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HUMAN LONGEVITY, INDIVIDUAL LIFE DURATION, AND THE GROWTH OF THE OLDEST-OLD POPULATION

Edited by
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Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population

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IN MEMORIAM: VÄINÖ KANNISTO (1916–2002)

After a long and distinguished career as a demographer and statistician with the United Nations (1957–1981), Väinö Kannisto illustrated the concept of active ageing through outstanding research accomplishments in his old age. While continuing on several missions for the United Nations up until 1990,[1] he pioneered modern research in the demography of the oldest-old. He started this research around age 70 and his work between age 72 and 85 became a monument in old-age mortality research.

He was one of the first to study mortality above the age of 100 years, publishing as early as 1988 a paper on the survival of centenarians in *Population Studies*. In the 1990s, with the help of Roger Thatcher, he developed the Oldest-Old Mortality Database, known today as the Kannisto-Thatcher Database on Old Age Mortality (http://www.demogr.mpg.de). Three books, which laid the foundation of our current knowledge on mortality of the oldest-old, were published by Odense University Press from this database: *Development of Oldest-Old Mortality, 1950–1990: Evidence from 28 developed countries* in 1994; *The Advancing Frontier of Survival* in 1996; and *The Force of Mortality at Ages 80 to 120* in 1998. Through these studies, he and his collaborators have found that significant declines in oldest-old mortality started in many industrialized countries during the third quarter of the twentieth century. This is widely considered as one of the major findings in demographic research on ageing.

He made important contributions to the methodology of old-age mortality research as well. Again with Thatcher, in 2002, Kannisto proposed a simple procedure to extend the method of extinct generations developed by Vincent in 1951 in order to accurately compute the mortality rates at extreme ages. He also proposed the two-parameter logistic model (Kannisto model), which effectively summarizes age variations in old-age mortality with the minimal number of parameters.

Väinö Kannisto was also deeply interested in the relationship between the mortality level and the population health status. In 1991, he published a major paper in *Genus* where he explored the possible impact of the change in mortality selection on the individual level of frailty among survivors. Kannisto returned to this topic in 1997 when he published a paper on the impact of the Finnish famine on mortality.

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[1] More information on the career of Kannisto is available in Vaupel, J.W. (2002) "Dr Väinö Kannisto: A reflection", *Demographic Research*, 6 (Article 5) http://www.demographic-research.org/Volumes/Vol6/5/

In the last years of his life, as a member of the IUSSP committee on Longevity and Health, Väinö Kannisto pushed us to go deeply into two phenomena accompanying the increase in life expectancy, i.e. the 'compression of mortality' and the 'rectangularisation of the survival curves'. He proposed a number of indicators to monitor these phenomena, including the C family indicators to measure the concentration of deaths and the R family indicators to measure the rectangularisation of the survival curve. He built on Lexis' work on the normal life duration and underlined the importance of the modal age at death as an indicator of longevity as well as the standard deviation of deaths above the modal age.

Kannisto's work was mainly published in demographic journals such as *Population Studies*; *Genus*; *Population and Development Review*; *Population*; and *Demographic Research.* His primary co-authors were Roger Thatcher and James Vaupel. Kannisto was the first demographer awarded the Longevity Prize of the Ipsen Foundation in 1997.

Väinö Kannisto was born on September 24, 1916 in Helsinki and he died unexpectedly on 16 February 2002 in Lisbon, interrupting his ongoing work. He was 85 years old. Several times during our committee meetings, he stressed that active life is much more important than long life. His life, including the extraordinarily creative years after age 70, was exemplarily active, productive, and fruitful.

Jean-Marie Robine

References

Kannisto, V. (1988) "On the survival of centenarians and the span of life", *Population Studies,* 42:389–406.

Kannisto, V. (1991) "Frailty and survival", *Genus,* 47(3–4):101–118.

Kannisto, V. (1994) *Development of Oldest-Old Mortality, 1950–1990: Evidence from 28 Developed Countries*. Odense: Odense University Press (Odense Monographs on Population Aging 1).

Kannisto, V. (1996) *The Advancing Frontier of Survival*. Odense: Odense University Press.

Kannisto, V. (1999) *Measuring the Compression of Mortality*. Paper distributed at the European Population Conference, EAPS.

Kannisto, V. (2000a) *Central and Dispersion Indicators of Individual Life Duration*: *New Methods*. International Union for the Scientific Study of Population, Seminar on: Human Longevity, Individual Life Durations and Growth of the Oldest–Old, Montpellier, 23–26 October.

Kannisto, V. (2000b) "Measuring the compression of mortality", *Demographic Research* 3 (Article 6). http://www.demographic-research.org/Volumes/Vol3/6/

Kannisto, V. (2001) "Mode and dispersion of the length of life", *Population*, 13(1):159–171.

Kannisto, V., Christensen, K., and Vaupel, J. W. (1997) "No increased mortality in later life for cohorts born during famine", *American Journal of Epidemiology*, 145(11):987–994.

Kannisto, V., Lauristen, J., Thatcher, A. R., *et al* (1994) "Reductions in mortality at advanced ages: several decades of evidence from 27 countries", *Population and Development Review*, 20:793–809.

Kannisto, V., Turpeinen, O., and Nieminen, M. (1999) "Finnish life tables since 1751" *Demographic Research*, 1(1):1–27. (Available online at www.demographic-research.org).

Lexis, W. (1878) Sur la Durée Normale de la Vie Humaine et sur la Théorie de la Stabilité des Rapports Statistiques. *Annales de Démographie Internationale,* 2(5):447–460.

Thatcher, A. R., Kannisto, V., and Vaupel, J. W. (1998) *The Force of Mortality at Ages 80 to 120*. Odense: Odense University Press.

Thatcher, R. V., Kannisto, V., and Andreev, K. (2002) "The survivor ratio method for estimating numbers at high ages", *Demographic Research*, 6(1):1–18. (Available online at www.demographic-research.org).

Vincent, P. (1951) La mortalité des vieillards. *Population*, 6:181–204.

Vaupel, J. W., Carey, J. R., Christensen, K., Johnson, T. E., Yashin. A. I., Holm. N. V., Iachine, I. A., Kannisto, V., Khazaeli, A. A., Liedo, P., Longo, V. D., Zeng, Y., Manton, K. G., and Curtsinger, J. W. (1998) "Biodemographic trajectories of longevity", *Science,* 280:855–860.

PREFACE

JEAN-MARIE ROBINE[1], EILEEN CRIMMINS[2],
SHIRO HORIUCHI[3], AND ZENG YI[4]
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What do we know about human longevity? The scientific community regularly meets to examine and re-examine this question, which persists in intriguing us. We all keep proceedings of such meetings on our shelves, such as the CIBA Foundation Colloquia on Ageing held in 1959, the world conference *Ageing: A challenge to Science and Society* held in Vichy in 1975; *Between Zeus and the Salmon*, gathering the contributions to the US National Research Council Committee on Population presented in Washington in 1996; and the proceedings of the series *Research and Perspectives in Longevity*, convened by the Foundation IPSEN.

Such books gathering current knowledge from several perspectives—biology, demography, medicine, sociology—form a crossroads for the diffusion of new ideas and hypotheses. Thus, in October 1977 the Council of the International Union for the Scientific Study of Population (IUSSP) created a new scientific committee on 'factors affecting mortality and the length of life'. The reason was the necessity for demographers and actuaries to develop closer links with other social and biomedical disciplines. The first seminar, held at Fiuggi Terme (Italy) in May 1980, gathered among others, John Pollard, Antonio Golini, Samuel Preston and Jacques Vallin with Leonard Hayflick, Roy Walford, Albert Jacquard, Jean-Noel Biraben and Bernard Benjamin. The resulting book, *Biological and Social Aspects of Mortality and the Length of Life*, became a reference work for many years and remains a model for our committee.

Twenty years later, in 1999, the International Union for the Scientific Study of Population convened a new scientific committee on 'longevity and health', to update our knowledge on the length of life. The scientific objectives were to study human longevity, the dynamics of health transitions, the emergence and proliferation of centenarians, and demo-epidemiological projections, together with the forecast of future health status.

To provide answers to these different questions, it was decided to arrange three seminars, each of them dealing with one of the main objectives: (i) a critical assessment of our knowledge about human longevity, mortality at older ages and the distribution of individual

life durations, held in Montpellier, France in 2000; (ii) the definition(s) of the different health concepts and the relations which link them together, held in Beijing in 2001; and (iii) the evolution of the diverse socioeconomic factors that may be linked with a positive evolution of functional abilities, and that may positively or negatively influence older people's living conditions and quality of life in general, held in New York in 2003.

Two books have resulted from these three seminars: this one focusing on longevity—*Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*; and the other one focusing on healthy ageing—*Longer Life and Healthy Ageing*. In addition, a special issue of *Genus* (2005) focuses on the causes and prospects of increasing longevity.

In addition, the committee organized in 2004 an international conference in Beijing on the 'demographic window' which brought together demographers and population economists from Western and Asian countries, to exchange the latest scientific knowledge on population dynamics, the change in population age structure, and its impact on economic and social development. This conference led to a special issue of *Asian Population Studies* (2005).

An editorial committee selected a subset of the many excellent papers presented at the Montpellier meeting in 2000 for publication in this volume. They have been reviewed by the editorial committee and by an external reviewer and appropriate revisions and updating to 2005 have been made. The final revised papers are presented here.

ACKNOWLEDGEMENTS

The committee (Jean-Marie Robine, Yves Carrière, Eileen Crimmins, Shiro Horiuchi, Vaïnö Kannisto†, Zeng Yi) thanks all those agencies and people that made this work possible. First, the International Union for the Scientific Study of Population, for sponsorship of the Seminar held in Montpellier (France) on October 23–25, 2000. We also thank the *Centre de Lutte Contre le Cancer* (CRLC) and the School of Medicine of the University of Montpellier, the Centre for Healthy Ageing and Family Studies at Peking University, the Laboratory of Populations at the Rockefeller University, the Asian Metacentre at the Singapore National University, and the U.S. National Institute on Ageing (grants 7P01AG08761 and R13 AG021466-01). The committee is much indebted to Isabelle Romieu for assisting the committee, organizing the seminar in Montpellier, and for editorial assistance.

INTRODUCTION

JEAN-MARIE ROBINE[1], EILEEN CRIMMINS[2],
SHIRO HORIUCHI[3], AND ZENG YI[4]
[1]*INSERM, University of Montpellier;* [2]*University of Southern California;* [3]*Rockefeller University;* [4]*Duke University and Peking University*

This book is intended to assess our current knowledge on human longevity and on the relationships linking longevity and health. Research in this area—demographic, epidemiological, genetic and evolutionary—has developed at an accelerating pace in recent years, revealing many radical and unexpected findings. Throughout most of the Western world, expectation of life has increased to a much greater degree than most actuaries ever expected, potentially threatening the solvency of pension systems and upsetting population projections. Record life expectations have been reliably recorded and their trend measured with new databases. The rapid growth of the 'oldest-old' population—90 and over, and especially of centenarians and super-centenarians—has attracted much attention. A completely unexpected deceleration of the increase in the force of mortality among the oldest-old has challenged accepted opinion about the form of the human mortality curve, and thus fuelled speculation about the expansion of the human life-span.

Argument continues about whether the human survival curve, as well as the curve of morbidity onset, is becoming rectangularised or whether the tail of its distribution will simply be extended to older and older ages. The causes of death of the oldest-old, now known to be different in many important ways from those of the younger old, have raised questions about frailty, the selection of survivors, the morbidity, the health and medical needs of the very elderly. In trying to resolve these questions, biology and demography often come together. Important biodemographic issues include the impact of early-life events on the future longevity of individuals, the heritability of longevity between parents and children, the existence of long-lived families and the relationship between longevity and fertility and the optimum ages for procreation.

Comparisons of physiological processes and life-cycle strategies of different species (yeast, worms, flies, mice and even large monkeys) have been essential for the development of higher-level theories of ageing from an evolutionary viewpoint. Other biological work has developed markers of ageing in persons of good health and, on a different track, begun to isolate "longevity" genes. A great variety of biological findings, on the effects upon ageing of caloric restriction, antioxidants, inflammation, telomere length, growth hormones, and

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genes such as ApoE, and of numerous changes in environmental conditions, all await location in a coherent overall model. This complexity in relationship between the biological and environmental factors makes it clearer that the expression of longevity is a complex, multifactorial, phenotypic trait, largely governed by environment (Robine 2003; Vaupel *et al*. 2003), and less and less a fixed species characteristic (Buffon 1749; Cutler 1985; Walford 1985; Hayflick 1996).

This first volume from the IUSSP Committee on Longevity and Health deals with the limits of human longevity, the distribution of individual life duration, and the growth of the oldest-old population. It discusses the availability and reliability of data—the biological, environmental and social factors affecting length of life and the oldest-old and some of the demographic effects of recent and future changes in survival upon human social structure. In the chapters that follow, experts in biology, demography, epidemiology, medical gerontology, and sociology attempt to answer many questions related to human longevity.

The book is organized in 5 sections. In the first section dealing with theoretical and comparative biological concepts, research questions related to human longevity are summarized by Jean-Marie Robine and put in the broader context of species diversity by Steven Austad and of biodemography by James Carey and Debra Judge. In the second section dealing with empirical and analytical studies of ageing and of oldest-old population, empirical data on the mortality trajectory for the oldest-old in China are introduced by Zeng Yi and James Vaupel. New indicators of individual life duration are presented by Väinö Kannisto, and Wilma Nusselder examines the rectangularisation of the survival curve at advanced ages in the Netherlands. Evidence for exceptional male longevity in Sardinia is shown by Michel Poulain and his colleagues and the quality of data on reported age among the elderly in Quebec is examined by Robert Bourbeau and Bertrand Desjardins. In the third section, dealing with the causes of death and biological frailty, France Meslé studies in detail the quality and the comparability of the data and Shiro Horiuchi examines the distribution of the causes of death of the oldest old. Kaare Christensen and Anne Maria Herskind analyse the heritability of longevity and Douglas Ewbank examines the genetic factors associated with human life span. In the fourth section dealing with gender and social determinants, Marja Jylha and Tiina Luukkaala investigate the social determinants in mortality in the oldest old and John Wilmoth and Mike Dennis examine the social determinants in older adult mortality in the United States. The gender differences in mortality among the oldest-old are examined by Jacques Vallin. In a final section, dealing with causes of the trend in mortality and morbidity, possible explanations of the decline in mortality among the oldest-old are explored from a medical point of view by Bernard Jeune and from a demographic perspective by Graziella Caselli, James Vaupel, and Anatoli Yashin. Lastly, the marital status and family support of the oldest-old in Great Britain are presented by Emily Grundy and Michael Murphy. The diversity of these 18 chapters underlines the resolutely multidisciplinary approach adopted by the committee to carry out a critical assessment of our knowledge about human longevity.

Section 1
Theoretical and Comparative Biological Concepts

SECTION 1. THEORETICAL AND COMPARATIVE BIOLOGICAL CONCEPTS

The first chapter by Jean-Marie Robine presents a broad review of research issues in the study of human longevity. It suggests that research in this area can be divided into four main disciplines: (i) demography (increase in life expectancy, mortality trajectory, concentration of ages at death, rectangularisation of the survival curve, emergence of population at extreme ages); (ii) epidemiology (health and causes of death of the oldest-old, epidemiological transition and compression of morbidity); (iii) biodemography (heritability of longevity, relationship between longevity and fertility, impact of early-life events on longevity, interspecies comparison); and (iv) biology (ageing theories, biomarkers and longevity genes). Most of these issues are discussed in the chapters of this book. This review strongly suggests that there is no age limit to human longevity and raises the point of the importance of the plasticity of the human mortality trajectory upon environmental conditions.

In Chapter 2, Steven Austad puts our knowledge on longevity in the broader context of species diversity and proposes four generalizations: (i) larger mammalian species live longer than smaller ones; (ii) certain taxonomic groups such as bats and marsupials are exceptions to this relationship between body size and longevity; (iii) within species, smaller individuals are generally longer-lived than larger individuals; and (iv) females are the longer-lived sex, although numerous exceptions can be found. For example, in a special study in which four mouse and three rat genotypes were reared under identical conditions, Austad shows that male mice typically live longer than female mice, while the reverse is true for rats. In addition, although there is a large unexplained variation in longevity, even among genetically identical animals in identical environments, there is no evidence from the enhanced longevity induced by caloric restriction of a longevity "wall" beyond which mice and rats cannot live. This detailed chapter demonstrates the importance of interspecies comparison to enhance our knowledge on longevity, especially on questions such as data quality, maximum life span, and species variation in longevity. The substantial variability in longevity observed in genetically identical animals under uniform laboratory conditions remains a mystery.

Chapter 3 is limited to social species. In that chapter, James Carey and Debra Judge propose a general theory of longevity extension in social species, particularly adapted to humans. In a biodemographic framework they try to explain the longevity-oriented question posed two decades ago by George Sacher: "Why do we live as long as we do?" In this general theory, longevity is no longer merely viewed as the result of an absence of mortality but as a self-reinforcing and positively selected life history trait in social species. The authors claim that a small increase in longevity is amplified as (i) reduction in mortality at young ages

increases natural selection for mechanisms of maintenance and repair at *all* older ages as well as increasing the potential for intergenerational transfers; (ii) intergenerational transfers of resources from old to young increase fitness of the young and thus favour the presence of older individuals in a population; and (iii) the division of labour increases both efficiency and innovation at all levels resulting in increased resources that can be invested. The next step would be to test the various propositions made.

CHAPTER 1. RESEARCH ISSUES ON HUMAN LONGEVITY

JEAN-MARIE ROBINE
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In this introductionnary chapter, we present the wide range of current findings and research issues in longevity, and identify questions still unanswered that should be investigated in the years to come.

This review is based mostly upon work on human longevity published between 1998 and 2004. However, some older work is invoked given its continued importance today. We have followed a five-part plan, starting with demographic questions surrounding longevity (Part 1), followed by epidemiological questions on the health of extremely old people (Part 2). We then address strictly bio-demographic issues (Part 3) mixing biology and demography, most often in a family framework. Part 4 examines biological questions focusing on markers and on the role played by genes. A final part deals briefly with databases on human longevity.

The questions are sorted into themes and sub-themes in each Part I. Demographic issues thus cover (i) increase in life expectancy, (ii) fall in mortality amongst the oldest-old, (iii) mortality trajectories with age, (iv) life durations and age distribution at death, (v) rectangularisation of the survival curve, (vi) tail of distribution and extreme ages, (vii) emergence of oldest-old (ninety-year olds, centenarians and supercentenarians). Epidemiological issues cover (i) health of oldest-old, (centenarians) and of their children. They also address (ii) causes of mortality of the oldest-old, and (iii) epidemiological transition and compression of morbidity. Biodemographic issues are addressed under (i) heritability of longevity between parents and children and the existence of long-lived families, and (ii) the relationship between longevity and fertility or optimum procreation ages. They also cover (iii) the impact of early-life events on the future longevity of individuals, and (iv) species comparison. The biological issues are both theoretical—continuing still covering ageing theories—and practical, seeking (i) to identify biological markers of ageing in good health, and (ii) to isolate longevity genes.

Could it be that a study of longevity in the lower species provides clues into research on human longevity under a "from fly to man" schema? (Carey 1997). Possibly, but there is a vast amount of accumulated knowledge specific to human longevity and it is time to ask ourselves what the study of human longevity could bring to the study of longevity in other species. In a word, it is the study of the quality of life. Most publications on longevity of *C. Elegans* or flies are content to report the effect of such and such a genetic or environmental manipulation on the average and on the maximum survival observed.

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Nothing, or very little, is said about related variables such as the weight or development of the manipulated individuals, their fertility and general functional state (mobility and activity), or their cognitive state and their behaviour. For man, it is clear that longevity is of no interest in itself and is worth something only if it is not to the detriment of the quality of life. The study of life expectancies in good functional health is a good example of the state of research (Robine *et al*. 2003). We shall not address these issues in this review: they were, however, addressed for the first time during the most recent meeting of the *Fondation Ipsen* Longevity Seminar Program, where several presentations were made of work on the survival in good health of various animal species (Carey *et al*. 2005).

But what do we mean by longevity, 'life expectancy', 'life span' 'maximum life span', 'maximum age reported at death', 'length of life', 'mean life duration', 'age at death', 'expectation of life' . . . ? These terms are used with varying degrees of definition, particularly in English-speaking published works. The resulting long-standing confusion (Greenwood 1928; Deevey 1947) has survived much criticism, despite many authors' efforts (Manton *et al*. 1999; Hayflick 2002). It is explained that the number of disciplines embarked on the study of longevity and the growing interest in this topic attract an increasing number of researchers. It underlines the need for a basic manual for the study of longevity, common to both the social and the biological sciences (Carey 2003), and it justifies the attempts at clarification undertaken by this review.

1. Longevity and Demography

1.1. INCREASE OF LIFE EXPECTANCY AT BIRTH

The first question that intrigues demographers is how far average life expectancy at birth can increase. Will it continue to increase by three months every year in the most advanced countries in the demographic transition, reaching 100 years for women in at least one country in the world in around 2060, as suggested by Oeppen and Vaupel (2002); or shall we henceforth measure its increase in days or hours, as suggested by Olshanky and his team (Olshanky *et al*. 2001a)? The debate is far from settled (Leslie 2003); but progress in those countries with the best life expectancy at birth—Japan, Hong Kong, France and Switzerland—shows no signs of slowing down (Hong Kong Census and Statistics Department 2002; Heiniger and Wanders 2002; Beaumel *et al*. 2004; Ministry of Health and Welfare of Japan 2003). 85 years of age has been considered the ultimate limit for average life expectancy for some time (Fries 1980; Fries and Crapo 1981; Hayflick 1981; Olshansky *et al*. 1990) and the fact that the current average life expectancy has already exceeded this value for Japanese women is most probably an important stage in the progress of human longevity (Ministry of Health and Welfare of Japan 2003; Robine *et al*. 2003).

Secondly, can the developed countries, the United States in particular, continue to forecast life expectancies for the 2050s that remain less than those for Japan in the 2000s? It is clear that forecasts should be revised upwards in the majority of countries and that new methodological work on demographic forecasting techniques is necessary (Horiuchi 2000; Tuljapurkar *et al*. 2000). It is surely important to determine the time required for one or another country to catch up with the more advanced countries in the epidemiological

transition and not just to be content with extrapolating national mortality trends (Oeppen and Vaupel 2002).

Although developed as early as the 17th century (Graunt 1661), life expectancy at birth was only adopted as a population longevity indicator in the 1920s–1930s (Dublin 1923; Dublin *et al*. 1926; Dublin and Lotka 1934, 1945). Life expectancy at birth, with a value very sensitive to infant mortality, related perfectly well to the then current health priorities, focusing on the fight against infectious diseases that were at that time particularly devastating for young children. Hence, when virtually nobody imagined that the mortality of old people (i.e. people over 65) could be reduced, increase in longevity could only stem from a reduction in premature mortality. Today it is this same sensitivity to the fall in infant mortality, whereas the fall in mortality predominantly concerns old people, which causes life expectancy at birth to be questioned as an indicator of population longevity [see Part 1.4 on Life duration (modal age at death)].

Be that as it may, life expectancy remains the flagship indicator for demographers and work since 1990 has been a constant quest to understand its limits (Manton 1991; Vallin 1992; Carnes and Olshansky 1993; Vallin 1993; Olshansky and Carnes 1994; Vallin and Caselli 1997; Gavrilov and Gavrilova 1998; Wilmoth 1998a, 1998b, 2000; Olshansky *et al*. 2001a; Riley 2001; Wilmoth 2001; Bongaarts and Feeney 2002; Olshansky and Carnes 2002; Vaupel 2002; White 2002; Wilmoth 2002; Carnes *et al*. 2003).

1.2. FALL IN MORTALITY IN THE OLDEST-OLD

Although life expectancy at birth continues to increase by three months every year in Japan, France and Switzerland—whereas infant mortality does not exceed five per 1000 in these countries—the mortality of old and even very old people is falling drastically, and has been for at least thirty years. Paradoxically, this fall in itself has not been studied greatly, beyond statistical descriptions, and little is still known of its causes and mechanisms (Horiuchi 1991; Vaupel and Lundstrom 1994; Kannisto 1988; Kannisto *et al*. 1994; Manton and Vaupel 1995; Wilmoth 1995; Myers 1996; Catalano 2002).

The fall in mortality of old people deserves to be studied independently from work on life expectancy (see above) or on mortality trajectories (see Part 1.3 on Mortality trajectories below)—the more so such this fall is far from homogeneous in the developed countries. The poor Danish and Dutch scores illustrate this perfectly (Nusselder and Mackenbach 2000; Jansen *et al*. 2003). What are the specific factors (medical, economic, social, political, environmental, etc.) determining the fall in mortality of very old people in the most developed countries? What is the magnitude of discrepancies between the countries and what causes them? These are some of the important questions for future research.

1.3. MORTALITY TRAJECTORIES WITH AGE

This is a major biomathematical question that has fascinated demographers and biologists since their respective disciplines commenced. Is there a law of mortality? And if so, what is it? It has been known for some time that mortality increases with age, but is there an age, and if yes, what is it, at which death the following year is a certainty?

Research into laws of mortality has been marked by foundation work by English mathematicians, particularly de Moivre (1756) on the increase of mortality with age, Gompertz (1825) on the exponential progression, called Gompertzian, of mortality, and Perk (1932) on so-called logistical trajectories. But it also owes a great deal to biologists, who since Buffon (1749) have been pointing out that the mortality of old people is lower than expected (Greenwood and Irwin 1939; Comfort 1964), a phenomenon recognised by Gompertz himself (Gompertz 1825; Carnes *et al*. 1996; Olshansky and Carnes 1997).

From 1950 onwards, the extinct generation method suggested by Vincent (1951) and its modern extensions (Meslé and Vallin 2000a; Thatcher *et al*. 2002) could be used to calculate the mortality rate for the oldest-old accurately. Creating a database covering several countries has increased the number of observations (Vincent 1951; Dépoid 1973), but these remained limited until the K-T Database created by Kannisto and Thatcher that includes mortality data from 28 developed countries (Kannisto, 1994). This database is the foundation for all modern work on mortality trajectories, suggesting logistic trajectories (Kannisto 1996; Thatcher *et al*. 1998; Thatcher 1999b) or quadratic trajectories (Vaupel *et al*. 1998).

The International Database on Longevity (IDL) was set up predominantly to distinguish between these two trajectories; its objective is to calculate accurately mortality rates between 105 and 115 years of age (Robine and Vaupel 2002). There is no doubt today that mortality slows down over the age of 85 and that mortality rates observed at 95 or 100 years of age are lower than expected (Horiuchi and Wilmoth 1998; Vanfleteren *et al*. 1998; Manton 1999; Lynch and Brown 2001; Weitz and Fraser 2001; Kestenbaum and Fergusson 2002; Barbi *et al*. 2003).

Figure 1 summarises our knowledge about mortality trajectories with age. Since Gompertz (1825), demographers have all considered that mortality increases exponentially with age, with mortality rates doubling approximately every eight years. In 1951, Vincent was able to estimate for the first time that the age at which the probability of dying in the same year was close to one is 110 years (Vincent 1951). Twenty years later, Dépoid (1973) would find a limit age of 117 years based on the same hypotheses and methods. The collapse of mortality is considerable: but nobody was interested in the question at that time and doubts have never been raised over Vincent's conclusions. The duration of human life was considered limited to 110 years and a characteristic of the species (Buffon 1749; Cutler 1985; Walford 1985; Hayflick 1996), controlled by clock genes (Fries 1980; Hayflick 1981). The Kannisto and Thatcher database had to be created before this biological dogma was questioned. Mortality follows a logistic trajectory with age, tending towards a mortality ceiling without ever reaching it (Thatcher *et al*. 1998), or a quadratic trajectory, where mortality diminishes with age, having passed a maximum at around 110 years (Vaupel *et al*. 1998). The mortality rates between 110 and 114 years of age, calculated extremely accurately thanks to the IDL (Robine and Vaupel 2002) show that mortality does not increase, or only very slightly, after 110 years of age. These observations push the exponential trajectories definitively to one side (Gompertz or Makenham), but still do not make the distinction between the logistic and quadratic trajectories, with the latter only diverging significantly after 115 years of age. These results nevertheless show that human longevity has no limits in terms of age and there are no biologically-controlled limits (clock genes or other mechanisms

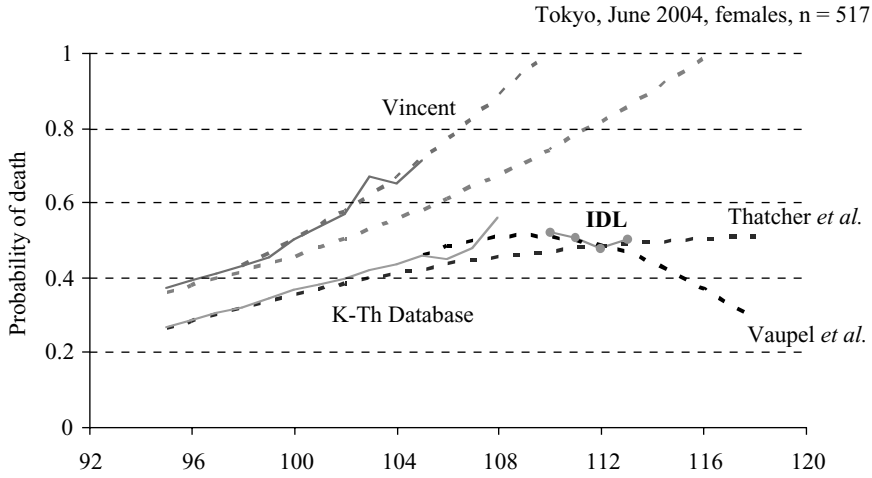

Figure 1. Mortality trajectory beyond 95 years of age. *Source*: International Database on Longevity (IDL), 2004.

linked to natural selection). If there really is a limit, it is for mortality levels that do not reach an annual mortality rate of 60%, even in people of 110 years of age or more, even for the most frail, under mortality conditions currently found in the most developed countries.

These results need explaining, for they fuel the fear that old people will always be both increasingly numerous and increasingly older. What determines the mortality ceiling? Can it drop significantly in the future? Several, even complementary, explanations have been put forward to explain the slowing down in mortality of the oldest-old, such as genetic heterogeneity of populations (Vaupel *et al*. 1979), the redundancy of biological maintenance, repair and defence mechanisms in the human body (Gavrilov and Gavrilova, 2001 and 2003), the very special configuration of generations at the heart of the demographic transition (Bonneux *et al*. 1998), and considerable progress in the economic, physical, medical, and social environment of the oldest (Robine, 2001 and 2003). In 1939, Greenwood and Irvin were already noting "Even the juvenile of 60, if ordinarily intelligent, eschews the violent exercises of the child of 40. Centenarians rarely appear in public. A statistical rate of mortality might show no increase with age, if the demands made on the vital forces diminished *pari passu* with the decay of vigour" (Greenwood and Irwin 1939). This question was entirely theoretical in 1939; but in 2006, with the accumulation of ninety-year-olds and centenarians housebound or in retirement homes, the determining factors of mortality trajectories with age should be investigated urgently, to find out just where the mortality ceilings can be lowered. Remember that, in the 25 years between 1975 and 2000, the mortality rate for women centenarians in Japan decreased from 50 to 35% (Robine *et al*. 2003a).

The study of mortality trajectories is one subject where work on animal species amplifies work on man (Carey *et al*. 1992; Vaupel *et al*. 1998).

1.4. LIFE DURATION AND AGE DISTRIBUTION AT DEATH

Modal age at death and age distribution at death, that measure individual life durations, have not been studied in depth, unlike life expectancy at birth and mortality trajectories with age. Demographers are unfamiliar with the mode. And yet it is this mode that indicates the most frequent life durations in the conditions of the moment. It is more than likely the best population longevity indicator (Horiuchi 2003). The most frequent life durations in Japan, where life expectancy at birth reaches 85 years of age for women, are in the order of 90 years of age (Ministry of Health and Welfare of Japan 2003). The modal age at death, which is highly sensitive to the drop in mortality of the oldest-old, relates clearly to the current epidemiological situation in the most developed countries; but its characteristics and determination are clearly different from life expectancy.

The distribution of ages at death attracted as much attention at the end of the 19th century from demographers and statisticians as mortality trajectories (Thiele 1871; Lexis 1878; Bertillon 1878; Perozzo 1879; Bodio 1887; Levasseur 1891; Pearson 1902). The aim was to determine the normal length of life durations based on work by Laplace and Quetelet (Laplace 1812; Quetelet 1835, 1848, 1871; Véron and Rohrbasser 2003).

As early as 1939 Greenwood and Irvin showed that modal age at death, measuring the most frequent life durations, was not invariable and increased over time (Freudenberg 1934; Phillips 1935; Greenwood and Irwin 1939). Many years would pass, however, before this idea would be universally acknowledged, particularly thanks to work by Benjamin and also Kannisto (Clarke 1950; Phillips 1954; Benjamin 1959, 1963, 1964, 1982, 1988; Kannisto 1999, 2000a, 2000b, 2001).

The question asked today is naturally just how far modal age at death, as an indicator of the most frequent life durations, can be increased, as for life expectancy at birth. The question relates also to whether life durations become uniform as mortality diminishes. It has always been assumed that increased life expectancy at birth goes hand in hand with reduced inequalities faced with death. This was undoubtedly true as long as the growth in life expectancy was due to the drop in infant mortality, but where are we now when it is caused by the drop in mortality of the oldest-olds? How does the standard deviation in life durations move on beyond the modal age at death? Is there a carry-forward of all ages to death towards the oldest-olds? Or are these ages concentrated beyond the mode (Robine 2001; Cheung 2003; Cheung *et al*. 2005a, 2005b)? This issue of compression of mortality has been studied above all in terms of rectangularisation of the survival curve, detailed in the following section (Levy 1996; Wilmoth and Horiuchi 1999).

1.5. RECTANGULARISATION OF THE SURVIVAL CURVE

Biologists were the first to become interested in the shapes and transformation of the survival curve, long before demographers showed any concern (Pearl and Doering 1923; Pearl and Miner 1935; Greenwood 1928; Deevey 1947; Comfort 1956, 1964; Strehler 1975; Gordon 1980). One explanation is that demographers were undoubtedly more interested in fertility and the drop in infant mortality than in life durations and population ageing. Doctors and biologists popularised the theory of the rectangularisation of the survival curve

in the 1980s (Fries 1980; Fries and Crapo 1981; Hayflick 1981). Nothing was settled in the heated debates that followed with demographers from the United States (Schneider and Brody 1983; Fries 1984; Myers and Manton 1984a and b; Fries, 1989; Olshansky *et al*. 1990; Rothenberg *et al*. 1991; Olshansky *et al*. 1991; Fries 2002). Some methodological progress was nevertheless achieved over time (Manton and Tolley 1991; Manton and Singer 1994; Manton and Stallard 1996; Eakin and Witten 1995; Coale 1996; Cheung, 2001; Yashin AI *et al*. 2001); and empirical studies started to pile up (Nagnur 1986; Hill 1993; Go *et al*. 1995; Nusselder and Mackenbach 1996, 1997; Nusselder 1998; Pelletier *et al*. 1997; Paccaud *et al*. 1998; Martel and Bourbeau 2003). According to Fries, growth in life expectancy goes hand in hand with rectangularisation of the survival curve that tends towards maximum distribution corresponding to a modal age at death of 85 years of age and a standard deviation of 4 years. This very high concentration of life durations should then be accompanied by a compression of morbidity in the last years of life (Fries 1980).

However, that is not supported by the experience of Japanese women, who, with a modal age at death of the order of 90 years of age, do not show such a standard deviation or such a concentration of ages at death. Nevertheless, the absence of a strict definition of the dimensions of the transformation for survival curves has not produced to date an accurate measurement of modifications to the survival curve which have accompanied, and still accompany, the epidemiological transition (Cheung *et al*. 2005).

1.6. TAIL OF DISTRIBUTION AND OLDEST-OLDS

The tail of distribution of the survival curve or of the death curve has been studied even less (Smith 1994). And yet it is ideal for monitoring the limits of human life. Indicators are few and are marred by a variety of defects (Faber 1982; Faber and Wade 1983; Bell *et al.* 1992; Finch and Pike 1996; Vaupel 2002). Work on the maximum age at death, starting with Gumbel (1937), shows that growth in maximum age reported at death has speeded up over the last few years (Wilmoth and Lundström 1996; Wilmoth *et al*. 2000; Robine and Saito 2003; Wilmoth and Robine 2003; Robine and Paccaud 2005). This is no doubt explained by the considerable increase in the number of centenarians, at least in part (Wilmoth and Robine 2003).

1.7. EMERGENCE OF THE OLDEST-OLD (NINETY-YEAR-OLDS, CENTENARIANS AND SUPERCENTENARIANS)

Paradoxically, more is known about centenarians than about ninety-year-olds. When it became apparent that the numbers of oldest-olds were really taking off (Vaupel et Jeune, 1995), attention focused on centenarians rather than ninety-year-olds, despite there being 35 times more people in their 90s than centenarians, for example in France in 2003 (Beaumel *et al*. 2004).

The first modern studies date back to the 1990s (Thatcher 1992); but it was only at the end of that decade that studies really began to proliferate (Skytthe and Jeune 1995; Vaupel and Jeune 1995; Smith 1997; Thatcher 1997; Wang *et al*. 1997; Krach and Velkoff

1999; Thatcher 1999a; Allard and Robine 2000; Zeng *et al*. 2001; Jeune and Skytthe 2001; McCormack 2001; Poulain *et al*. 2001; Thatcher 2001; Vallin and Meslé 2001; Robine *et al*. 2003a and b; Robine and Saito 2003; Robine and Paccaud 2005). They all show a numerical explosion in the number of centenarians. Increase rhythms vary from country to country, however, producing significant differences in the time taken to double the number of centenarians (Centenarian Doubling Time—CDT) and in the centenarian rate per 10,000 people aged 60 forty years earlier (Centenarian Rate—CR) (Robine *et al*. 2005). This increase is explained mainly by the fall in mortality after the age of 80 (Thatcher 1992; Vaupel and Jeune 1995; Thatcher 2001; Robine and Paccaud 2005); and it is surely the fall in mortality after 100 years of age, combined with the increase of numbers at 100 years of age, that explains the current numerical explosion of the over-105s noted in both France and Japan (Ministry of Health and Welfare 1963–2004).

The exponential increase in centenarian numbers noted in many countries (Robine *et al*. 2005), combined with the fall in mortality over and above 100 years of age (Robine *et al*. 2003a) has speeded up the increase in maximum age reported at death that has been observed over, the last two or three decades (Wilmoth and Robine, 2003). Beyond the case of Jeanne Calment, who died in 1997 at the age of 122 (Ritchie 1995; Robine and Allard 1998), more and more individuals are reaching the age of 110 (Meslé *et al*. 2000; Coles 2001 onwards; Coles 2004). The International Database on Longevity (IDL) can be used to monitor the emergence of this population of supercentenarians (110 years of age and above) in great detail (Robine and Vaupel 2001, 2002). It can also be used to verify the ages.

Age verification of the oldest-olds is a classic problem in historical demography (Thoms 1873; Charbonneau and Desjardins 1990). The case of Louis Joubert, for example, deceived the most critical observers (Bowerman 1939; Charbonneau 1990; Wilmoth *et al*. 1996). North America is known historically for exaggerating ages, particularly in coloured populations (Myers and Shudde 1955; Myers 1966; Hill *et al*. 2000). The most amazing stories of longevity, however, emerged from Latin America and the Soviet Union during the 1970s (Mazess and Forman 1979; Arkhipov 1980; Palmore 1984; Bennett and Garson 1986). Are Okinawa and Sardinia the current fairytale lands (Koenig 2001; Poulain *et al*. 2004)? Age verification remains a prerequisite for any study on longevity (Perls *et. al*. 1999; Allard and Robine 2000). It is a fundamental point of the IDL (Wilmoth *et al*. 1996; Desjardins 1999; Jeune and Vaupel 1999; Robine and Allard 1999; Thatcher 1999c; Rosenwaike and Stone 2003). The absence of verification falsifies the calculation of mortality rates in the oldest-olds (Preston *et al*. 1999; Robine and Vaupel 2002) [See Part 1.3].

The work of the Danish team led by Jeune has shown clearly that cases of centenarians prior to 1800 are in all likelihood false, that these disputed cases decrease with the development of statistics in the 19th century, that true centenarians are surely exceptional between 1800 and 1900, that they are rare but no longer exceptional until 1945, and that they become excessive after the Second World War (Jeune 1995; Kjaergaard 1995). Is this Danish schema, taken up partly in Japan (Robine and Saito 2003), valid for the China of today (Wang *et al*. 1998; Wang 2001)?

2. Longevity and Epidemiology

2.1. HEALTH OF THE OLDEST-OLD (NINETY-YEAR-OLDS, CENTENARIANS AND SUPERCENTENARIANS)

Extensive debate has surrounded the health of centenarians for some years. Before this time, the health of ninety-year-olds and centenarians was rarely studied. This is due to their modest numbers before the 21st century (Wigzell 1970). Most observers thought for a long time that centenarians were in good health and that this was the main reason for their survival. The simple idea was that individuals in good health survived longer. Centenarians, therefore, must have remained in good health for longer (Hitt *et al*. 1999). The team from the Danish Centre for Demographic Research contests this idea (Andersen-Ranberg *et al*. 1999) and claims that the state of health declines regularly with age up to 100 years and beyond. The health of centenarians would thus be in line with that of seventy-, eighty- and ninety-year-olds. The most recent research has nevertheless identified three profiles of morbidity in centenarians: survivors, delayers and escapers. Escapers are individuals who reach the age of 100 by escaping the main fatal diseases associated with ageing. Delayers are individuals who have pushed back the age when these diseases appear to at least 80 years of age, and survivors are individuals who have reached 100 by surviving these diseases diagnosed before the age of 80. According to the New England Centenarian Study (NECS), 24% of men and 43% of women centenarians are survivors, 44% of men and 42% of women are delayers, and 32% of men and 15% of women centenarians are escapers (Evert *et al*. 2003).

In fact, there are still very few studies on the health of centenarians and virtually none on ninety-year-olds. The principal modern studies are the French study 'In search of the secret of living to 100' from the *Fondation Ipsen* (Fondation Ipsen 1991; Allard *et al*. 1996), the Danish study on centenarians (Andersen-Ranberg *et al*. 1999), the Japanese study on centenarians (Tauchi *et al*. 1999), the New England Centenarian Study (Evert *et al*. 2003) and the Italian study on centenarians (Gueresi *et al*. 2003).

An important issue to be addressed in any study of the health of centenarians is their cognitive state. One current hypothesis is that almost all centenarians must be demented, given the advance in prevalence of Alzheimer's disease with age. In fact, a series of recent studies show that around one third of centenarians are not thought to be demented (Blansjaar *et al*. 2000; Andersen-Ranberg *et al*. 2001; Dewey and Copeland, 2001; Hagberg *et al*. 2001; Silver *et al*. 2001; Robine and Jagger 2002; Ankri and Poupard 2003). In a recent study, Perls estimates that 15 to 25% of centenarians are cognitively intact and that 90% of the others have pushed back the appearance of cognitive deficiencies until the age of 90 (Perls 2004). According to Kliegel and his colleagues, those who develop dementia at the highest ages will go through a shorter period of cognitive decline before death (Kliegel *et al*. 2004); and this refers back to the theories of the compression of morbidity [see Part 2.3]. A few studies have concentrated on the psychology of centenarians. Here also the basic idea is that centenarians must show particular psychological characteristics (Samuelsson *et al*. 2001, Hagberg *et al*. 2001). It is usually difficult for researchers to list centenarians in a continuum of ages and to consider them as part of a whole.

The emerging concept of frailty should make it easier to appreciate the health, robustness, and frailty of centenarians better. This approach has been adopted by the European teams for the projects European Challenge for Health Ageing (ECHA, directed by De Benedictis) and Genetics of Healthy Aging (GEHA, directed by Franceschi). A further important, but rarely-studied, point is the quality of life of these very old people (Baltes 2003).

Research teams have gradually become interested in the health of children of centenarians, to attempt to understand if they age better than controls. There seems to be a positive link between the longevity of parents and their children's health (Barzilai *et al*. 2001; Frederiksen *et al*. 2002; Reed *et al*. 2003; Terry *et al*. 2003). Coronary diseases, high blood pressure, diabetes, and strokes occur far later in children of centenarians. This does not appear to be the case, however, for cancer or osteoporosis (Terry *et al*. 2004).

2.2. DEATH OF THE OLDEST-OLD (NINETY-YEAR-OLDS, CENTENARIANS AND SUPERCENTENARIANS)

The causes of death of the oldest-old are poorly understood (Kohn 1982; Smith 1993; Fogata *et al*. 1996; Lloyd-Jones *et al*. 1998; D'Amico *et al*. 1999). The oldest-old most frequently suffer from multiple deficiencies and pathologies. The proportion of ill-defined causes of death increases considerably with age. Remember that the modal age of death is today in the order of 90 years of age for women in Japan. In these conditions, it is likely that we know less and less what humans die from. Research into the causes of mortality at 90 years of age and beyond would be welcomed.

Since the work by Clarke on "anticipated" mortality and "senescent" mortality (Clarke 1950) and by Bourgeois-Pichat on "endogenous" and "exogenous" mortality (Bourgeois-Pichat, 1952), several researchers have tried to divide the causes of death between those due to ageing and the others, with the hope, once again, of finding limits to human longevity. What would be human longevity in the absence of diseases and accidental causes? In practical terms, it seems very difficult to separate this out (Bourlière 1987; Carnes and Olshansky 1997; Horiuchi 1997; Horiuchi and Wilmoth 1997; Vallin and Berlinguer 2002). The current classifications of causes of death coincide with disease classifications. These respond to clinical objectives of identifying the disease and choosing suitable treatment and have no scientific purpose; they do not in themselves identify the causes of death linked to ageing of the individual and his loss of robustness. It is therefore impossible at present to verify if centenarians die of old age or from specific diseases, or worse still, through negligence.

2.3. EPIDEMIOLOGICAL TRANSITION

The emergence of ninety-year-old and centenarian populations throws new doubt on the now traditional theories of epidemiological transition and its explanations (Omran 1971; Preston 1975; McKeown 1976; McKeown 1979; Caldwell 1979; Mosley and Chen 1984; Morel 1991). Successive adjustments have been proposed (Olshansky and Ault 1986; Riley 1990; Preston 1992; Myers and Lamb 1993; Meslé and Vallin 2000b; Riley 2001; Robine 2001; Meslé and Vallin 2002; Myers *et al*. 2002). But that is far from enough (Robine and Michel 2004). A theory remains to be found that explains how we reached the current

stage, with its trajectories of mortality with age, the emergence of the oldest-old, factors determining their states of health—in particular their functional state—and the causes of their death. Above all, a theory remains to be found that can be used to improve forecasts for the future. Where do the current transitions lead us?

One particularly burning question is to understand whether the extending lifetime is one of good health or of bad health, with an ever-increasing accumulation of degenerative diseases and disability. In other words, is the lengthening of life duration accompanied by compression of morbidity or a pandemic of disabilities and dementia? Health expectancy and life expectancy without disability have more particularly been developed to answer these questions (Palmore 1987). The question is far from settled and is the subject of diverse research programs (Vita *et al*. 1998; Ferrucci *et al*. 1999; Nusselder *et al*. 2000; Hubert *et al*. 2002; Fries 2002; Robine *et al*. 2003c; Crimmins 2004).

Studying morbidity, or disability, in pathological or poly-pathological terms is surely not enough to understand current epidemiological transitions. Just as biology does not explain a great deal in the absence of environment, so diseases alone do not explain a great deal in the absence of the ability of the individual to defend himself. The study of the state of health of individuals in terms of the ability to face up to the stresses of life should help us advance on this point. This refers us back to the current notions of frailty and robustness and heightens the importance of nutritional status (Kannisto 1991; Fried *et al*. 2001; Alter 2004).

3. Longevity and Biodemography

3.1. HERITABILITY OF LONGEVITY

The study of family components in longevity has been a classic of biodemography since work by Pearl in the 1930s, particularly the study of the relationship between the longevity of parents and of their children (Pearl 1931; Philippe 1980; Jacquard 1982; Desjardins and Charbonneau 1990; Bocquet-Appel and Jakobi 1991; Abernethy and Hip 1990). All these studies show that there is a significant family component in longevity, but it is always fairly difficult to distinguish what is owed to genes from what is owed to the shared family environment (Cournil *et al*. 2000; Gavrilov and Gavrilova, 2001b; Cournil and Kirkwood 2001; Kerber *et al*. 2001; Matthijs *et al*. 2002). The Gavrilovs have shown recently that the relationship between the longevity of parents and of their children is far from linear. It is even stronger when the parents achieve a greater age (Gavrilov and Gavrilova 2001b).

Perls and his team have recently re-examined several of these family relationships under the New England Centenarian Study, such as family concentrations of long-lived subjects (Perls *et al*. 2000) or the longevity of centenarian siblings (Perls *et al*. 1998a). In particular, Pearls and Wilmoth have shown that brothers and sisters of centenarians have mortality rates reduced by half at all stages in their lives compared with their affiliation cohort (Perls *et al*. 2002). Elsewhere, the study of twins is the preferred method of isolating the genetic contribution to longevity (McGue *et al*. 1993; Herskind *et al*. 1996; Ljungquist *et al*. 1998), or, now, the genetic contribution to the functional decline of the oldest-old (Gurlang *et al*. 2004).

3.2. LONGEVITY AND PROCREATION

Since Kirkwood and Rose suggested the existence of a trade-off between longevity and fertility—humans having to choose between immortality and reproduction (Kirkwood and Rose 1991) studies have focused regularly on the relationship between longevity and fertility (Le Bourg *et al*. 1993). Perls and his colleagues, for example, observe that women who procreate late live longer (Perls *et al*. 1998b; Mûller *et al*. 2002); whereas others suggest that the birth of a son reduces the mother's longevity, at least during pre-industrial times (Helle *et al*. 2002).

Other teams take advantage of newly-available genealogical data to re-examine the relationship between parental age and the longevity of the children. The idea is that there is an optimum age for procreation, bolstering the longevity of the children (Gavrilov *et al*. 1996a and b; Gavrilov and Gavrilova 1997a and b; Gavrilov *et al*. 1997; Gavrilova *et al*. 1998; Westendorp and Kirkwood 1999, 2001; Promislow 1998; Gavrilov and Gavrilova 2001b; Kerber *et al*. 2001). The conclusions are far from convincing. In particular, the age of parents when future centenarians are born is no different from the age of parents when controls belonging to the same birth cohorts are born (Robine *et al*. 2003d).

3.3. LONGEVITY AND CHILDHOOD EVENTS

Biodemographic research has gradually embraced the study of the possible impact of events in early childhood on the longevity of individuals. Kannisto and his colleagues have thus studied the impact of famines (Kannisto *et al*. 1997), whilst others have studied the impact of the season of birth (Gavrilov and Gavrilova 1999; Doblhammer and Vaupel 2001). Thus, Doblhammer and Vaupel have shown that children born in Autumn have a greater chance of survival past their 50s. These results are consistent with the fact that at the turn of the 20th century, children born in Autumn had a higher birth weight than children born at other times of the year (Doblhammer and Vaupel 2001). These results of course suggest a link to the food resources available throughout the year in the economic and social conditions of the late 19th and early 20th centuries. Other events from early childhood have been studied since (Gavrilova *et al*. 2003; Gavrilov and Gavrilova 2003). In particular, Finch and Crimmins relate the drop in infant mortality to the drop in mortality at 70 years of age and above, 70 years later, within the same cohorts. They thus partly explain the drop in mortality of the oldest-old from a reduction in infections and improved food in early childhood (Finch and Crimmins 2004).

3.4. SPECIES COMPARISON

Lastly, species comparison remains a major subject in biodemography, be it trajectories of mortality (Vaupel *et al*. 1998), life duration distribution (Horiuchi 2003) or frailty and life expectancy in good functional health (Carey *et al*. 2005), as do numerous biological and environmental mechanisms involved in longevity in good health, such as caloric restriction (Mattison *et al*. 2003; Magwere *et al*. 2004; Masternak *et al*. 2004) and its links with the insulin/IGF-1 pathway (Arantes-Oliveira *et al*. 2003) or the carrying forward of degenerative diseases (Coley *et al*. 2003).

It is clear that the majority of biodemographical questions remain unanswered. These are major, frequently fascinating, issues. They include the longevity/fertility trade-off, an optimum age for procreation and the impact of the season of birth on longevity. Many of these issues assume "natural" fertility, in other words a difficult environment like that in the 19th century or before the industrial revolution. They also assume the existence of statistical data and chronological series on variables like the fertility rate, birth weight, food consumption, and life durations. These two series of conditions are largely contradictory. Natural fertility and difficult economic environments are frequently paired with the absence of statistics. Statistical availability is frequently paired with a favourable economic environment and controlled fertility, all of which makes these questions impossible to study. The 19th and 20th centuries offer a rare window on the two series of conditions co-existing in some European countries, which explains the emphasis of current biodemographical research. The results are appropriate for the populations at the junction of these two centuries. But it is highly unlikely that there is a now a significant relationship between the fertility of today's young women (0, 1, 2, 3 children maximum) and their future longevity or even a relationship between the season of birth of today's children and their future longevity.

4. Longevity and Biology

It is still not understood why man gets older and is incapable of maintaining his body in good working order whilst life and genetic heritage have been handed down from generation to generation, without major alterations, for thousands of years. Since work by Williams (1957) and Kirkwood and Rose (1991), no major advances have been made in the evolutionary theories on ageing (Carnes and Olshansky 1993). Olshansky, Carnes, and their teams are continuing their work on biological limits to longevity (Olshansky *et al*. 2001; Olshansky and Carnes 2002; Carnes *et al*. 2003), whilst the Gavrilovs suggest that the ageing of individuals and human longevity can be explained by the theory of reliability of complex systems (Gavrilov and Gavrilova 2001a). But beyond research into major theories to explain all the observations, biologists are focusing above all on studying biological markers relating to longevity and ageing in good health and the related genes.

4.1. BIOLOGICAL LONGEVITY MARKERS

Numerous biological parameters have thus been studied in centenarians, such as fibronectin concentration (Labat-Robert *et al*. 2000), or of antioxidants (Mecocci *et al*. 2000; Hyland *et al*. 2002), heart rate (Paolisso *et al*. 1999a and b) and many more, particularly in centenarians in good health studied by Italian research teams (Bagnara *et al*. 2000; Paolisso *et al*. 2000; Savarino *et al*. 2001; Rabini *et al*. 2002; Atzmon *et al*. 2002; Barzilai *et al*. 2003, Gangemi *et al*. 2003). More recent studies have covered the ability to face up to stress, measured by the production of Heat Shock Proteins (HSP) (Ambra *et al*. 2004; Marini *et al*. 2004; Simar *et al*. 2004), immune, anti-inflammatory responses (Van den Biggelaar *et al*. 2004), research into specific antibodies (Meroni *et al*. 2004) and beta-carotene concentration (Hu *et al*. 2004). These studies frequently take place in conjunction with observations of other laboratory animal species such as yeast *Saccharomyces cerevisiae* (Chen *et al*. 2003), worms *Caenorhabditis elegans* (Arantes-Oliveira *et al*. 2003), flies *Drosophila Melanogaster* (Magwere *et al*. 2004), mice (Masternak *et al*. 2004), dogs

(Coley *et al*. 2003) and monkeys (Mattison *et al*. 2003). A recent study has shown that HDL and LDL particles in centenarians and their children are greater than in the controls and that such a phenotype is associated with a lower frequency of high blood pressure and cardio-vascular diseases. This result is linked to the Cholesteryl Ester Transfer Protein (CETP) gene (Barzilai *et al*. 2003).

Elsewhere, caloric restriction seems to halt ageing and increase longevity. It reduces the weight of individuals and the quantities of insulin, IGFI, glucose and the thyroid hormone contained in the blood. A strong link exists between the insulin/IGF pathway and longevity, found in *C. elegans*, *Drosophila melanogaster* and mice as well as humans (Bonafe *et al*. 2003; Kojima *et al*. 2004).

4.2. LONGEVITY GENES

Research into genes associated with longevity, particularly longevity in good health, is the major interest at the start of the 21st century (Jazwinski 1996; Kirkwood 1997; Finch and Tanzi 1997; Bartke *et al*. 2001; Longo and Finch 2003) and the principal motivation for current studies on centenarians and ninety-year olds, such as the New England Centenarian Study (NECS) in the United States and the European Challenge for Healthy Ageing (ECHA) and the Genetics of Healthy Ageing (GEHA) in Europe. Several studies are currently investigating genes linked to longevity (Bladbjerg *et al*. 1999; Perls *et al*. 2000; Perls 2001; Barzilai and Shuldiner 2001; Puca *et al*. 2001; Blanché *et al*. 2001; Kaeberlein *et al*. 2002; Barzilai 2003; Geesaman *et al*. 2003; Rose *et al*. 2003; Perls *et al*. 2002; Perls 2003) or are studying the assocation between the length of telomeres and mortality (Bodnar *et al*. 1998; Campisi *et al*. 2001; Takuto *et al*. 2002; Cawthon *et al*. 2003).

The only gene so far found to be clearly associated with longevity is the Apolipoprotein E gene, ApoE (Blanché 2003). An association between longevity and a locus on the chromosome 4 has recently been discovered (Puca *et al*. 2001); but it has proved impossible to reproduce on a second sample (Geesaman *et al*. 2003). Teams are seeking genes to counteract the principal degenerative diseases, such as cancer (Bonafe *et al*. 2002; Tyner *et al*. 2002), cardio-vascular diseases (Zuliani *et al*. 2002) and Alzheimer's disease (Siverman *et al*. 1999; Blazer *et al*. 2001; Fillenbaum *et al*. 2002; Eichner *et al*. 2002; Choi *et al*. 2003) with other teams seeking genes associated with the immune system, such as the HLA system (Takata *et al* 1987; Ivanova *et al*. 1998; Lio *et al*. 2003) or studying the mitochondrion DNA (Tanaka *et al*. 1998; Vandenbroucke 1998; Kokaze *et al*. 2003). Some teams are studying progeria, a rare genetic disorder that causes accelerated ageing (Ly *et al*. 2000). Others try to test evolutionist theories of age-related diseases (Wick *et al*. 2003).

A few researchers have started to study the differences in life expectancy between countries that may be attributed to genetic variations (Ewbank 2004), whereas, others are developing new statistical methods to study longevity genetics (Yashin *et al*. 1999, 2000; Tan *et al*. 2002). Far more is known about the links between certain genes and longevity for other laboratory animal species, such as yeast, worms, flies and mice, and it is always tempting to use this information for humans (Bartke *et al*. 2001; Tyner *et al*. 2002; Longo and Finch 2003). Miller thus identifies six sorts of longevity genes: (i) genes that cause ageing,

(ii) genes that alter longevity because they increase the risk of developing certain diseases, (iii) genes acting on the type of old person you are, (iv) low-fitness genes that prolong life duration, probably by slowing it down, (v) alleles and combinations of alleles that alter life duration because they alter ageing and (vi) genes that slow ageing down (Miller 2001). Other classifications do exist, however (Martin 1999).

ApoE is the first gene to have been linked to longevity in humans (Louhija *et al*. 1994; Schächter *et al*. 1994), and therefore most is known about it. The ApoE allele e4 increases the risk of Alzheimer's disease and cardio-vascular disease. This allele is therefore encountered less frequently in centenarians, whereas the allele e2, associated with a reduced risk of Alzheimer's disease, is encountered more frequently (Silverman *et al*. 1999; Blanché *et al*. 2001; Blazer *et al*. 2001; Frisoni *et al*. 2001; Eichner *et al*. 2002; Fillenbaum *et al*. 2002; Choi *et al*. 2003). Studies have recently commenced on the possible contribution of the ApoE, with the distribution of the various alleles varying greatly from one country to the next, in the deviations in life expectancy observed in Europe (Ewbank 2004).

It is highly unlikely, however, that the longevity genes act independently from the environment, if indeed they exist (Christen 2003). The principal European projects on successful ageing genetics are the AKEA project, a study of centenarians in Sardinia directed by Deiana since 1997, the ECHA project (European Challenge for Healthy Ageing, 2002–2004) directed by De Benedictis, and the GEHA project (Genetics of Healthy Ageing, 2004–2009) directed by Franceschi (Abbott 2004). Other projects are in progress, however, such as the MALVA study (Gueresi *et al*. 2003). The common denominator in all these European projects is the simultaneous consideration of genetic and environmental factors through epidemiological surveys and related health examinations. The study of gene/environment interactions, possibly including additional factors such as chance (Finch and Kirkwood 2000), is the preferred approach to studying longevity determinants, even if it remains a difficult to carry out such studies. The study of the variability of life durations or ageing also remains a major topic (Finch 1998), as does the study of the plasticity of these various phenotypes to the environment and to its modifications (Vaupel *et al*. 2003).

The recent progress in the demography of longevity is partly due to the establishment of international databases, such as the Oldest-Old Mortality Database, better known as the Kannisto–Thatcher Database (Kannisto 1994), the Human Mortality Database (HMD), developed jointly by the University of California at Berkeley and the Max Planck Institute for Demographic Research at Rostock (www.mortality.org or www.humanmortality.de), and the International Database on Longevity (IDL), developed jointly by the University of Montpellier, the French National Institute for Demographic Studies (INED) and the Max Planck Institute for Demographic Research (Robine and Vaupel 2002). Similar databases in the other fields of longevity, epidemiology, biodemography, and biology would surely contribute to significant progress.

Lastly, it should be mentioned that throughout this review we have found no studies, or only very few, devoted to the economic and social consequences of this longevity revolution (Boulding 2003).

References

Abbott, A. (2004) “Growing old gracefully”, *Nature*, 428:116–118.

Abernethy, V., and Hip, R. (1990) “Parent characteristics and sex differential infant mortality: The case in Tennessee”, *Human Biology*, 62(2):279–290.

Allard, M., and Robine, J.-M. (2000) *Les centenaires français*. Etude de la Fondation IPSEN, 1990–2000. Paris: Serdi Edition.

Allard, M., Vallin, J., Andrieux, J. M., and Robine, J-M. (1996) “In search of the secret of centenarians: A demographic and medical survey about centenarians in France”. In: Caselli, G., Lopez, A. D. (eds.), *Health and Mortality Among Elderly Populations*. Oxford: Clarendon Press, pp. 61–86 (Chapter 4)

Alter, G. (2004) “Height, frailty, and the standard of living : Modeling the effects of diet and disease on declining mortality and increasing height”, *Population Studies*, 58(3):265–279

Ambra, R., Mocchegiani, E., Giacconi, R., Canali, R., Rinna, A., Malavolta, M., and Virgili, F. (2004) “Characterization of the hps70 response in lymphoblasts from aged and centenarian subjects and differential effectes of vitro zinc supplementation”, *Experimental Gerontology*, 39:1475–1484.

Andersen-Ranberg, K., Christensen, K., Jeune, B. *et al*. (1999) “Declining physical abilities with age: A cross-sectional study of older twins and centenarians in Denmark”, *Age and Ageing*, 28:373–377.

Andersen-Ranberg, K., Vasegaard, L., and Jeune, B. (2001) “Dementia is not inevitable: A population-based study of Danish centenarians”, *Journal of Gerontology*: *Psychososial Sciences*, 56B(3):P152–P159.

Ankri, J., and Poupard, M. (2003) “Prévalence et incidence des démences au grand âge. Analyse de la littérature”, *Rev. Epidemiol. Santé Publique*, 51:349–360.

Arantes-Oliveira, N., Berman, J. R., and Kenyon, C. (2003) “Healthy animals with extreme longevity”, *Science*, 302:611.

Arkhipov, I. J. A. (1980) “La longévité: essai d’interprétation du phénomène à partir de sa distribution géographique”, *La Revue de Gériatrie*, 5(8):405–407.

Atzmon, G., Gabriely, I., Greiner, W. *et al*. (2002) “Plasma HDL levels highly correlate with cognitive function in exceptional longevity”, *Journal of Gerontology*: *Medical Sciences*, 57A(11):M712–M715.

Austad, S. (2005) “Patterns in mammalian aging: Demography and Evolution”. In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Bagnara, G. P., Bonsi, L., Strippoli, P. *et al*. (2000) “Hemopoesis in healthy old people and centenarians”, *Journal of gerontology*: *Biologocal Sciences*, 55A(2):B61–B66.

Baltes, P. B. (2003) “Extending longevity: Dignity gain or dignity drain”, *Max Plank Research*, 3:15–19.

Barbi, E., Caselli, G., and Vallin, J. (2003) “Trajectories of extreme survival in heterogeneous populations”, *Population*, E58 (1): 43–66.

Bartke, A., Coschigano, K., Kopchick, J. *et al*. (2001) “Genes that prolong life: Relationships of growth hormone and growth to aging and life span”, *Journal of Gerontology*: *Biological Sciences*, 56A(8):B340–B349.

Barzilai, N. (2003) “Discovering the secrets of successful longevity”, *Journal of Gerontology*: *Medical Sciences*, 58A(3):225–226.

Barzilai, N., Atzmon, G., Schechter, C., *et al*. (2003) “Unique lipoprotein phenotype and genotype associated with exceptional longevity”, *The Journal of the American Medical Association*, 290(15): 2030–2040.

Barzilai, N., Gabriely, I., Gabriely, M., *et al*. (2001) "Offsring of centenarians have a favorable lipid profile", *Journal of the American Geriatric Society*, 491:76–79.

Barzilai, N., and Shuldiner, A. R. (2001) "Searching for human longevity genes: The future history of gerontology in the Post-genomic Era", *Journal of Gerontology*: Biological Sciences, 56A(2):M83–M87.

Beaumel, C., Désesquelles, A., Richet-Mastain, L., and Vatan, M. (2004) *La situation démographique en 2002*. Insee Société n°34.

Bell, F. C., Wade, A. H., and Goss, S. G. (1992) *Life Tables for the United States: 1900–2080*. Actuarial Study, No. 107. SSA Publication No. 11-11536. Administration Office of Actuary.

Benjamin, B. (1959) "Actuarial aspects of human lifespans". In: Wolstenholme, G. E. W., O'Connor, M. (eds.), *CIBA Foundation Colloquia on Ageing, Vol. 5*, *The Life Span of Animals*. Boston: Little, Brown and Company, pp. 2–20.

Benjamin, B. (1963) "Actuarial methods of mortality analysis: Adaptation to changes in the age and cause pattern", *Proceedings of the Royal Society*, B159:1–255.

Benjamin, B. (1964) "Demographic and actuarial aspects of ageing, with special reference to England and Wales", *Journal of the Institute of Actuaries*, 90:211–253.

Benjamin, B. (1982) "The span of life", *Journal of the Institute of Actuaries*, 109:319–357.

Benjamin, B. (1988) "Years of life lost and other mortality indices", *Journal of the Institute of Actuaries*, 115:709–719.

Bennett, N. G., and Garson, L. K. (1986) "Extraordinary longevity in the Soviet Union: Fact or artifact?" *The Gerontologist*, 26(4):358–361.

Bertillon, J. (1878) "Discussion sur le bulletin-modèle de mariage", *Annales de demographie internationale*, 5:472–473.

Bladbjerg, E. M., Andersen-Ranberg, K., de Maat, M. P. M., *et al*. (1999) "Longevity is independent of common variations in genes associated with cardiovascular risk", *Thrombosis and Haemostasis*, 82:1100–1105.

Blanché, H. (2003) "Les facteurs génétiques de la longévité", *Presse Medicale*, 32:365–369.

Blanché, H., Cabanne, L., Sahbatou, M., *et al*. (2001) "A study of French centenarians: Are ACE and APOE associated with longevity?" *CR Academic Science Life Sciences*, 324:129–135.

Blansjaar, B. A., Thomassen, R., and van Schaik, H. W. (2000) "Prevalence of dementia in centenarians", *International Journal of Geriatric Psychiatry*, 15:219–225.

Blazer, D. G., Fillenbaum, G., and Burchett, B. (2001) "The APOE-E4 allele and the risk of functional decline in a community sample of African American and white older adults", *Journal of Gerontology*: *Medical Sciences*, 56A(12):M785–M789.

Bocquet-Appel, J. P., and Jakobi, L. (1991) "La transmission familiale de la longévité à Arthez d'Asson (1685–1975)", *Population*, 46:327–347.

Bodio, L. (1887) "Quelques renseignments sur les conditions hygieniques et sanitaires de l'Italie", *Bulletin de l'Institut international de statistique*, II(part 1):264–84.

Bodnar, A. G., Ouellette, M., Frolkis, M., *et al*. (1998) "Extension of life-span by introduction of telomerase into normal human cells", *Science*, 279:349–352.

Bonafe, M., Barbi, C., Storci, G., *et al*. (2002) "What studies on human longevity tell us about the risk for cancer in the oldest old: Data and hypotheses on the genetics and immunology of centenarians", *Experimental Gerontology*, 37:1263–1271.

Bonafe, M., Barbieri, M., Marchegiani, F., *et al*. (2003) "Polymorphic variants of insulin-like growth factor I (IGF-I) receptor and phosphoinositide 3-kinase genes affect IGF-I plasma levels and human longevity: Cues for an evolutionarily concerved mechanism of life span control", *Journal of Clinical Endocrinology and Metabolism*, 88:3299–3304.

Bongaarts, J., and Feeney, G. (2002) "How long do we live?", *Population and Development Review*, 28(1):13–29.

Bonneux, L., Barendregt, J. J., and Van der Maas, P. J. (1998) "The expiry date of man: A synthesis of evolutionary biology and public health", *Journal of Epidemiology and Community Health*, 52:619–623.

Boulding, K. (2003) "Possible consequences of increased life expectancy", *Population and Development Review*, 29 (3):193–504.

Bourbeau, R., and Desjardins, B. (2005) "Mortality at extreme ages and data quality: The Canadian experience". In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Bourgeois-Pichat, J. (1952) "Essai sur la mortalité biologique de l'homme", *Population*, 7(3):381–394

Bourlière, F. (1987) "Vieillissement "normal" et vieillissement pathologique", *Gerontologica Perspecta*, 1:475–485.

Bowerman, W. G. (1939) "Centenarians", *Transactions of Actuaries*, 40:360–378.

Buffon, G.L.L. (1749). *Oeuvres Complètes*. Paris: P Duménil Editeur (Edition de 1836).

Caldwell, J. C. (1979) "Education as a factor in mortality decline: An examination of Nigerian data", *Population Studies*, 33(3):395–413.

Campisi, J., Kim, S. H., Lim, C. S., *et al*. (2001) "Cellular senescence, cancer and aging: The telomere connection", *Experimental Gerontology*, 36:1619–1637.

Carey, J. R. (1997) "What demographers can learn from fruit fly actuarial models and biology", *Demography*, 34(1):17–30.

Carey, J. R. (2003) *Longevity, the Biology and Demography of Life Span*. Princeton: University Press.

Carey, J., and Judge, D. S. (2005) "Life span extension in humans is self-reinforcing: A general theory of longevity". In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Carey, J. R., Liedo, P., Orozco, D., and Vaupel, J. W. (1992) "Slowing of mortality rates at older ages in large medfly cohorts", *Science*, 258:457–461.

Carey, J. R., Robine, J-M., Michel, J. P., and Christen, Y. (2005) *Longevity and Frailty*. Berlin: Springer.

Carnes, B., and Olshansky, S. J. (1993) "Evolutionary perspectives on human senescence", *Population and Development Review*, 19:793–806.

Carnes, A. B., and Olshansky, S. J. (1997) "A biologically motivated partitioning of mortality", *Experimental Gerontology*, 32(6):615–631.

Carnes, B., Olshansky, S. J., and Grahn, D. (1996) "Continuing the search for a law of mortality", *Population and Development Review*, 22:231–264.

Carnes, B. A., Olshansky, S. J., and Grahn, D. (2003) "Biological evidence for limits to the duration of life", *Biogerontology*, 4:31–45.

Caselli, G., Vaupel, J., and Yashin, A. (2005) "Explanation of the decline in mortality among the oldest-old: A demographic point of view". In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.) *Human Longevity, individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Catalano, R. (2002) "Economic antecedents of mortality among the very old", *Epidemiology*, 13:133–137.

Cawthon, R. M., Smith, K. R., O'brien, E., *et al*. (2003) "Association between telomere length in blood and mortality in people aged 60 years and older", *The Lancet*, 361:393–395.

Charbonneau, H. (1990). "Pierre Joubert a-t-il vécu 113 ans?" *Mem Soc Geneal Can-Fr*, 41:45–49.

Charbonneau, H., and Desjardins, B. (1990) "Vivre cent ans dans la vallée du Saint-Laurent avant 1800", *Annales de Démographie Historique*, 218–226.

Chen, C., Dewaele, S., Braeckman, B., Desmyter, L., Verstraelen, J., Borgonie, G., Vanfleteren, J., and Contreras, R. (2003) "A high-throughput screening system for genes extending life-span", *Experimental Gerontology*, 38: 1051–1063.

Cheung, J. (2001) *The Long-Term Trend of Non-Maori Mortality and its More Recent Compression Effect*. Presented at the Population Association of New Zealand biannual conference, Wellington.

Cheung, S. L. K. (2003) *Scalar Expansion and Normal Longevity in Hong Kong*. Hong Kong University of Science and Technology. PhD Thesis.

Cheung, S. L. K., Robine, J-M., Tu, E. J. C., and Caselli, G. (2005a) "Change in the distribution of normal life durations through the demographic transition: The case of Hong Kong", (unpublished manuscript).

Cheung, S. L. K., Robine, J-M., Tu, E. J. C., *et al*. (2005b) "Three dimensions of the survival curve: Horizontalization, verticalization and longevity extension", *Demography*, 42(2):243–252.

Choi, Y. H., Kim, J. H., Kim, D. K., *et al*. (2003) "Distributions of ACE and APOE polymorphisms and their relations with dementia status in Korean centenarians", *Journal of Gerontology*: *Medical Sciences*, 58A(3):227–231.

Christen, Y. (2003) "Les facteurs environnementaux de la longévité", *Presse Medicale*, 32:370–376.

Christensen, K., and Herskind, A. M. (2005) "Genetic factors associated with individual life duration: Heritability". In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Clarke, R. D. (1950) "A bio-acturial approach to forecasting rates of mortality", In: *Proceedings of the Centenary Assembly of the Institutes of Actuaries*, Cambridge: Cambridge University Press, Vol. 2, pp. 12–27.

Coale, A. J. (1996) "Age patterns and time sequence of mortality in national populations with the highest expectation of life at birth", *Population and Development Review*, 22(1):127–135.

Coles, L. S. (2001) "Table of world-wide living supercentenarians", *Journal of Anti-Aging Medicine*, 4(3):267–269.

Coles, L. S. (2004) "Demography of human supercentenarians", *Journal of Gerontology: Biological Sciences*, 59A(6):579–586.

Coley, D. M., Schlittler, D. L., Glickman, L. T., Hayeck, M., and Waters, D. J. (2003) "Exceptional longevity in pet dogs is accompanied by cancer resistance and delayed onset of major diseases", *Journal of Gerontology: Biological Sciences*, 58A(12):1078–1084.

Comfort, A. (1956) *The Biology of Senescence*. London: Routledge and Kegan Paul.

Comfort, A. (1964) *Aging: The Biology of Senescence*. Austin, TX: Holt, Rinehart and Winston, Inc.

Cournil, A., and Kirkwood, T. B. L. (2001) "If you would live long, choose your parents well", *Trends in Genetics*, 17(5):233–235.

Cournil, A., Legay, J-M., and Schächter, F. (2000) "Evidence of sex-linked effects on the inheritance of human longevity: A population-based study in the Valserine valley (French Jura), 18–20th centuries", *Philosophical Transactions of the Royal Society of London B*. *Biological Science*, 267:1021–1025.

Crimmins, E. M. (2004) “Trends in the health of the elderly”, *Annual Review of Public Health*, 25:79–98.

Cutler, R. G. (1985) “La biologie du vieillissement et de la longévité”, *Gerontologica Biomedica Acta*, 1:7–61.

D’Amico, M., Agozzino, E., Biagino, A., *et al*. (1999) “Ill-defined and multiple causes on death certificates–a study of misclassification in mortality statistics”, *European Journal of Epidemiology*, 15:141–8.

De Moivre, A. (1756) *The Doctrine of Chances*. Third edition.

Deevey, E. S. (1947) “Life tables for natural populations of animals”, *The Quarterly Review of Biology*, 22:283–314.

Dépoid, F. (1973). “La mortalité des grands vieillards”, *Population*, (4–5):755–792.

Desjardins, B., and Charbonneau, H. (1990) “L’héritabilité de la longévité”, *Population*, 3:603–616.

Desjardins, B. (1999) “Did Marie Louise Meilleur become the oldest person in the world?”. In: Jeune, B., Vaupel, J. W. (eds.), *Validation of Exceptional Longevity*. Odense: Odense University Press, pp. 189–194.

Dewey, M. E., and Copeland, J. R. M. (2001) “Dementia in centenarians”, *International Journal of Geriatric Psychiatry*, 16:538–539.

Doblhammer, G., and Vaupel, J. W. (2001) “Lifespan depends on month of birth”, *Proceedings of the National Academy of Sciences of the United States of America*, 98(5):2934–2939.

Dublin, L. I. (1923) “The possibility of extending human life”, *Metron*, 3(2):175–197.

Dublin, L. I., Kopf, E. W., and Lotka, J. A. (1926) “The components of death curves. An analysis of life table deaths by causes”, *The American Journal of Hygiene*, 7:S299–S333.

Dublin, L. I., and Lotka, J. A. (1934) “The history of longevity in the United States”, *Human Biology*, 1.

Dublin, L. I., and Lotka, J. A. (1945) “Trends in longevity”, *The Annals of the American Academy*, 5:123–134.

Eakin, T., and Witten, M. (1995) “How square is the survival curve of a given species?”, *Experimental Gerontology* 30:33–64.

Eichner, J. E., Dunn, S. T., Perveen, G., *et al*. (2002) “Apolipoprotein E polymorphism and cardiovascular disease: A HuGE review”, *The American Journal of Epidemiology*, 155(6):487–495.

Evert, J., Lawler, E., Bogan, H., *et al*. (2003) “Morbidity profiles of centenarians: Survivors, delayers, and escapers”, *Journal of Gerontology*: *Medical Sciences*, 58A(3):232–237.

Ewbank, D. C. (2004) “The APOE gene and differences in life expectancy in Europe”, *Journal of Gerontology*: *Biological Sciences*, 59A(1):16–20.

Ewbank, D. C. (2005) “Mortality among the least frail: Lessons from research on the APOE gene”. In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Faber, J. F. (1982) *Life tables for the United States: 1900–2050*. Actuarial Study, No. 87. SSA Publication No. 11–11534. Administration Office of Actuary.

Faber, J. F., and Wade, A. H. (1983 *) Life Tables for the United States: 1900–2050*. Actuarial Study, No. 89. SSA Publication No. 11-11536. Administration Office of Actuary.

Ferrucci, L., Izmirlian, G., Leveille, S. G., *et al*. (1999) “Smoking, physical activity and active life expectancy”, *American Journal of Epidemiology*, 149:645–653.

Fillenbaum, G. G., Blazer, D. G., Burcher, B. M., *et al*. (2002) "Apolipoprotein E ε4 and risk of mortality in African and white older community residents", *The Gerontologist*, 42(3):381–386.

Finch, C. E. (1998) "Variations senescence and longevity include the possibility of negligible senescence", *Journal of Gerontology*: *Series A Biological Science and Medical Science*, 53:B235–B239.

Finch, C. E., and Crimmins, E. M. (2004) "Inflammatory exposure and historical changes in Human life spans", *Science*, 305:1736–1739.

Finch, C. E., and Kirkwood, T. L. (2000) *Chance, Development, and Aging*. Oxford: Oxford University Press.

Finch, C. E., and Pike, M. C. (1996) "Maximum life span predictions from the gompertz mortality model", *Journal of Gerontology: Biological Sciences*, 51A(3):B183–B194.

Finch, C. E., Tanzi, R. E. (1997) "Genetics of aging", *Science*, 278:407–411.

Fogata, M. L., Naik, P. N., and Goldberg, T. H. (1996) "Causes of death in the very old", *Journal of the American Geriatric Society*, 44:1412–3.

Fondation IPSEN (1991) *100 tableaux pour 100 ans.* Fondation IPSEN. Paris: A la recherche du secrtet des centenaires, Document 1.

Frederiksen, H., MCGue, M., Jeune, B., *et al*. (2002) "Do children of long-lived paprents age more successfully?", *Epidemiology*, 13(3):334–339.

Freudenberg, K. (1934) "Die Gesetzmässigkeiten der menschilchen Lebensdauer. Ergebn. D", *Hygiene*, 15:335–441.

Fried, P. L., Tangen, C. M., Walston, J., *et al*. (2001) "Frailty in older adults: Evidence for a phenotype", *Journal of Gerontology: Series A Biological Sciences and Medical Sciences*, 56A(3):M146–M156.

Fries, J. F. (1980) "Aging, natural death, and the compression of morbidity", *The New England Journal of Medicine*, 303(3):130–135.

Fries, J. F. (1984) "The compression of morbidity: Miscellaneous comments about a theme", *The Gerontologist*, 24:354–359.

Fries, J. F. (1989) "The compression of morbidity: Near or far?", *Milbank Quarterly*, 67(2):208–232.

Fries, J. F. (2002) "Reducing disability in older age", *The Journal of the American Medical Association*, 288(24):3164–3166.

Fries, J. F., and Crapo, L. M. (1981) *Vitality and Aging: Implication of the Rectangular Curve*. San Francisco: W. H. Freeman and Company.

Frisoni, G. B., Louhija, J., Geroldi, C., *et al*. (2001) "Longevity and the ε2 allele of Apolipoprotein E: The finnish centenarians study", *Journal of Gerontology*: *Medical Sciences*, 56A(2):M75–M78.

Gangemi, S., Basile, G., Alba, R., *et al*. (2003) "Increased circulating interleukin-18 levels in centenarians with no signs of vascular disease: Another paradox in longevity?", *Experimental Gerontology*, 38:669–672.

Gavrilov, L. A., and Gavrilova, N. S. (1997a) "When fatherhood should stop", *Science*, 277:17–18.

Gavrilov, L. A., and Gavrilova, N. S. (1997b) "Parental age at conception and offspring longevity", *Review in Clinical Gerontology*, 7:5–12.

Gavrilov, L. A., and Gavrilova, N. S. (1998). "The future of long life", *Science*, 281(11):1611.

Gavrilov, L. A., and Gavrilova, N. S. (2003) "The quest for a general theory of aging and longevity", *Science of Aging Knowledge Environment*, www.sageke.sciencemag.org/cgi/content/full/sageke;2003/28/re5.

Gavrilov, L. A., Gavrilova, N. S., Evdokushkina, G. N., Semyonova, V. G., Gavrilova, A. L., Evdokushkina, N. N., and Lapshin, E. V. (1996a) "Determinants of human longevity: Parental age at conception and offspring longevity", *Longevity Report*, 10(54):7–15.

Gavrilov, L. A., Gavrilova, N. S., Kroutko, V. N., Evdokushkina, G. N., Semyonova, V. G., Gavrilova, A. L., Lapshin, E. V., Evdokushkina, N. N., Kushnareva Yu., E., (1996b) "Specific decrease in longevity of daughters conceived by old fathers", *Longevity Report*, 10(56):4–5.

Gavrilov, L. A., Gavrilova, N. S., Kroutko, V. N., Evdokushkina, G. N., Semyonova, V. G., Gavrilova, A. L., Lapshin, E. V., Evdokushkina, N. N., and Kushnareva Yu., E. (1997) "Mutation load and human longevity", *Mutation Research*, 377:61–62.

Gavrilov, L. A., and Gavrilova, S. N. (1999) "Season of birth and human longevity", *Journal of Anti-aging Medicine*, 2(4):365–366.

Gavrilov, L. A., and Gavrilova, S. N. (2003) "Early-life factors modulating lifespan". In: Rattan, S. I. S. (ed.), *Modulating Aging and Longevity*. Dordrecht: Kluwer Academic Publishers.

Gavrilov, L. A., and Gavrilova, N. S. (2001a) "The reliability theory of aging and longevity", *Journal of Theoretical Biology*, 213:527–545.

Gavrilov, L.A., and Gavrilova, N. S. (2001b) "Biodemographic study of familial determinants of human longevity", *Population*, 13(1):197–222.

Gavrilova, N. S., Gavrilov, L. A., Evdokushkina, G. N., Semyonova, V. G., Gavrilova, A. L., Lapshin, E. V., Evdokushkina, N. N., Kushnareva Yu E., Kroutko, V. N., and Andreyev A Yu. (1998) "Evolution, mutations, and human longevity: European royal and noble families", *Human Biology*, 70:799–804.

Gavrilova, S. N., Gavrilov, L. A., Evdokushkina, G. N., *et al*. (2003) "Early-life predictors of human longevity: Analysis of the XIXth century birth cohorts", *Annales de démographie historique*, (2):177–198.

Geesaman, B. J., Benson, E., Brewster, S. J., *et al*. (2003) "Haplotype-based identification of a microsomal transfer protein marker associated with the human lifespan", *Proceedings of the National Academy*, 100(24):14115–14120.

Go, C. G., Brustrom, J. E., Lynch, M. F., and Aldwin, C. M. (1995) "Ethnic trends in survival curves and mortality", *The Gerontologist*, 35(3):318–326.

Gompertz, B. (1825) "On the nature of the function expressive of the law of human mortality, and on a new mode of determining the value of life contingencies", *Philosophical Transactions of the Royal Society of London B* Biological Science, 115:513–585.

Gordon, T. J. (1980) *Changing Mortality Patterns. In the Future of Life Expectancy: Economic, Social and Medical Implications of Living Longer*. Society of Actuaries, Chicago. *Proceedings of a two-day symposium held* March 10–11, 1980.

Graunt, J. (1661) *Observations Naturelles et Politiques Répertoriées dans l'Index ci-après et faites sur les Bulletins de Mortalité*: Edition critique by E. Vilquin. Paris: INED.

Greenwood, F. R. S. (1928) " 'Laws' of mortality from the biological point of view ", *Journal of Hygiene*, XXVIII: 267–294.

Greenwood, M., and Irwin. J. O. (1939) "The Biostatistics of senility", *Human Biology*, 11(1):1–23.

Grundy, E. (2005) "Marital status and family support of the oldest old in Great Britain". In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.) *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Gueresi, P., Troiano, L., Minicuci, N., *et al*. (2003) "The MALVA (MAntova LongeVA) study: An investigation on people 98 years of age and over in a province of Northern Italy", *Experimental Gerontology*, 38:1189–1197.

Gumbel, E. L. (1937) “La durée extrême de la vie humaine”, *Actualités Scientifique et Industrielles 520*, Paris: Statistique mathématique, Hermann et Cie Editeurs.

Gurland, B. J., Page, W. F., and Plassman, B. L. (2004) “A twin study of the genetic contribution to age-related functional impairment”, *Journal of Gerontology: Medical Sciences*, 59A(8):859–863.

Hagberg, B., Bauer, A. B., and Poon, L. W. (2001) “Cognitive functioning in centenarians: A coordinated analysis of results from three countries”, *Journal of Gerontology: Psychological Sciences*, 56B(3):P141–P151.

Hayflick, L. (1981) “Prospects for human life extension by genetic manipulation”. In: Danon, D., Shock, N. W., Marois, M. (eds.), *Aging: A Challenge to Science and Society*, Vol. I. Oxford: Oxford University Press, pp. 162–179.

Hayflick, L. (1996) *How and Why we Age?* New York: Ballantine Books.

Hayflick, L. (2002) “Anarchy in gerontological terminology”, *The Gerontologist*, 42(3):416–421.

Heiniger, M., and Wanders, A.C. (2002) *Portrait démographique de la Suisse*. Berne: Office fédéral de la statistique.

Helle, S., Lummaa, V., and Jokela, J. (2002) “Sons reduced maternal longevity in preindustrial humans”, *Science*, 296:1085.

Herskind, A. M., McGue, M. J., Holm, N. W., Sorense, T. I., Harvale, B., and Vaupel, J. W. (1996) “The heritability of Human Longevity: A population-based study of 2872 Danish Twin Pairs born 1870–1900”, *Human Genetics*, 97:319–323.

Hill, G. B., (1993) “The entropy of the survival curve: An alternative measure”, *Canadian Studies in Population* 20(1): 43–57.

Hill, M. E., Preston, S. H., and Rosenwaike, I. (2000) “Age reporting among white American aged 85 +: Results of a record linkage study”, *Demography*, 37(2):175–186.

Hitt, R., Young-Xu, Y., Silver, M., and Perls, T. (1999) “Centenarians: The older you get, the healthier you have been”, *The Lancet*, 353:652.

Hong Kong Census and Statistic Department. (2002) *Hong Kong Life Tables 1996–2031*. Hong Kong Government Printer.

Horiuchi, S. (1991) “Assessing effects of mortality reduction on population aging”, *Population Bulletin of the United Nations*, 31:38–51.

Horiuchi, S. (1997) “Postmenopausal acceleration of age-related mortality increase”, *Journal of Gerontology*, 52A(1):B78–B92.

Horiuchi, S. (2000) “Greater lifetime expectations”, *Nature*, 405:744–745.

Horiuchi, S. (2003) “Interspecies differences in the life span distribution: Humans versus invertebrates”. In: Carey, J. R., Shripad, T. (eds.), *Population and Development Review*, Vol. 29, pp. 127–151.

Horiuchi, S. (2005) “Causes of death among the oldest-old: Age-related changes in the causes-of-death distribution”. In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Horiuchi, S., and Wilmoth, J. R. (1997) “Age patterns of the life table aging rate for major causes of death in Japan, 1951–1990”, *Journal of Gerontology*, 52A(1):B67–B77.

Horiuchi, S., and Wilmoth, J. R. (1998) “Deceleration in the age pattern of mortality at older ages”, *Demography*, 35(4):391–412.

Hu, P., Reuben, D. B., Crimmins, E. M., Harris, T. B., Huang M-H., and Seeman, T. E. (2004) "The effect of serum Beta-Carotene concentration and burden of inflammation on all-cause mortality risk in hight-functioning older persons: Mac Arthur studies of successful aging", *Journal of Gerontology: Medical Sciences*, 59A(8):849–854.

Hubert, H. B., Bloch, D. A., Oehlert, J. W., and Fries, J. F. (2002) "Lifestyle habits and compression of morbidity", *Journal of Gerontology*, 57A(6):M347–M351.

Human Mortality Database. University of California, Berkeley (USA), and Max Planck Institute for Demographic Research (Germany). Available at www.mortality.org or www.humanmortality.de (data downloaded on November 2004).

Hyland, P., Duggan, O., and Turbitt, J. (2002) "Nonagenarians from the Swedish NONA immune study have increased plasma antioxidant capacity and similar levels of DNA damage in perpherical blood mononuclear cells compared to tounger control subjects", *Experimental Gerontology*, 37:465–473.

International Database on Longevity. Max Planck Institute for Demographic Research (Germany). Available at www.demogr.mpg.de/general/structure/division1/lab-sl/90.htm

Ivanova, R., Hénon, N., Lepage, V., *et al*. (1998) "HLA-DR alleles display sex-dependent effects on survival and discriminate between individual and familial longevity", *Human Molecular Genetics*, 7:187–194.

Jacquard, A. (1982) "Heritability of human longevity". In: Preston, S. V. (ed.) *Biological and Social Aspects of Mortality and the Length of Life*. Liège: Ordina Edition, pp. 303–313.

Jansen, F., Nusselder, W. J., Looman, C. W. N., Mackenbach, J. P., and Kunst, A. E. (2003) "Stagnation in mortality decline among elders in the Netherlands", *The Gerontologist*, 43(5):722–734.

Jazwinski, S. M. (1996) "Longevity, genes and aging", *Science*, 273:54–59.

Jeune, B. (1995) "In search of the first centenarians". In: Jeune, B., Vaupel, J. W. (eds.), *Exceptional Longevity: From Prehistory to the Present*. Odense: Odense University Press. (Odense Monographs on population Aging 2).

Jeune, B. (2005) "Explanation of the decline in mortality among the oldest-old: A medical point of view". In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Jeune, B., and Skytthe, A. (2001) "Centenarians in Denmark in the past and the present", *Population*, 13(1):75–94.

Jeune, B., and Vaupel, J. W. (1999). *Validation of Exceptional Longevity*. Odense: Odense University Press.

Jylha, M., and Luukkaala, T. (2005) "Social determinants of mortality in the oldest-old: Social class and the individual way of life". In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Kaeberlein, M., Jegalian, B., and McVey, M. (2002) "AGEID: A database of aging genes and interventions", *Mechanisms of Aging and Development*, 123:1115–1119.

Kannisto, V. (1988) "On the survival of centenarians and the span of life", *Population Studies*, 42:389–406.

Kannisto, V. (1991) "Frailty and survival", *Genus*, 47(3–4):101–118.

Kannisto, V. (1994) *Development of Oldest-Old Mortality, 1950–1990: Evidence from 28 Developed Countries*. (Odense Monographs on Population Aging 1) Odense: Odense University Press.

Kannisto, V. (1996). *The Advancing Frontier of Survival*. Odense: Odense University Press.

Kannisto, V. (1999) *Measuring the Compression of Mortality*. Paper distributed at European Population Conference, EAPS, IUSSP, NIDI, SN, NVD.

Kannisto, V. (2000a). *Central and Dispersion Indicators of Individual Life Duration*: New Methods. International Union for the Scientific Study of Population, Seminar on Human Longevity, Individual Life Durations and Growth of the Oldest-Old, Montpellier, 23–26 October.

Kannisto, V. (2000b) "Measuring the Compression of Mortality", *Demographic Research* 3 (Article 6). http://www.demographic-research.org/Volumes/Vol3/6/

Kannisto, V. (2001) "Mode and dispersion of the length of life", *Population*, 13(1):159–171.

Kannisto, V. (2005) "Central and dispersion indicators of individual life duration: New methods". In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Kannisto, V., Christensen, K., and Vaupel, J. W. (1997) "No increased mortality in later life for cohorts born during famine", *The American Journal of Epidemiology*, 145(11):987–994.

Kannisto, V., Lauristen, J., Thatcher, A. R., *et al*. (1994) "Reductions in mortality at advanced ages: Several decades of evidence from 27 countries", *Population and Development Review*, 20:793–809.

Kerber, R. A., O'Brien, E., and Smith, K. R. (2001) "Familial excess longevity in Utah genealogies", *Journal of Gerontology*: *Biomedical Science*s, 56A(3)B130–B139.

Kestenbaum, B. M., and Fergusson, B. R. (2002) "Mortality of the extreme aged in the United States in the 1990s. Based on improved Medicare data". *North American Actuarial Journal*, 6(3):38–44.

Kirkwood, T. B. L. (1997) "Genetics and the future of human longevity", *Journal of the Royal College of Physicians of London*, 31(6):669–673.

Kirkwood, T. B. L., and Rose, M. R. (1991) "Evolution of senescence: Late survival sacrificed for reproduction", *Philosophical Transactions of the Royal Society of London B*, 332:15–24.

Kjoergaard, T. (1995) "Alleged Danish centenarians before 1800". In: Jeune, B., Vaupel, J. W. (eds), *Exceptional longevity: From Prehistory to the Present*, Odense: Odense University Press. pp. 47–54.

Koenig, R. (2001) "Sardinia's mysterious male Methuselahs", *Science*, 291(16):2074–2076.

Kohn, R. R. (1982) "Cause of death in very old people", *Journal of the American Medical Association*, 247:2793–2797.

Kojima, T., Hidehiko, K., Aizu, T., Aria, Y., Takayama, M., Nakazawa, S., Ebihara, Y., Inagaki, H., Masui, Y., Gondo, Y., Sakaki, Y., and Hirose, N. (2004) "Association analysis between longevity in the Japanese population and polymorphic variants of genes involved in insulin and insulin-like growth factor 1 signaling pathways", *Experimental Gerontology*, 39:1595–1598.

Kokaze, A., Ishikawa, M., Matsunaga, N., Yoshida, M., Sekine, Y., Sekiguchi, K., Satoh, M., Harada, M., Teruya, K., Takeda, N., Uchida, Y., Tsunoda, T., and Takashima, Y. (2003) "Longevity-associated mitochondrial DNA 5178 A/C polymorphism modulates effects of daily drinking and cigarette consumption on serum triglyceride levels in middle-aged Japanese men", *Experimental Gerontology*, 38:1071–1076.

Krach, C. A., and Velkoff, V. A. (1999) *Centenarians in the United States*. Washington, DC: US Department of Health and Human Services (Current Populations Reports, Special Studies).

Kliegel, M., Moor, C., and Rott, C. (2004) "Cognitive status and development in the oldest old: A longitudinal analysis from the Heildelberg centenarain study", *Archives of Gerontology and Geriatrics*, 39:143–156.

Labat-Robert, J., Marques, M. A., and N'Doye, S. (2000) "Plasma fibronectine in French centenarians", *Archives of Gerontology and Geriatrics*, 31:95–105.

Laplace, P. S. (1812) *Théorie Analytique des Probabilités*. Paris: Veuve Courcier.

Le Bourg, E., Thon, B., Légaré, J., Desjardins, B., and Charbonneau, H. (1993) "Reproductive life of French-Canadians in the 17–18th centuries: A search for a trade-off between early fecundity and longevity", *Experimental Gerontology*, 28:217–232.

Leslie, M. (2003) "Rising expectations", *Science of Aging Knowledge Environment*, 47:ns 7.

Levasseur, E. (1891) *La population francaise,* Tome II, Paris: Arthur Rousseau Editeur, pp. 143–184 (Chapter 13).

Levy, M. L. (1996) "La rectangularization de la courbe des survivants". In: AIDELF (ed.) *Morbidité, Mortalité: Problèmes de Mesure, Facteurs d'évolution, Essai de Prospective*. Paris: PUF, pp. 576–579.

Lexis, W. (1878) "Sur la Durée Normale de la Vie Humaine et sur la Théorie de la Stabilité des Rapports Statistiques", *Annales de Démographie Internationale*, 2(5):447–460.

Lio, D., Pes, G. M., Carru, C., *et al*. (2003) "Association between the HLA-DR alleles and longevity: A study in Sardinian population", *Experimental Gerontology*, 38:313–317.

Ljungquist, B., Berg, S., Lanke, J., McClean, G., and Pedersen, N. L. (1998). "The effect of genetic factors for longevity: A comparaison of identical and fraternal twins in the Swedish Twin Registry", *Journal of Gerontology: Series A Biological Science and Medical Science*, 53A:M441–M446.

Lloyd-Jones, D. M., Martin, D. O., Larson, M. G., *et al*. (1998) "Accuracy of death certificates for coding coronary heart disease as the cause of death", *Annals of Internal Medicine*, 129:1020–1026.

Longo, V. D., and Finch, C. (2003) "Evolutionary medicine: From dwarf model systems to healthy centenarians?", *Science*, 209:1342–1346.

Louhija, J., Miettinen, H. E., Kontula, K., *et al*. (1994) "Ageing and genetic variation of plasma apolipoproteins. Relative loss of apolipoprotein E4 phenotype in centenarians", *Journal of Artherosclerosis and Thrombosis*, 14:1084–1089.

Ly, D. H., Lockhart, D. J., Lerner, R. A., *et al*. (2000) "Mitotic misregulation and human aging", *Science*, 287:2486–2492.

Lynch, S. M., and Brown, J. C. (2001) "Reconsidering mortality compression and deceleration: An alternative model of mortality rates", *Demography*, 38:79–95.

Magwere, T., Chapman, T., and Partridge, L. (2004) "Sex differences in the effect of dietary restriction on life span and mortality rates in female and male Drosophila Melanogaster", *Journal of Gerontology: Biological Sciences*, 59A(1):3–9.

Manton, K. G. (1991) "New biotechnologies and the limits to life expectancy". In: Lutz, W. (ed.), *Future demographic trends in Europe and North America*. New York: Academic Press, pp. 97–115.

Manton, K. G. (1999) "Dynamic paradigms for human mortality and aging", *Journal of Gerontology: Biological Sciences*, 54A(6):B247–B254.

Manton, K. G., and Singer, B. (1994) "What's the fuss about the compression of mortality?", *Chance*, 7:21–30.

Manton, K. G., and Stallard, E. (1996) "Longevity in the United States: Age and sex-specific evidence on life span limits from mortality patterns 1960–1990", *Journal of Gerontology: Biological Sciences*, 51A(5):B362–B375.

Manton, K. G., and Tolley, H. D. (1991) "Rectangularization of the survival curve implications of an ill-posed question", *Journal of Aging and Health*, 3(2):172–193.

Manton, K. G., and Vaupel, J. W. (1995) "Survival after the Age of 80 in the United States, Sweden, France, England, and Japan", *New England Journal of Medicine*, 333:1232–1235.

Manton, K. G., Stallard, E., and Corder, L. (1999) "The limits og longevity and their implications for heath and mortality in developed countries". In: *Health and Mortality: Issues of Global Concern*. New York: United Nations, pp. 324–343 (Chapter XIV).

Marini, M., Lapalombella, R., Canaider, S., Farina, A., Monti, D., De Vescovi, V., Morellini, M., Bellizi, D., Dato, S., De Benedictis, G., Passarino, G., Moresi, R., Tesei, S., and Franceschi, C. (2004) "Heat shock response by EBV-immortalized B-lymphocytes from centenarians and control subjects: A model to study the relevance of stress response in longevity", *Experimental Gerontology*, 39:83–90.

Martel, S., and Bourbeau, R. (2003) "Compression de la Mortalité et Rectangularisation de la Courbe de Survie au Québec au Cours du XX^{e} Siècle", *Cahiers Québécois de Démographie*, 32(1):43–75.

Martin, G. M. (1999) "Genes that modulate longevity and senescence", In: Robine, J-M., *et al*. (eds.), *The Paradoxes of Longevity*. Berlin: Springer, pp. 11–21.

Masternak, M. M., Al-Regaiey, K., Bonkowski, M. S., Panici, J., Sun, L., Wang, J., Przybylski, G. K., and Bartke, A. (2004) "Divergent effects of caloric restriction on gene expression in normal and long-lived mice", *Journal of Gerontology: Biological Sciences*, 59A(8):784–788.

Matthijs, K., Van de Putte, B., and Vlietinck, R. (2002) "The inheritance of longevity in a Flemish village (18th–20th Century)", *European Journal of Population*, 18:59–81.

Mattison, J. A., Lane, M. A., Roth, G. S., and Ingram, D. K. (2003) "Calorie restriction in rhesus monkeys", *Experimental Gerontology*, 38:35–46.

Mazess, R. B., and Forman, S. H. (1979) "Longevity and age exageration in Vilcabamba, Ecuador", *Journal of Gerontology*, 34(1):94–98.

McCormack, J. (2001) "The emerging face of centenarians in Australia", Gerontology, 47(suppl 1):533–534.

McGue, M. J., Vaupel, J. W., Holm, N., and Harvald, B. (1993) "Longevity is moderately heritable in a sample of danish twins born 1870–1880", *Journal of Gerontology*, 48:B237–B244.

McKeown, T. (1976) *The modern rise of population.* London: Edward Arnold.

McKeown, T. (1979) *The Role of Medicine: Dream, Mirage, or Nemesis*. Princeton: Princeton University Press.

Mecocci, P., Polidori, M. C., Troiano, L., *et al*. (2000) "Plasma antioxidants and longevity: A study on healthy centenarians", *Free Radical Biology and Medicine*, 28(8):1243–1248.

Meroni, P. L., Mari, D., Monti, D., Coppola, R., Capri, M., Salvioli, S., Tincani, A., Gerli, R., and Franceschi, C. (2004) "Anti-beta 2 glycoprotein I antibodies in centenarians", *Experimental Gerontology*, 39:1459–1465.

Meslé, F. (2005) "Causes of death among the oldest-old: Validity and comparability". In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Meslé, F., and Vallin, J. (2000a) *Comment améliorer la précision des tables de mortalité aux grands âges: le cas de la France?*—Paris, INED, p. 26. (Communication présentée au Colloque de l'AIDELF "Vivre plus longtemps, avoir moins d'enfants, quelles implications ?", Byblos, Liban).

Meslé, F., and Vallin, J. (2000b) "Transition sanitaire: Tendances et perspectives", *Médecine/Science*, 16:1161–1171.

Meslé, F., and Vallin, J. (2002) "Increase in life expectancy and Concentration of ages at death", In: Robine, J-M., *et al*. (eds.) *Determining Health Expectancies*. Chichester: John Wiley & sons, pp. 13–33.

Meslé, F., Vallin, J., and Robine, J-M. (2000) "Vivre plus de 110 ans en France", *Gérontologie et Société*, 94:101–120.

Miller, R. A. (2001) “A position paper on longevity genes”, *Sageke.sciencemag*.org 9/vp6.

Ministry of Health and Welfare. (1963–2003) *Zenkoku koureisha meibo* (A list of centenarians in Japan).

Ministry of Health and Welfare (2003) *Life tables for Japan 2002*. Statistics and information department, Minister’s Secretariat, Ministry of Health, Labor and Welfare.

Morel, M. F. (1991) “The care of children: The influence of medical innovation and medical institutions on infant mortality 1750–1914”. In: Schofield, R., Reher, D., Bideau, A. (eds.), *The Decline of Mortality in Europe*. Oxford: Clarendon Press, pp. 196–219.

Mosley, W. H., and Chen, L. C. (1984) “An analytical framework for the study of child survival in developing countries”. In: Mosley, W. H., Chen, L. C. (eds.), *Child Survival: Strategies for Research (Population and Development Review, A Supplement to Volume 10)*, New York: The Population Council, pp. 25–45.

Mûller, H-G., Chiou, J. M., Carey, J. R., *et al*. (2002) “Fertility and life span: Late children enhance female longevity”, *Journal of Gerontology*: *Biomedical Sciences*, 57A(3):B202–B206.

Myers, G., and Lamb, V. (1993) “Theoretical perspectives on healthy life expectancy”. In: Robine, J-M., Mathers, C. D., Bone, M. R., Romieu, I. (eds.), *Calculation of Health Expectancies; Harmonization, Consensus Achieved and Future Perspectives*. Montrouge: John Libbey Eurotext, pp. 109–119.

Myers, G. C., and Manton, K. G. (1984a) “Compression of mortality: Myth or reality?”, *The Gerontologist*, 24(4): 346–353.

Myers, G. C., and Manton, K. G. (1984b) “Recent changes in the U.S. age at death distribution: Further observations”, *The Gerontologist*, 24(6):572–575.

Myers, G. C., Lamb, V. L., and Agree, E. M. (2002) “Patterns of disability change associated with the epidemiological transition”. In: Robine, J-M., *et al*. (eds.) *Determining health expectancies*. Chichester: John Wiley & sons. pp. 59–74.

Myers, J. C. (1996) “Comparative mortality trends among older persons in developed countries”, In: Caselli, G., Lopez, A. D. (eds.), *Health and Mortality among Elderly Populations*. Oxford, UK: Clarendon Press, pp. 87–111.

Myers, R. J. (1966) “Validity of centenarian data in the 1960 census”, *Demography*, 3:470–476.

Myers, R. J., and Shudde, L. O. (1955) “Mortality experience of Union civil war veterans”, *Transactions of Society of Actuaries*, 7:63–68.

Nagnur, D., (1986) “Rectangularization of the survival curve and entropy: The Canadian experience 1921–1981”, *Canadian Studies in Population*, 13:83–102.

Nusselder, W. (1998) *Compression or Expansion of Morbidity ? A Life-table Approach*. Thesis, Erasmus University Rotterdam. Amsterdam: Thesis Publishers.

Nusselder, W. (2005) “Recent trends in life expectancy and rectangularisation of the survival curve at advanced ages in the Netherlands”. In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Nusselder, W. J., and Mackenbach, J. P. (1996) “The rectangularization of the survival curve in Netherlands, 1950–1992”, *Gerontologist*, 36:773–782.

Nusselder, W. J., and Mackenbach, J. P. (1997) “Rectangularization of the survival curve in the Netherlands: An analysis of underlying causes of death”, *Journal of Gerontology: Social Sciences*, 52B(3):S145–S154.

Nusselder, W. J., and Mackenbach, J. P. (2000) “Lack of improvement of life expectancy at advanced ages in the Netherlands”, *International Journal of Epidemiology*, 29:140–148

Nusselder, W. J., Looman, C. W. N., Marang Van De Mheen, P. J., *et al*. (2000) “Smoking elimination produces compression of morbidity”, *Journal of Epidemiology and Community Health*, 54:566–574.

Oeppen, J., and Vaupel, J. W. (2002) "Broken limits to life expectancy", *Science*, 296:1029–1031.

Olshansky, S. J., and Ault, A. B. (1986) "The fourth stage of the epidemiologic transition: The age of delayed degenerative diseases", *Milbank Quarterly*, 64(3):355–391.

Olshansky, S. J., and Carnes, B. A. (1994) "Demographic perspectives on human senescence", *Population and Development Review*, 20:57–80.

Olshansky, S. J., and Carnes, B. A. (1997) "Ever since Gompertz", *Demography*, 34(1):1–15.

Olshansky, S. J., and Carnes, B. A. (2002) "A biodemographic interpretation of life span", *Population and Development Review*, 28(3): 501–513.

Olshansky, S. J., Carnes, B. A., and Cassel, C. (1990) "In search of Methuselah: Estimating the upper limits to human longevity", *Science*, 250:634–640.

Olshansky, S. J., Carnes, B. A., and Butler, R. (2001b) "If humans were built to last", *Scientific American*, 284(3):50–55.

Olshansky, S. J., Carnes, B. A., and Désesquelles, A. (2001a) "Prospects for human longevity", *Science*, 291:1491–1492.

Olshansky, S. J., Rudberg, M. A., Carnes, B. A., *et al*. (1991) "Trading off longer life for worsening health. The expansion of morbidity hypothesis", *Journal of Aging and Health*, 3(2):194–216.

Omran, A. R. (1971) "The epidemiologic transition: A theory of Epidemiology of population change", *The Milbank Memorial Fund Quarterly*, 49:509–538.

Paccaud, F., Sidoti Pinto, C., Marazzi, A., and Mili, J. (1998) "Age at death and rectangularization of the survival curve: Trends in Switzerland, 1969–1994", *Journal of Epidemiology and Community Health*, 52:412–415.

Palacios, R. (2002) "The future of global ageing", *International Journal of Epidemiology*, 31:786–791.

Palmore, E. B. (1984) "Longevity in Abkhazia: A reevaluation", *The Gerontologist*, 24(1):95–96.

Palmore, E. B. (1987) "Some errors and irrelevancies in the debate over compression of morbidity", *Gerontologica Perspecta*, 1:30–31.

Paolisso, G., Manzella, D., Barbieri, M., *et al*. (1999b) "Baseline heart rate variability in healthy centenarians: Differences compared with aged subjects (>75 years old)", *Clinical Science*, 97:579–584.

Paolisso, G., Manzella, D., Rizzo, M. R., *et al*. (2000) "Effect s of glucose ingestion on cardiac autonomic nervous system in healthy centenarians", *European Journal of Clinical Investigation*, 30:277–284.

Paolisso, G., Tagliamonte, M. R., Rizzo, M. R., *et al*. (1999a) "Mean arterial blood pressure and serum levels on the molar ratio of insulin-likes growth factor-1 to its binding proteine-3 in healthy centenarians", *Journal of Hypertension*, 17:67–73.

Pearl, R. (1931) "Studies on human longevity. IV. The inheritance of longevity. Preliminary report", *Human Biology*, 3:245–269.

Pearl, R., and Doering, C. R. (1923) "A comparison of the mortality of certain lower organisms with that of man", *Science*, 1468:209–212.

Pearl, R., and Miner, J. R. (1935) "Experimental studies on the duration of life. XIV the comparative mortality of certain lower organisms", *The Quarterly Review of Biology*, 10:60–79.

Pearson, K. (1902) "On the modal value of an organ or character", *Biometrika*, 1(2):260–261.

Pelletier, F., Legare, J., and Bourbeau, R. (1997) "Mortality in Quebec during the nineteenth century: From the state to the cities", *Population Studies*, 51:93–103.

Perks, W. (1932) "On some experiments on the graduation of mortality statistics", *Journal of the Institute of Actuaries*, 63:12–40.

Perls, T. (2001) "Genetic and phenotypic markers among centenarians", *Journal of Gerontology*: *Medical Sciences*, 56A(2):M67–M70.

Perls, T. (2003) "Genetics of exceptional longevity", *Experimental Gerontology*, 38:725–730.

Perls, T. (2004) "Dementia-free centenarians", *Experimental Gerontology*, 39:1587–1593.

Perls, T., Kunkel, L., and Puca, A. (2002) "The genetics of exceptional human longevity", *Journal of the American Geriatrics Society*, 50:359–368.

Perls, T., Terry, D. F., Silver, M., *et al*. (2000) "Centenarians and the genetics of longevity", *Results and Problems in Cell Differentiations*, 29:1–20.

Perls, T., Wilmoth, J., Levenson, R., *et al*. (2002) "Life-long sustained mortality advantage of siblings of centenarians", *Proceedings of the National Academy of Sciences of the United States of America*, 99(12):8442–8447.

Perls, T. T., Bubrick, E., Wager, C. G., Vijg, J., and Kruglyak, L. (1998a). "Siblings of centenarians live longer", *Lancet*, 351:1560.

Perls, T. T., Alpert, L., and Fretts, R. C. (1998b) "Middle-aged mothers live longer", *Nature*, 389:133 (Scientific correspondence).

Perls, T. T., Bochen, K., Freeman, N., *et al*. (1999) "Validity of reported age and centenarian prevalence in a New England sample", *Age and Ageing*, 28:193–197.

Perozzo, L. (1879) "Distribuzione dei morti per eta", *Annali di Statistica*, 2nd series, 5:75–93.

Philippe, P. (1980) "Longevity: Some familial correlates", *Social Biology*, 27(3):211–219.

Phillips, W. (1935) "A basic curve of death", *Journal of the Institute of Actuaries*, 80:S289–S325.

Poulain, M., Chambre, D., and Foulon, M. (2001) "Survival among Belgian centenarians (1870–1894 cohorts)", *Population*, 13:117–38.

Poulain, M., Pes, G. M., Grasland, C., Carru, C., Ferrucci, L., Baggio, G., Franceschi, C., and Deiana, L. (2004) "Identification of a geographic area characterized by extreme longevity in the Sardinia island: The AKEA study", *Experimental Gerontology*, 39:1423–1429.

Poulain, M., Pes, G., Carru, C., Ferrucci, L., Baggio, G., Franceschi, C., and Deiana, L. (2005) "The validation of exceptional male longevity in Sardinia". In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Preston, S. H. (1975) "The changing relation between mortality and level of economic development", *Population Studies*, 29:231–48.

Preston, S. H. (1992) "Cohort succession and the future of the oldest old". In: Suzman, R. M., Willis, D. P., Manton, K. G. (eds.), *The Oldest-Old*. Oxford: Oxford University Press, pp. 50–57.

Preston, S. H., Elo, I. T., and Stewart, Q. (1999) "Effects of age misreporting on mortality estimates at older ages", *Population Studies*, 53:165–177.

Promislow, D. E. L. (1998) "Longevity and the barren aristocrat", *Nature*, 396:719–720.

Puca, A. A., Daly, M. J., Brewster, S. J., Matisse, T. C., Barret, J., Shea-Drinkwater, M., Kang, S., Joyce, E., Nicoli, J., Benson, E., Kunkel, L. M., and Perls, T. (2001) "A genome-wide scan for linkage to human exceptional longevity identifies a locus on chromosome 4", *Proceedings of the National Academy of Sciences of the United States of America*, 98(18):10505–10508.

Quetelet, A. (1835) *Sur l'homme et le développement de ses facultés, essai d'une physique sociale*. Pairs: Bachelier; reprint paris: Fayard, 1991.

Quetelet, A. (1848) *Du systéme social et des lois qui le régissent.* Pairs: Guillaumin, Book 1.

Quetelet, A. (1871) *Anthropométrie ou mesure des différentes facultés de l'homme*. Brussels: Muquardt.

Rabini, R. A., Moretti, N., and Staffolani, R. (2002) "Reduced susceptibility to peroxidation of erythrocyte plasma membranes from centenarians", *Experimental Gerontology*, 37:457–663.

Reed, T., Carmelli, D., Robinson, T. S., *et al*. (2003) "More favourable midlife cardiovascular risk factor levels in male twins and mortality after 25 years of follow-up is related to longevity of their parents", *Journal of Gerontology*: *Medical Sciences*, 58A(5):425–431.

Riley, J. C. (1990) "The risk of being sick: Morbidity trends in four countries", *Population and Development Review*, 16(3):403–432.

Riley, J. C. (2001) *Rising Life Expectancy: A Global History*. Cambridge: Cambridge University Press.

Ritchie, K. (1995) "Mental status examination of an exceptional case of longevity J.C. aged 118 years", *British Journal of Psychiatry*, 166:229–235.

Robine, J.-M. (2001) "A new biodemographic model to explain the trajectory of mortality", *Experimental Gerontology*, 36,899–914.

Robine, J.-M. (2001) "Redefining the stages of the epidemiological transition by a study of the dispersion of life spans: The case of France", *Population*", 13(1):173–194.

Robine, J.-M. (2003) "Life course, environmental change, and life span", *Population and Development Review*, 29:229–38.

Robine, J.-M., and Allard, M. (1998) "The oldest human", *Science*, 279:1834–1835.

Robine, J.-M., and Allard, M. (1999) "Jeanne Calment: Validation of the duration of her life". In: Jeune, B., Vaupel, J. W. (eds.) *Validation of Exceptional Longevity*. (Odense Monographs on Population Aging 6) Odense: Odense University Press, pp. 145–172.

Robine, J.-M., Cournil, A., Henon, N., and Allard, M. (2003d) "Have centenarians had parents younger than the others", *Experimental Gerontology*, 38:361–365.

Robine, J.-M., and Jagger, C. (2002) "What do we know about the cognitive status of centenarians", In: Finch, C., Robine, J.-M., Christen, Y. (eds.), *Brain and Longevity*. Berlin: Springer, pp. 145–152.

Robine, J.-M., Jagger, C., Mathers, C. D., Crimmins, E. M., and Suzman, R. M. (2003c) *Determining health expectancies*. Chichester: Willey.

Robine, J.-M., and Michel, J. P. (2004) "Looking forward for a general theory on population aging", *Journal of Gerontology*: *Medical Sciences*, 59A(6):590–597.

Robine, J.-M., Paccaud, F. (2005) "Nonagenarians and centenarians in Switzerland, 1860–2001: A demographic analysis", *Journal of Epidemiology and Community Health*, 59:31–37.

Robine, J.-M., Romieu, I., and Allard, M. (2003b) "Les centenaires français et leur état de santé fonctionnelle", *La Presse Médicale*, 33:360–364.

Robine, J.-M., and Saito, Y. (2003) "Survival beyond age 100: The case of Japan", *Population and Development Review*, 29:208–28.

Robine, J.-M., Saito, Y., and Jagger, C. (2003a) "The emergence of extremely old people: The case of Japan", *Experimental Gerontology*, 38:735–739.

Robine, J.-M., and Vaupel, J. W. (2001) "Supercentenarians: Slower ageing individuals or senile elderly?", *Experimental Gerontology*, 36:915–930.

Robine, J.-M., and Vaupel, J. W. (2002) "Emergence of supercentenarians in low-mortality countries", *North American Actuarial Journal*, 6(3):54–63.

Robine, J.-M.,Caselli, G., *et al*. (2005). "An unprecedented increase in the number of centenarians", *Genus*, LXl(1):57–82.

Rose, G., Dato, S., Altomare, K., *et al*. (2003) "Variability of the SIRT3 gene, human silent information regulator Sir2 homologue, and survivorship in elderly", *Experimental Gerontology*, 38:1065–1070.

Rosenwaike, I., and Stone, L. F. (2003) "Verification of the ages of supercentenarians in the United States: Results of a matching study", *Demography*, 40(4):727–739.

Rothenberg, R., Lentzner, H. R., and Parker, R. A. (1991) "Population aging patterns: The expansion of mortality", *Journal of Gerontology*, 46:S66–S70.

Samuelsson, G., and Johnson, A. M. (2001) "Centenarians in France, Georgia, Hungary and Sweden: Social characteristics", *Indian Journal of Gerontology*, 15(1–2):29–52.

Savarino, L., Grandi, D., Ciapetti, G., *et al*. (2001) "Serum concentrations of zinc and selenium in elderly: Results in healthy nonagenarians and centenarians", *Experimental Gerontology*, 36:327–339.

Schächter, F., Faure-Delanef, L., Guenot, F., et al. (1994) "Genetic association with human longevity at APOE and ACE loci", *Nature Genetics*, 6:29–32.

Schneider, E. R. L., and Brody, J. A. (1983) "Aging, natural death, and the compression of morbidity: Another view", *The New England Journal of Medicine*, 304(14):854–855.

Silver, M. H., Jilinskaia, E., and Perls, T. T. (2001) "Cognitive functional status of age-confirmed centenarians in a population-based study", *Journal of Gerontology: Psychosocial Sciences*, 56B(3):P134–P140.

Simar, D., Malatesta, D., Koechlin, C., Cristol, J. P., Vendrell, J. P., and Caillaud, C. (2004) "Effect of age on Hsp72 expression in leucocytes of healthy active people", *Experimental Gerontology*, 39:1467–1474.

Silverman, J. M., Smith, C. J., and Marin, D. B. (1999) "Identijying families with likely protective factors against Alzheimer disease", *American Journal of Human Genetics*, 64:832–838.

Skytthe, A., and Jeune, B. (1995) "Danish centenarians after 1800". In: Jeune, B., Vaupel, J. W. (eds.), *Exceptional longevity: From Prehistory to the Present*. Odense: Odense University Press (Monographs on population Aging 2).

Smith, D. W. E. (1993) *Human Longevity*. New York, NY: Oxford University Press.

Smith, D. W. E. (1994) "The tails of survival curves", *BioEssays*, 16(12):907–911.

Smith, D. W. E. (1997) "Centenarians: Human longevity outliers", The *Gerontologist*, 37(2):200–207.

Strehler, B. L. (1975) "Implications of aging research for society". In: *Theoretical Concepts of Developmental and Age Changes*. *Federation Proceedings*, 34(1):5–8.

Takata, H., Suzuki, M., Ishii, T., *et al*. (1987) "Influence of major histocompatibility complex region genes on human longevity among Okinawan-Japanese centenarians and nonagenarians", *The Lancet*, 10:824–826.

Takuto, K., Izumiyama-Shimomura, Honma, N., *et al*. (2002) "Telomere lengths are characteristic in each human individual", *Experimental Gerontology*, 37:523–531.

Tan, Q., Yashin, A. I., Bladbjerg, E. M., *et al*. (2002) "A case-only approach for assessing gene by sex interaction in Human longevity", *Journal of Gerontology*: *Biological Sciences*, 57A(4):B129–B133.

Tanaka, M., Gong, J. S., Zhang, J., *et al*. (1998) "Mitochondrial genotype associated with longevity", *Lancet*, 351:185–186 (Research letter).

Tauchi, H., Sato, T., and Watanabe, T. (1999) *Japanese Centenarians. Institute for Medical Science of Aging*, Aichi: Aichi Medical University.

Terry, D. F., Wilcox, M., MCCormick, M. A., *et al*. (2003) "Cardiovascular advantages among the offspring of centenarians", *Journal of Gerontology*: *Medical Sciences*, 58A(4):367–371.

Terry, D. F., Wilcox, M., MCCormick, M. A., *et al*. (2004) "Cardiovascular delay in centenarian offspring", *Journal of Gerontology*: *Medical Sciences*, 59A(4):385–389.

Thatcher, A. R. (1992) "Trends in numbers and mortality at high ages in England and Wales", *Population Studies*, 46:411–426.

Thatcher, R. (1997) "Trends and prospects at very high ages". In: Charlton, J., Murphy, M. (eds.), *The Health of Adult Britain 1841–1994*. London: The Stationery Office (Vol 1 and 2).

Thatcher, A. R. (1999a) "The demography of centenarians in England and Wales", *Population Trends*, 162 (Part1):5–43.

Thatcher, A. R. (1999b). "The long-term pattern of adult mortality and the highest attained age", *Journal of the Royal Statistical Society Series A*, A 162, 5–43.

Thatcher, A. R. (1999c) "Katherine Plunket: A well documented supercentenarian in 1930". In: Jeune, B., Vaupel, J. W. (eds.), *Validation of Exceptional Longevity*. Odense: Odense University Press, pp. 135–138.

Thatcher, A. R. (2001) "The demography of centenarians in England and Wales", *Population*, 13:139–156.

Thatcher, A. R., Kannisto, V., and Vaupel, J. W. (1998) *The Force of Mortality at Ages 80 to 120*. Odense: Odense University Press.

Thatcher, R. V., Kannisto, V., and Andreev, K. (2002). "The survivor ratio method for estimating numbers at high ages", *Demographic Research*, 6(1):1–12. (Available online at www.demographic-research.org).

Thiele, T. N. (1871) "On a mathematical formula to express the rate of mortality throughout the whole of life, tested by a series of observations made use of by the Danish life insurance company of 1871", *Journal of the Institute of Actuaries and Assurance Magazine*, XVI:S313–S329.

Thoms, W. J. (1873) *Human longevity*. London: John Murray.

Tuljapurkar, S., Li, N., and Boe, C. (2000) "A universal pattern of mortality decline in the G7 countries", *Nature*, 405:789–792.

Tyner, S. D., Venkatachalam, S., Chol, J. *et al*. (2002) "p53 mutant mice that display early ageing-associated phenotypes", *Nature*, 415(3):45–53.

Vallin, J. (1992) "Quelles hypothèses peut-on faire sur l'évolution future de la mortalité". In: Tapinos, G. (ed.), *La France dans deux générations: Population et société dans le premier tiers du XXI ième siècle*. Paris: Arthème Fayard.

Vallin, J. (1993) "Future of health expectancy". In: Robine, J-M., *et al*. (eds.), *Calculation of Health Expectancies, Harmonization, Consensus Achieved and Future Perspectives*. Montrouge: John Libbey.

Vallin, J. (2005) "Mortality differences by sex among the oldest-old". In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Vallin, J., and Berlinguer, G. (2002). "De la mortalité endogène aux limities de la vie". In: *Démographie: analyse et synthèse III. Les déterminants de la mortalité*. (Chapter 48).

Vallin, J., and Caselli, G. (1997) "Toward a new horizon in demographic trends: The combined effects of 150 years life expectancy and new fertility models". In: Robine, J-M., Vaupel, J. W., Jeune, B., Allard, M. (eds.), *Longevity: To the Limits and Beyond*. Berlin: Springer.

Vallin, J., and Meslé, F. (2001) "Vivre au-delà de 100 ans", *Population et Société*, 365:4.

Van Den Biggelaar, A. H. J., Huizinga, T. W. J., De Craen, A. J. M., Gussekloo, J., Heijmans, B. T., Frölich, M., and Westendorp, R. G. J. (2004) "Impaired innate immunity predicts frailty in old age. The Leiden 85-plus study", *Experimental Gerontology*, 39:1407–1414.

Vandenbroucke, J. P. (1998) "Maternal inheritance of longevity", *Lancet*, 351:1064 (Correspondence).

Vanfleteren, J. R., De Vreese, A., and Braeckman, P. (1998). "Two-parameter logistic and Weibul equations provide better fits to survival data from isogenic population of Caenorhabditis elegans in axenic culture than does the Gompertz model", *Journal of Gerontology*: *Series A Biological Science and Medical Science*, 53A:B393–B403.

Vaupel, J. W. (2002) "Life expectancy at current rates vs current conditions: A reflexion stimulated by Boogaarts and Feeney's 'How long do we live?"', *Demographic Research*, 7(8):365–378.

Vaupel, J. W. (2002) "Post-Darwinian Longevity. MPIDR Working Paper WP 2002-043 September", *Demographic Research*. http://www.demogr.mpg.de

Vaupel, J. W., and Jeune, B. (1995) "The emergence and proliferation of centenarians". In: Jeune, B., Vaupel, J. W. (eds.), *Exceptional Longevity: From Prehistory to the Present*. Odense: Odense University Press (Monographs on population Aging 2).

Vaupel, J. W., and Lundstrom, H. (1994) "The future of mortality at older ages in developed countries". In: Lutz, W. (ed.), *The Future Population of the World: What Can We Assume Today*? London, UK: Earthscan Publications, pp. 295–315.

Vaupel, J. W., Manton, K. G., and Stallard, E. (1979) "The impact of heterogeneity in individual frailty on the dynamics of mortality", *Demography*, 16:439–454.

Vaupel, J. W., Carey, J. R., Christensen, K., Johnson, T. E., Yashin, A. I., Holm, N. V., Iachine, I. A., Kannisto, V., Khazaeli, A. A., Liedo, P., Longo, V. D., Zeng, Yi., Manton, K. G., and Curtsinger, J. W. (1998) "Biodemographic trajectories of longevity", *Science*, 280:855–860.

Vaupel, J. W., *et al*. (2003) "Aging. It's never too late", *Science*, 301(5640):1679–1681.

Véron, J., and Rohrbasser, J. M. (2003) "Wilhelm lexis: The normal length of life as an expression of the 'nature of things", *Population*, 58(3):303–322.

Vincent, P. (1951) "La mortalité des vieillards", *Population*, 6:181–204.

Vita, A. J., Terry, R. B., Hubert, H. B., and Fries, J. F. (1998) "Aging, health risks, and cumulative disability", *New England Journal of Medicine*, 338:1035–1041.

Walford, R. (1985) *Maximum Life Span*. New York: WW Norton & Company.

Wang, Z. (2001) *Age Validation, Demographic Characteristics and Functional Status among Chinese Centenarians.* Dissertation, University of Southern Denmark, Faculty of Health Sciences.

Wang, Z., Yi, Z., Jeune, B., and Vaupel, J. W. (1997) "A demographic and health profile of centenarians in China". In: Robine, J-M., *et al*. (eds.), *Longevity : To the Limits and Beyond*. Berlin, Springer-Verlag.

Wang, Z., Yi, Z., Jeune, B., and Vaupel, J. W. (1998) "Age validation of Han Chinese centenarians", *Genus*, 54(1–2):123–141.

Weitz, J. S., and Fraser, H. B. (2001) "Explaining mortality rate plateaus", *Proceedings of the National Academy of Sciences of the United States of* America, 98(26):15383–15386.

Westendorp, R. G., and Kirkwood, T. B. L. (1999) "Human longevity at the cost of reproductive success", *Nature*, 396:743–746.

Westendorp, R. G., and Kirkwood, T. B. L. (2001) "Maternal and paternal lines of familial longevity", *Population*, 13(1):223–236.

White, K. M. (2002) "Longevity advances in high-income countries, 1955–1996", *Population and Development Review*, 2002;28:59–76.

Wick, G., Berger, P., Jansen-Dürr, P., *et al*. (2003) "A Darwinian-evolutionary concept of age-related diseases", *Experimental Gerontology*, 38:13–25.

Wigzell, F. W. (1970) "The functional state of nonagenarians", *Geriatrics*, 170–178.

Williams, G. C. (1957) "Pleiotropy, natural selection, and the evolution of senescence", *Evolution*, 11:398–411.

Wilmoth, J. R. (1995) "Are mortality rates falling at extremely high ages? an investigation based on a model proposed by Coale and Kisker", *Population Studies*, 49:281–295.

Wilmoth, J. R. (1997) "In search of limits: What do demographic trends suggest about the future of human longevity". In: Kenneth, W. W., Caleb, E. F. (eds.), *Between Zeus and the Salmon: The Biodemography of Longevity*. Washington, DC: National Academy Press, pp. 38–64.

Wilmoth, J. R. (1998a) "Is the pace of Japanese mortality decline converging toward international trends?", *Population and Development Review*, 24(3):593–600.

Wilmoth, J. R. (1998b) "The future of human longevity: A demographer's perspective", *Science*, 280:395–397.

Wilmoth, J. R. (2000) "Demography of longevity: Past, present, and future trends", *Experimental Gerontology*, 35(9–10):1111–1129.

Wilmoth, J. R. (2001) "How long can we live? A review essay", *Population and Development Review*, 27:791–800.

Wilmoth, J. R. (2002) "Human longevity in historical perspective". In: Paola, S. T. (ed.), *Physiological Basis of Aging and Geriatrics*, 3rd edition, Boca Raton, FL: CRC Press, pp. 11–24.

Wilmoth, J. R., and Dennis, M. (2005) "Social differences in older adult mortality in the United States: Questions, data, methods, and results". In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Wilmoth, J. R., and Lundström, H. (1996) "Extreme longevity in five countries: Presentation of trends with special attention to issues of data quality". *European Journal of Population*, 12:63–93.

Wilmoth, J. R., and Horiuchi, S. (1999) "Rectangularization revisited: Variability of age at death within human populations", *Demography*, 36(4):475–495.

Wilmoth, J. R., and Robine, J.-M. (2003) "The world trend in maximum life span", *Population and Development Review*, 29:239–257.

Wilmoth J. R., Skytthe, A., Friou, D., and Jeune, B. (1996) "The oldest man ever? A case study of exceptional longevity", *Gerontologist*, 36:783–788.

Wilmoth, J. R., Deegan, L. J., Lundstro, H., *et al*. (2000) "Increase of maximum life-span in Sweden, 1861–1999", *Science*, 289:2367–2368.

Yashin, A. I., *et al*. (2001) "The new trends in survival improvement require a revision of traditional gerontological concepts", *Experimental Gerontology*, 37:157–167.

Yashin, A. I., De Benedictis, G., Vaupel, J. W., *et al*. (1999) "Genes, demography, and life span: The contribution of demographic data in genetic studies on aging and longevity", *American Journal of Human Genetics*, 65:1178–1193.

Yashin, A. I., De Benedictis, G., Vaupel, J. W., *et al*. (2000) "Genes and longevity: Lessons from studies of centenarians", *Journal of Gerontology: Biological Sciences*, 55A(7):B319–B328.

Zeng, Y., and Vaupel, J. (2005) "Oldest old mortality in China". In: Robine, J-M., Crimmins, E., Kannisto, V., Carrière, Y. (eds.), *Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population*. Berlin: Springer.

Zeng, Y., Vaupel, J. W., Xiao, Z., *et al*. (2001) "The healthy longevity survey and the active life expectancy of the oldest old in China", *Population*, 13(1):95–116.

Zuliani, G., Cherubini, A., and Volpato, S. (2002) "Genetic factors associated with the absence of atherosclerosis in octogenarians", *Journal of Gerontology*: *Medical Sciences*, 57A(9):M611–M615.

CHAPTER 2. PATTERNS IN MAMMALIAN AGEING: DEMOGRAPHY AND EVOLUTION

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Abstract

From our limited knowledge of comparative mammalian longevity four generalizations may be made: (1) overall, larger mammal species live longer than smaller ones; (2) certain taxonomic groups such as bats and marsupials are exceptions to this body size–longevity relationship; (3) within species, there is suggestive evidence that smaller individuals are generally longer-lived than larger individuals; and (4) in most mammal species, females are the longer-lived sex, although numerous exceptions can be found. In the unique data set represented by the NIA/NCTR Biomarkers of Ageing study in which four mouse and three rat genotypes were reared under identical conditions, it is evident that male mice typically live longer than female mice, while the reverse is true for rats. In addition, although there is a large unexplained variation in longevity, even among genetically identical animals in identical environments, there is no evidence from the enhanced longevity of caloric restriction of a longevity "wall" beyond which mice and rats cannot live.

1. Introduction

We currently possess scant knowledge about ageing in most other animal species, other than realizing that the range of longevities within the animal kingdom is enormous, and that humans lie towards the longer-lived end of the continuum. However, even this scant knowledge reveals some tantalizing glimpses into the universe of animal patterns of ageing, which might tell us a great deal about how nature, that is evolution, has moulded senescence. For instance, although most animal species survive less than a year in nature (given the fact that most described species are short-lived arthropods), longevity approaching or surpassing one, even two, centuries is known to occur in a wide range of animal groups from crustaceans to molluscs to fishes, reptiles, and nonhuman mammals (Finch and Austad 2001). Evolutionary theory (Charlesworth 1994; Rose 1991) provides a conceptual context for understanding some correlates of slow ageing—namely, occupation of ecological niches with reduced extrinsic hazards, possession of exceptionally effective anti-predator defences such as shells, spines, or exceptionally large body size, exceptionally low metabolic rate,

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and low reproductive rates. However, detailed patterns of animal ageing are still elusive because of limitations of our knowledge about the timing and course of ageing among sufficient numbers of species.

Mechanistically, there has been substantial progress over the past one to two decades in identifying fundamental mechanisms of ageing. An emerging consensus is that such mechanisms involve efficiency in minimizing damage from oxygen radicals, and reducing activity in the insulin biochemical pathway. These mechanism affect longevity in both invertebrates and vertebrates (Sohal and Weindruch 1996; Tatar *et al.* 2003).

Perhaps surprisingly, long life seems to be associated with resistance to a wide variety of physiological insults either on the organismal or cellular level. That is, even though individuals or specific cell types from different species may be indistinguishable under the microscope, they differ enormously in functional details, such as resistance to stress (Martin *et al*. 1996; Wang *et al*. 2004). For instance, a mutation in a gene called *age-1* in the tiny roundworm *C. elegans* increases longevity by about 65% and also increases the worms' ability to survive exposure to ultraviolet radiation, heat, and several chemicals that produce oxygen radicals (Martin *et al*. 1996). In addition, the impact of ambient oxygen concentration on the number of population doublings undergone by normal cultured skin cells is much greater for cells from short-lived house mice than long-lived humans (Campisi 2001). Also, the ability of primary skin cells to survive in the face of oxidative and nonoxidative insult was directly correlated with life span among a sample of eight mammalian donor species (Kapahi *et al*. 1999). As we continue making progress in dissecting these fundamental ageing processes in a few model species, insights should be developed which will help illuminate larger, interspecific, demographic patterns of ageing.

The remainder of this review will focus on what is known, and not known, about demographic patterns of ageing among mammals and assorted nonmammalian vertebrates, with the intent of placing our knowledge of humans in a larger biological context.

2. Demographic Data Quality

The quality of any data set depends upon the question that data set is designed to ask. By this criterion, data quality for a number of mammal species is paradoxically both very good and very poor. In comparison with human demographers, who frequently work with sample sizes of hundreds of thousands or millions, researchers studying mammals operate with comparatively small samples. On the other hand, studies of certain laboratory species control for genetic and environmental variables in ways that human studies can never approach.

First, considering data from natural environments, despite decades of field studies of a reasonably wide array from among the 4000+ extant mammal species, there is little data that allows reasonably precise descriptions of mortality rate changes with age. Problems with field data have to do with small sample sizes, year to year variability in environmental conditions obscuring underlying biological trends, and uncertainty about age at which animals actually die. Large mammals live too long for most field studies to monitor individuals throughout their lives (but see Packer *et al*. 1988 on African lions). By contrast, studies of shorter-lived small species generally consist of substantially larger samples of

animals monitored throughout life. However, in these species death is usually not directly detected but is assumed when animals disappear from trapping grids. Disappearance from a trapping grid can also be due to dispersal out of the trapping area. In addition, field researchers frequently note differential trapping success among sex and age classes due to differential mobility, dispersal tendency, or the willingness to enter traps. Therefore biases due to dispersal may not be random.

Even modest quality field data may still be useful for a rough indication of how long mean or median longevity in a particular environment may be, or how age-independent mortality patterns change with environmental variables; and the very best field data might even suggest whether actuarial ageing actually occurs in nature. That is, whether age-specific mortality rate tends to increase, or reproductive output decrease, with age or not. For instance, Promislow (1990) examined 59 published life tables of mammals in the wild, and contrary to a good deal of gerontological speculation (Hayflick 2000), found statistically significant evidence for senescence (measured by an increase in mortality rate with age) in 44% (26) of the species and a nonsignificant trend in a further 34% (20) of the species. Holmes and Austad (1995) asked a similar question about birds, which, because they are more easily observed in nature, have somewhat higher quality life tables. They found that 80% of 59 avian life tables exhibited a trend of increasing mortality rate with age and in 25% of the tables the trend was statistically significant. Thus even with the manifold problems associated with vertebrate life tables from field data, we find that animals often do senesce in nature (although it is unlikely that they reach the stage of advanced decrepitude achievable in protected environments such as laboratories or modern cities).

Field data, even in the form of unique observations, also have the potential to highlight particular species or groups that are exceptionally long-lived. Thus, for instance, we know that bats generally live exceptionally long lives, as revealed by incidental mark-recapture observations in natural populations. These observations find individuals of many species no larger than mice living into their teens, twenties, or even thirties. Indeed, the maximum observed longevity from field populations of a sample of 64 bat species is 3.5 times as long as for nonflying mammals of the same body size (Wilkinson and South 2002), even though most bat field studies were not designed to detect exceptional longevity. Six bat species have authenticated ages of greater than 30 years; five of these records are from wild populations. Most remarkable of all, the 7 g Brandt's bat, *Myotis brandtii,* has survived in the wild up to at least 38 years (Wilkinson and South 2002).

Even with these exceptional longevities, due to the rigors of life in nature, there are probably few or no oldest-old, as we designate the term in humans, to be found in nature. That is, life in nature is too harsh for animals to reach ages of substantial frailty. As an example, the longest-lived African lion (*Panthera leo*) recorded in more than two decades of field work encompassing hundreds of individuals is 18 years, whereas zoo records for this species approach twice that longevity (Nowak 1999).

Captive longevity data for hundred of species are now available, due to the long history of keeping mammals in zoos, wildlife parks, and laboratory facilities (see Carey and Judge 2000 for a compendium). Because captive conditions shelter animals from the obvious unpredictable vicissitudes of nature, intrinsic ageing rates are likely to be more apparent in captivity and comparative trends may be evaluated. A note of caution is required

concerning information on longevity of captive mammals. Even today, husbandry practices are poorly developed for many captive species, and highly variable between facilities. As a consequence, mortality rates for even reasonably common species often fail to increase with age, as is common in populations dominated by extrinsic causes of death (see, for instance, Allman *et al.* 1998 for selected primate species).

Due to the above problems with captive populations, most comparative studies have focused not on survival curves or age-specific mortality rates, but instead on maximum longevity records—the Jeanne Calments of zoology—as the metric most likely to reveal something about relative differences in ageing rates among species. Needless to say, maximum longevity records are also susceptible to problems related to sample sizes, as well as problems related to variably developed husbandry techniques. For instance, comparing the best information on captive longevity records of 42 genera of commonly maintained primates over a seventeen year interval, 1982–1999 (Jones 1982; Jones 1999 as cited in Nowak 1999), one finds that maximum longevity has increased by more than 33% in nearly half of the genera, and more than doubled in 12% of them (Figure 1). Therefore, even with

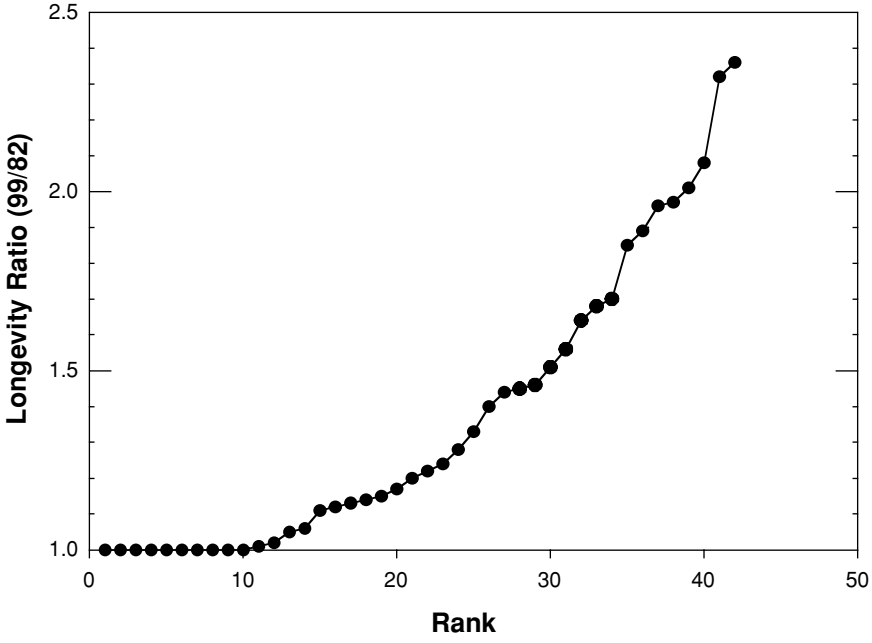

Figure 1. Increase in maximum longevity for 42 genera of captive primates between 1982 and 1999. Ordinate measures maximum longevity reported in 1999 versus that reported by the same researcher (M. L. Jones) in 1982. The 42 genera were ranked by the relative increase in reported maximum longevity. Not included is the datum for *Phaner furcifer* (Fork-marked Lemur), which showed a ten-fold increase in longevity over this time period, because the 1982 record (1.2 y) was obviously not indicative of its true longevity. Sources Jones 1982; Nowak 1999.

the large number of species now kept in zoos and wildlife facilities, we may yet have only the vaguest idea of what constitutes the oldest-old age for any but a few species.

Despite these caveats, the following trends can be detected from the captive comparative data. First, as has been known for some time, larger mammal species tend to be longer-lived than smaller species, although the data are widely scattered (Austad and Fischer 1991). Second, certain taxonomic groups (bats, primates, monotremes) are exceptionally long-lived for their body size, whereas other groups (e.g. marsupials) tend to be particularly short-lived. Third, *within* a number of species such as dogs, rats, mice, and horses, genetically smaller individuals are generally longer-lived than larger individuals (Li *et al*. 1996; Miller 2001). It has been hypothesized that the same is true for humans (Samaras and Elrick 1999), although data contrary to this hypothesis are also in the literature (Fogel and Costa 1997). Fourth, as with humans, most mammal species females probably live longer than males, although exceptions are not difficult to find (Austad and Holmes 1998; Smith 1993). Surprisingly, there have been few empirical investigations of mechanisms of sex differences in longevity, perhaps because such differences are subtle in laboratory rodents. With respect to this last point, a demographic trend which has never previously been reported, although it is evident in data from the NIA/NCTR Biomarkers study (see below) is that males are typically the slightly longer-lived sex in laboratory mice, whereas females are slightly longer-lived in laboratory rats (Table 1). The subtlety of these sex differences may explain why there have not been mechanistic investigations into the phenomenon.

We know more about the demography of ageing in laboratory rodents (house mice, *Mus musculus* and Norway rats, *Rattus norvegicus*) than any other mammal species except humans. However, because demographic studies of rodents are typically small (<50 individuals), descriptions of the oldest-old among even these species is lacking. It is unclear whether the sorts of statistical outliers as found in studies of invertebrates (Carey *et al*. 1992) occur in laboratory rodents. For instance, a rather typical laboratory study of 56 animals observed the oldest mouse (C57BL/6) survived 1577 days (McCracken, personal communication, 1998); whereas a much larger study (nearly 3,000 animals) of the same mouse genotype under identical conditions found its oldest mouse lived only about 3% longer (1628 days) (Turturro *et al*. 1999). By contrast, in another mouse genotype, B6D2F1,

Table 1. Percent sex difference in mean longevity among mouse and rat genotypes fed a standard laboratory diet ad lib in the NIA/NCTR Biomarkers Study.

Genotype	Longer-lived Sex	Percent Longer-Lived
Mice		
C57BL/6	Male	3.3
DBA/2	Male	6.2
B6D2F1	Male	11.8
B6C3F1	Male	5.8
Rats		
F344	Female	14.4
Brown-Norway	Female	5.3
F344BNF1	Female	6.6

there was a 22% greater longevity found in a large (nearly 3,000 animals) compared to a smaller study (N = 56) study. In order to understand more about the late-life mortality dynamics of laboratory rodents, more large studies will be required.

3. Intraspecific Variation in Longevity

Since it may be relevant to the ongoing debate about morbidity and mortality compression as longevity is extended, as well as the putative existence of a species-specific life span (Carey *et al*. 1992; Fries 1980; Wilmoth and Horiuchi 1999), it may be worth summarizing what is known about *variability* in longevity among laboratory rodents and other model species compared with similar information about humans. The logic of doing this is that, in particular among research species in which we know how to substantial lengthen life, the idea that longevity within a species has some empirical limit (Fries 1980) might be testable. Specifically, as more individuals live longer because of life-lengthening diets, for instance, a greater proportion of them should approach the theoretical longevity "wall." Thus the survival curve should necessarily become more rectangular and variation in longevity should decrease (Figure 2).

On the topic of variation in longevity, recent research has noted that there seems to be a general, irreducible variation in longevity (Finch and Kirkwood 2000). These authors have convincingly demonstrated that even genetically identical individuals maintained under the most similar environmental conditions still exhibit substantial variability in longevity and other life history traits such as reproductive rate and reproductive longevity. As an empirical

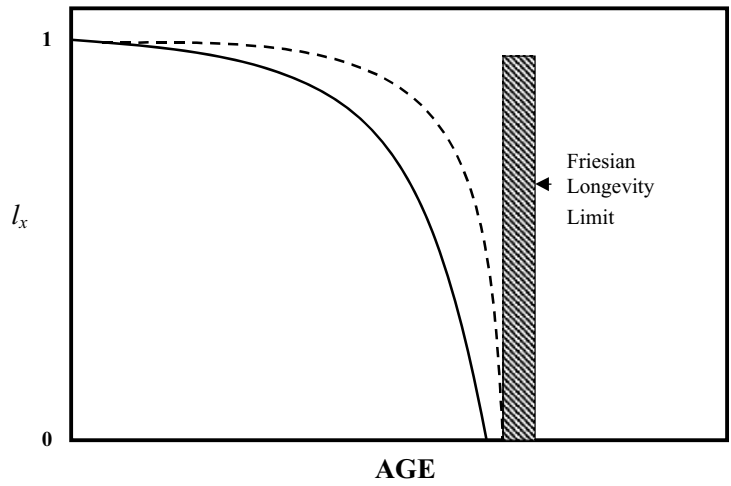

Figure 2. Schematic showing why caloric restriction, which increases longevity by as much as 50% (see Tables 3 and 4), should reduce the variation in age at death, given that the limited life span hypothesis were valid. The vertical axis (l_x) is the proportion surviving to age *x*.

baseline against which to judge variability in other animal species, consider the fact that the human population of the United States in 1980, with all its genetic and environmental heterogeneity, social class, and life style differences, exhibited a coefficient of variation (= CV, the ratio of standard deviation to mean, expressed as percent) in age-at-death of 50% (Table 1). Not surprisingly, less genetic (and probably environmental) variation has been observed among dizygotic twins living to at least 15 years of age within a narrowly-defined birth cohort from Denmark. For comparison, these twins exhibited a coefficient of variation in age-at-death of approximately half the magnitude (24.5%, sexes combined) of the U.S. population, whereas monozygotic twins (data also censored for deaths before age 15) from the same birth cohort had slightly less variability (CV = 22.4%) (McGue *et al*. 1993). Human twins, of course, do not share identical environments even as children, much less as adults. Thus although monozygotic twins will be genetically identical, environmental effects beginning prenatally—surprisingly monozygotic twins differ more in birth weight than do dizygotic twins—and continuing throughout life would be expected to introduce considerable longevity variation among twins (Finch and Kirkwood 2000).

Astonishingly then, greater variation in longevity (CV = 34%) than in either monozygotic or dizygotic human twins was observed in a study of the tiny nematode, *Caenorhabditis elegans*, under conditions specifically designed to maximize phenotypic uniformity. The study population consisted of genetically identical individuals living together in the same culture flask, in which the liquid medium was stirred to eliminate microenvironmental variation (Johnson and Wood 1982, cited in Finch and Kirkwood 2000). In other respects aside from longevity, *C. elegans* is remarkably invariant phenotypically. All individuals even have the same number of somatic cells and cell types. Variability in *C. elegans* turns out itself to be quite variable. In two replicate populations grown under identical conditions using the same genetically identical animals, Johnson (1987) found a more than two-fold between-experiment difference in life span variability (Table 1)—one experiment yielding variability almost as large as that of the US population, the other variability almost as small as among monozygotic Danish twins. In either case, there was massively more variation than I suspect most biologists would have expected. An additional series of observations using a genetically heterogeneous population found variability about midway in between that in the two experiments using a single genotype (Table 2).

Could this variation be due to unperceived variability in behaviour among animals too small to monitor individually, or might there have been some sort of microenvironmental variability that was impossible to control even in continuously mixing liquid in a laboratory flask? Behaviour can have a substantial impact on longevity in poikilothermic animals, so one possibility is that the variation in longevity represents unobserved behavioural variation. For instance, it is well known that house fly longevity is strongly affected by activity level, probably via changes in metabolic rate, and can thus be affected by seemingly trivial conditions like the opportunity for flight or the size of the container in which they are housed (Sohal 1986).

One way to address this issue is to observe how uniformity of conditions affects the variability of longevity in organisms in which metabolic rate does not have an automatic impact on longevity and in which microenvironmental conditions are more easily observed and controlled—organisms like laboratory rodents, for instance.

Table 2. Variability in age-at-death in selected species.

Group	Coefficient of Variation (%)	Mean	Reference
(U.S. 1980)			
Human Males*	**50.0**	69.8 yr	Faber 1982
Females*	**50.1**	77.5	
(Denmark, b. 1870–1880)			
Human MZ Female Twins**	**22.6**	73.3	McGue *et al*. 1993
Males**	**22.1**	71.9	
Human DZ Female Twins**	**25.1**	70.9	
Males**	**23.9**	70.3	
Laboratory mice (females)	**27.8**	864 d	Biomarkers study
(males)	**26.1**	910	
Laboratory rats (females)	**17.3**	968 d	Biomarkers study
(males)	**20.8**	899	
C. elegans (N2): Expt. 1	**23.4**	18.1 d	Johnson 1987
Expt. 2	**49.5**	20.0	
C. elegans (Heterogeneous)	**39.4**	23.0	Brooks *et al*. 1994

*deaths in first year of life excluded.
*deaths in first 15 years of life excluded.

The US National Institute on Ageing in collaboration with the National Centre for Toxicological Research (NCTR) began a massive laboratory rodent study called the Biomarkers of Ageing Program in 1988. The study continued for ten years. Four mouse and three rat genotypes (all individuals within a genotype are genetically identical) were reared and individually housed throughout life under identical conditions in a specific pathogen-free laboratory environment on several standardized diets. Subsets of individuals were killed every six months and subjected to a complete pathological analysis; others were shipped to outside investigators for additional projects. In all, some 60,000 rodents passed through the program (Sprott 1999; Turturro *et al*. 1999). Results of many of the studies were published in the November and December, 1999 issues of the *Journal of Gerontology: Biological Sciences*.

Because such exquisite effort was taken to standardize both genetics and environment in these populations, they offer a unique opportunity to examine the limits of uniformity in mammalian longevity. Also, because all genotypes were fed under both *ad libitum* and standardized calorically-restricted conditions (caloric restriction is well-known to increase longevity by as much as 50% in laboratory rodents), it is possible to assess whether increased longevity automatically leads to reduced variability—as the limited life span paradigm would suggest. The following results are summarized from "longevity groups" of 50–56 animals monitored from birth to death in the NIA/NCTR Biomarkers Study (Tables 3 and 4).

Several points, not previously reported, immediately emerge from the data. First, caloric restriction leads to a statistically greater enhancement in mean longevity in mice as compared

Table 3. Variability in longevity among house mice from the Biomarkers of Ageing Program (source, McCracken, personal comm. 1998).

Genotype	Feeding regime	Sex	Mean longevity (d)	Res/Al%	CV
C57BL/6	Ad lib	Male	813		21.8
	Restricted	Male	989	21.6	18.6
	Ad lib	Female	787		23.8
	Restricted	Female	954	21.2	28.4
(Breeding	Ad lib	Male	678		34.9
Diet)	Restricted	Male	925	36.4	28.2
(Breeding	Ad lib	Female	620		29.4
Diet)	Restricted	Female	953	53.7	28.6
DBA/2	Ad lib	Male	545		47.6
	Restricted	Male	717	31.6	28.8
DBA/2	Ad lib	Female	513		51.6
	Restricted	Female	703	37.0	40.1
B6D2F1	Ad lib	Male	964		22.4
	Restricted	Male	1258	30.5	16.0
	Ad lib	Female	862		20.5
	Restricted	Female	1122	30.2	21.9
B6C3F1	Ad lib	Male	959		23.5
	Restricted	Male	1257	31.1	19.3
	Ad lib	Female	906		16.9
	Restricted	Female	1216	34.2	17.5

CV = Coefficient of Variation. Res/Al% = Proportion increase in mean longevity in the calorically-restricted compared with the ad lib fed animals, expressed as a percent.

with rats (Mann-Whitney U Test on the proportional increase in mean longevity, $p < 0.05$). Although one often hears that caloric restriction reliable increases longevity by 25–40%, in fact the effect has a greater range. The smallest effect (11.5% increase in mean longevity) was in female F344 rats: the largest (53.7%) in C57BL/6 mice fed a "breeding" diet. The "breeding" diet fed these mice reduced longevity in both sexes when compared with the standard "maintenance" diet; however, this life shortening effect was smaller among the calorically restricted animals. Second, under standardized laboratory conditions, genetically uniform rodents, not surprisingly, generally do exhibit lower variability in longevity than human twins living in the chaotic real world. Mean coefficient of variation for longevity among rats (across all diets and sexes) was 19.1%, or somewhat less than either group of human twins. Male F344 rats, for instance, display a CV of only 13.7% (Table 4). However, low variability is not guaranteed. Among mice (all genotypes, sexes, diets combined), mean coefficient of variation for longevity was 27.0%, or slightly greater than either group of human twins. Genetically identical female DBA/2 mice, to take the extreme example, exhibit even greater variability than that found among the genetically heterogeneous American population living under dramatically varying conditions (Table 3). Why rats have generally lower variability than mice is unknown.

Table 4. Variability in longevity among rats from the Biomarkers of Ageing Program (source, McCracken, personal comm. 1998).

Genotype	Feeding regime	Sex	Mean longevity (d)	Res/Al%	CV
F344	Ad lib	Male	721		13.7
	Restricted	Male	876	21.5	16.7
	Ad lib	Female	825		15.5
	Restricted	Female	920	11.5	18.8
(Diet 2)	Ad lib	Male	700		19.1
	Restricted	Male	891	27.3	19.0
	Ad lib	Female	790		15.6
	Restricted	Female	906	14.7	22.2
Brown-Norway	Ad lib	Male	863		22.9
	Restricted	Male	993	15.1	34.2
Brown Norway	Ad lib	Female	909		16.7
	Restricted	Female	1124	23.7	20.1
F344BNF1	Ad lib	Male	931		26.5
	Restricted	Male	1218	30.8	14.2
	Ad lib	Female	969		14.2
	Restricted	Female	1298	34.0	15.6

CV = Coefficient of Variation. Res/Al% = Proportion increase in mean longevity in the calorically-restricted compared with the ad lib fed animals, expressed as a percent.

Regardless of species, genotype clearly has a major impact on level of variability, perhaps by regulating sensitivity to uncontrolled or uncontrollable environmental variables during fetal development, such as maternal age or the sex of one's intrauterine neighbours. Both of these variables have been shown to affect some aspects of ageing, although their affect on longevity has not been documented (Finch and Kirkwood 2000). Indeed one specific mouse chromosome region (chromosome 11, near the centromere) has been observed to be explain about 60% of the variation in longevity among a series of inbred strains derived from two inbred progenitor strains (a B6 × D2 recombinant inbred series) (De Haan *et al.* 1998). Third, it has previously been noted that highly inbred animals frequently display more variability in a variety of traits than F_1 hybrids between inbred strains (which although genetically identical will have different alleles at many genetic loci), probably due to increased developmental stability associated with genetic heterozygosity (Phelan and Austad 1994). No such clear trend is evident among these rat and mouse genotypes. The least variable rat genotype is an inbred strain (F344) rather than a hybrid; and one of the inbred mouse strains (C57BL/6) exhibits longevity variability approximately as low as the values from the two hybrid populations. Furthermore the lone hybrid rat genotype displays no less variability than several of the pure strain values. Thus the generalization that inbred populations are more variable that hybrid populations does not hold for rodent longevity.

There is also little evidence supporting the mortality compression hypothesis. In mice, the variation in longevity is frequently (7 of 10 comparisons)—although not universally—reduced as life is extended as the hypothesis would predict (Table 3).

However, in rats, variability was more likely to increase (6 of 8 comparisons) than decrease (Table 4).

In sum, variation in longevity among laboratory rodents under conditions of exemplary environmental, and complete genetic, uniformity remains substantial. Indeed in some genotypes, the variability approaches that of the American population at large. The source of this variability remains a mystery, but it is under partial genetic control. Given the range of variability observed and the life-extending effect of caloric restriction, there was no evidence that life extension necessarily leads to reduced variability in age at death as the mortality compression hypothesis would predict.

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References

Allman, J., Kumar, R., and Hasenstaub, A. (1998) "Parenting and survival in anthropoid primates: Caretakers live longer", *Proceedings of the National Academy of Sciences USA*, 95:6866–6869.

Austad, S. N., and Fischer, K. E. (1991) "Mammalian aging, metabolism, and ecology: Evidence from the bats and marsupials", *Journals of Gerontology*, 46:B47–B53.

Austad, S. N., and Holmes, D. J. (1998) "Evolutionary approaches to probing ageing mechanisms". In: Yu, B. P. (ed.), *Methods in Aging Research*, Boca Raton, FL: CRC Press, pp. 437–452.

Brooks, A., Lithgow, G. J., and Johnson, T. E. (1994) "Mortality rates in a genetically heterogeneous population of *Caenorhabditis elegans*", *Science*, 263:668–671.

Campisi, J. (2001) "From cells to organisms: Can we learn about aging from cells in culture?" *Experimental Gerontology*, 36(4–6):607–618.

Carey, J. R., and Judge, D. S. (2000) *Longevity Records: Life Spans of Mammals, Birds, Amphibians, Reptiles, and Fish*. Odense Monographs on Population Aging. Odense, DK: Odense University Press, pp. 241.

Carey, J. R., Liedo, P., Orozco, D., and Vaupel, J. W. (1992) "Slowing of mortality rates at older ages in large medfly cohorts", *Science*, 258:457–461.

Charlesworth, B. (1994) *Evolution in Age-Structured Environments*, 2nd edn., Cambridge, UK: Cambridge University Press.

De Haan, G., Gelman, R., Watson, A., Yunis, E., and Van Zant, G. (1998) "A putative gene causes variability in lifespan among genotypically identical mice", *Nature Genetics*, 19:114–116.

Faber, J. F. (1982) "Life tables for the United States: 1900–2050". *U.S. Department of Health and Human Services, Social Security Administration*. SSA Pub. No. 11-11534.

Finch, C. E., and Kirkwood, T. B. L. (2000) *Chance, Development, and Aging*. Oxford, UK: Oxford University Press.

Finch, C. E., and Austad, S. N. (eds.) (2001) "Symposium on slowly-aging organisms", *Experimental Gerontology*, special issue.

Fogel, R. W., and Costa, D. L. (1997) "A theory of technophysio evolution, with some implications for forecasting population, health care costs, and pension costs", *Demography*, 34(1):49–66.

Fries, J. F. (1980) "Aging, natural death, and the compression of morbidity", *New England Journal of Medicine*, 303:130–135.

Hayflick, L. (2000) "The future of ageing", *Nature*, 408:267–269.

Holmes, D. J., and Austad, S. N. (1995) "Birds as animal models for the comparative biology of aging: A prospectus", *Journals of Gerontology: Biological Sciences*, 50A:B59–B66.

Johnson, T. E. (1987) "Aging can be genetically dissected into component processes using long-lived lines of *Caenorhabditis elegans*", *Proceedings of the National Academy of Sciences, USA*, 84:3777–3781.

Johnson, T. E., and Wood, W. B. (1982) "Genetic analysis of life-span in *Caenorhabditis elegans*", *Proceedings of the National Academy of Sciences, USA*, 79:6603–6607.

Jones, M.L. (1982) "Longevity of captive mammals", *Zoologische Garten*, 52:113–128.

Kapahi, P., Boulton, M. E., and Kirkwood, T. B. L. (1999) "Positive correlation between mammalian life span and cellular resistance to stress", *Free Radicals in Biology and Medicine*, 26:495–500.

Li, Y., Deeb, B., Pendergrass, W., and Wolf, N. (1996) "Cellular proliferative capacity and life span in small and large dogs", *Journals of Gerontology: Biological Sciences*, 51A:B403–B408.

Martin, G. M., Austad, S. N., and Johnson, T. E. (1996) "Genetic analysis of ageing: Role of oxidative damage and environmental stresses", *Nature Genetics*, 13:25–34.

McGue, M., Vaupel, J. W., Holm, N., and Harvald, B. (1993) "Longevity is moderately heritable in a sample of Danish twins born 1870–1880". *Journals of Gerontology: Biological Sciences*, 48:B237–B244.

Miller, R. A. (2001) "Genetics of increased longevity and retarded aging in mice". In: Masoro, E. J., Austad, S. N. (eds.), *Handbook of the Biology of Aging*, 5th edn. San Diego: Academic Press, pp. 369–395.

Nowak, R. M. (1999) *Walker's Mammals of the World*, 6th edn. Baltimore: Johns Hopkins University Press.

Packer, C., Herbst, L., Pusey, A. E., Bygott, D., Hanby, J. P., Cairns, S. J., and Mulder, M. B. (1988) "Reproductive success of lions". In: Clutton-Brock, T. H. (ed.), *Reproductive Success*. Chicago: University of Chicago Press, pp. 363–383.

Phelan, J. P., and Austad, S. N. (1994) "Selecting animal models of human aging: Inbred strains often exhibit less biological uniformity that F_1 hybrids", *Journals of Gerontology*, 49:B1–B11.

Promislow, D. E. L. (1990) "Senescence in natural populations of mammals: A comparative study", *Evolution*, 45:1869–1887.

Rose, M. R. (1991). *Evolutionary Biology of Aging*. Oxford, UK: Oxford University Press.

Samaras, T. T., and Elrick, H. (1999) "Height, body size, and longevity", *Acta Medica Okayama*, 53:149–169.

Smith, D. W. E. (1993) *Human Longevity*. Oxford, UK: Oxford University Press.

Sohal, R. S. (1986) "The rate of living theory—a contemporary interpretation". In: Collatz, K.-G., Sohal, R. S. (eds.), *Insect Aging*. Berlin: Springer, pp. 23–44.

Sohal, R. S., and Weindruch, R. (1996) "Oxidative stress, caloric restriction, and aging", *Science*, 273:59–63.

Sprott, R. L. (1999) "Biomarkers of Aging", *Journals of Gerontology: Biological Sciences,* 54A:B464–B465.

Tatar, M., Bartke, A., and Antebi, A. (2003) "The endocrine regulation of aging by insulin-like signals", *Science*, 299(5611):1346–1351.

Turturro, A., Witt, W. W., Lewis, S., Hass, B. S., Lipman, R. D., and Hart, R. W. (1999) "Growth curves and survival characteristics of the animals used in the biomarkers of aging program", *Journals of Gerontology: Biological Sciences*, 54A:B492–B501.

Wang, H. D., Kazemi-Esfarjani, P., and Benzer, S. (2004) "Multiple-stress analysis for isolation of *Drosophila* longevity genes", *Proceedings of the National Academy of Science, USA*, 101(34):12610–12615.

Wilkinson, G. S., and South, J. M. (2002) "Life history, ecology and longevity in bats", *Aging* Cell, 1:124–131.

Wilmoth, J. R., and Horiuchi, S. (1999) "Rectangularization revisited: Variability of age at death within human populations", *Demography*, 36:475–495.

Wolf, N. S., Penn, P. E., Fei, R.G., and Pendergrass, W. R. (1995) "Caloric restriction: Conservation of in vivo cellular replicative capacity accompanies life-span extension in mice", *Experimental Cell Research*, 217:317–323.

CHAPTER 3. LIFE SPAN EXTENSION IN HUMANS IS SELF-REINFORCING: A GENERAL THEORY OF LONGEVITY

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Abstract

We propose that longevity is not merely the result of an absence of mortality but a self-reinforcing and positively selected life history trait in social species. We develop the argument that a small increase in longevity is amplified as (1) reductions in mortality at young ages increases natural selection for mechanisms of maintenance and repair at *all* older ages as well as increasing the potential for intergenerational transfers; (2) intergenerational transfers of resources from old to young increase fitness (e.g. through improved health, skill, and competitive ability) of the young and thus favour the presence of older individuals in a population; and (3) the division of labour increases both efficiency and innovation at all levels resulting in increased resources that can be invested. This is a theory framed around the longevity-oriented question posed two decades ago by George Sacher "Why do we live as long as we do?" rather than the more prevalent question today "Why do we age?" We describe the foundational principles and the main phases of our model for the evolution of longevity mediated through social organization and apply the concept specifically to human populations.

Introduction

Sacher (1978) notes that the approach to one basic question in the biology of aging "*Why do we grow old*?" is guided largely by a research paradigm involving model systems designed to compare ontogenetic functions in old and young animals. One of his primary concerns with this ageing-oriented approach to understanding longevity was that the far-reaching physiological, cellular and molecular correspondence between model systems (mice) and humans concealed a paradox: If model species are so similar to humans in molecular make-up that they can serve as models, why do mice age as much in 2 years as humans do in 80 years? This paradox motivated him to ask his second question: "Why do we live as long as we do?" This question cannot be answered within the framework of ontogenetic research on ageing, but rather requires the development of an evolutionary-comparative

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paradigm concerned with longevity. We use life span in the sense articulated by Wilmoth and the participants of the Santorini Conference on Longevity (Goldwasser, in press) and use longevity in a general manner to more specifically focus on prolonged or increasing life spans.

Despite the arguments by Sacher (1978) and others (e.g. Hayflick 2000) in support of developing a longevity-oriented theory of the finitude of life, no such theory has ever been published. Our objective in this paper is to describe a general theory of longevity extension in social species, particularly as it applies to humans. These central concepts derive from patterns identified in vertebrate life span data (Carey and Judge 2000), insects life spans (Carey 2001b), and humans (Kannisto *et al*. 1994; Tuljapurkar *et al*. 2000; Vaupel *et al*. 1998; Wilmoth *et al*. 2000), environmental factors associated with the evolution of extended longevity in insects (Carey 2001a; Carey 2001b), and the preliminary idea that longevity extension in humans is self-reinforcing[1] as first proposed by Carey and Judge (2001). Our theory also builds on and extends work by Fogel (1993, 1994, 1997) on what he and his co-workers refer to as "technophysio evolution"—a theory explaining the decline in morbidity and mortality since 1700.

A theory of longevity that extends beyond the classical evolutionary theory of ageing is important for several reasons. First, whereas senescence is a by-product of evolution (Medawar 1955), life span is an evolved life-history trait that results from positive selection. Second, unlike the evolutionary theory of senescence which is based solely on individual natural selection (Williams, 1957), this theory includes processes of sexual selection and kin selection, bringing life history theory more fully to bear on questions concerned with the latter portion of the life cycle. Third, longevity-oriented theory allows consideration of behaviours that are characteristic of older individuals including divisions of labour and intergenerational transfers (Beshers and Fewell 2001). Fourth, mortality factors unrelated to ageing (accidents, acute diseases, socio-economic factors) can be considered and therefore a longevity-oriented theory fosters a greater integration of demographic (Hauser and Duncan 1959) and gerontological (Finch 1990) pedagogies.

Comparative Demography of Longevity

Our purpose in this section is to situate human longevity in a broad biological context. We first describe a general classification system concerning factors that favour the evolution of extended longevity and then provide a brief sketch of longevity extension in social wasps including a discussion of its relevance to humans.

A GENERAL CLASSIFICATION SCHEME

The literature on ageing and longevity includes descriptions of a small number of life span correlates, including well-known relationships between longevity and both body mass and

[1] Self-reinforcing is synonymous with the terms 'positive feedback' used in systems engineering and 'autocatalytic processes' used in biochemistry and refers to a process that speeds up at a rate that increases with time because the process catalyzes (or feeds on) itself.

relative brain size (Austad 1997; Comfort 1961; Hakeem 1996) and the observation that animals that possess armour (e.g. beetles, turtles) or capability of flight (e.g. birds, bats) are often long-lived (Austad 1997; Kirkwood 1992). The evolutionary theory of senescence suggests that animals better able to escape stochastic mortality sources such as predators (e.g. via armoured defences or better escape mechanisms) live longer and thus the force of selection at older ages is increased and the evolution of longer pre-senescent life span is possible. But major inconsistencies exist within even this small set of correlates. For example, there are several exceptions regarding the relationship of extended longevity and large body size—(e.g. bats are generally small but most species are long-lived)—and this positive relationship may be either absent or reversed within-orders.[2] Likewise, the observation that flight ability and extended longevity are correlated does not provide any insight into why within-group (e.g. birds) differences in life span exist, nor does it account for the variation in longevity in insects where adults of the majority of species can fly.

An alternative approach for identifying broad correlates of longevity emerged from an examination of several large-scale databases containing the maximum recorded life spans of both vertebrate and invertebrate species (Carey 2001a; Carey 2001b; Carey and Judge 2000). Across a wide taxonomic spectrum, many long-lived species appeared to cluster within 1-of-2 general ecology and/or life history criteria: (1) species that live in either unpredictable environments (e.g. deserts) or where food resources are scarce (e.g. caves, deep water); or (2) species that exhibit extended parental care, and/or live in groups with complex or advanced social behaviour. This led to a classification system regarding the life-span determinants of species with extended longevity (Table 1) that we believe is general and applies to a wide range of invertebrate and vertebrate species: (1) *Environmentally Selected*. This category includes animals whose life histories evolved under conditions in which food is scarce and where resource availability is uncertain or environmental conditions are predictably adverse part of the time.[3] The extended longevity of animals in this category evolved through natural selection;[4] and (2) *Socially Selected*. This category includes species that exhibit extensive parental investment, extensive parental care, and eusociality.[5] The extended longevity of animals in this category results from natural, sexual, and kin selection.[4]

This classification system places the relationship of life span and two conventional correlates, relative brain size and flight capability, in the context of life history. That is, brain size is related to the size of the social group and the degree of sociality (Dunbar 1992;

[2] For example, body mass and life span are negatively correlated within the Pinnipeds (seals and walruses) and are un-correlated within the Chiroptera (bats).

[3] Some of the longest-lived small and medium-sized mammals including gerbils, rock hyrax, and feral asses live in deserts where rainfall and, thus reproduction, is episodic and unpredictable (Bronson 1998).

[4] Evolutionary theory considers three types of selection with variations within each of the types (Futuyma 1998). N*atural selection* is the direct reproductive outcome of differential survival and/or mortality of individuals. S*exual selection* is the process whereby traits are selected as a function of their contribution to acquiring more or better mates. K*in selection* is a form of selection wherein traits are reproduced differentially through their beneficial effects on the reproduction of other relatives.

[5] Eusocial insects (ants, bees, wasps, termites) have overlapping generations, are colonial, and show cooperative care of young and a reproductive division of labour. The naked mole rat, *Heterocephalus glaber*, is the only mammal that displays true eusociality. This sub-Saharan species lives in colonies of 10 to 100 individuals with a single dominant "queen" who selects and mates with one to three breeding males. Longevity in captivity can be in excess of 21 years (Faulkes 1998).

Table 1. Categories of factors that favour the evolution of extended life span in insects, arachnids and vertebrates selected examples species or groups. Life span (years) in parentheses (Carey 2001b; Carey and Judge 2000).

Selection Factors[1] / Taxonomic Group	Examples[2]
Environmentally-selected life spans (conditions of resource uncertainty and/or scarcity)	
Insects/acarina	*Heliconius* butterflies (0.9); cave beetles (4); orchard bees (1); paper wasp queens (1); soft ticks (20); treehole mosquitoes; flour beetles (4); monarch butterfly (1); African locusts (2); tarantulas (10); bed bugs (1)
Mammals	Gray seal (46); dromedary camel (40); horseshoe bat (30); little brown bat (30); flying fox (31); African wild ass (47); white rhinoceros (45); short-nosed echidna (50); wombat (26); gray seal (46); crabeater seal (36); ringed seal (46); Caspian seal (50); kangaroo rat (10); Greater Egyptian gerbil (8); hairy armadillo (20); rock hyrax (14)
Birds	Great blue heron (23); marabou (41); southern ground hornbill (70); sandhill crane (22); whooping crane (40); Cheriway caracara (26)
Reptiles & Amphibians	American toad (30); Japanese giant salamander (55); Eastern hellbender (25); greater siren (25); common boa constrictor (39); American alligator (56); Chinese alligator (38); West African dwarf crocodile (42); salt water crocodile (42); slowworm (54); Mexican burrowing python (33); loggerhead turtle (33); common snapping turtle (47); alligator snapping turtle (59); stinkpot (55); Eastern indigo snake (25); San Diego gopher snake (20); Aldabra tortoise (152); tuatara (77)
Fish	White sturgeon (100); Beluga sturgeon (118); European eel (88); carp (38); wrasse (53); sole (45); rockfish (140); Bunnylake brook trout (24); arctic char (41); spur dogfish (60)
Socially-selected life spans (kinship, cooperation, parental care, monogamy, and helpers)	
Insects/acarina	Tsetse fly (1); dung beetles (2); *Bembix* spp—progressive provisioning wasp (1); *Polistes* spp; aposematic Saturnid butterflies (1); bumblebees (1); ant queens (30); termite queens (30)
Mammals	Bowhead whale (40); blue whale (65); pilot whale (65); sperm whale (70); golden jackal (16); spotted hyena (40); naked mole rat (21); black legged mongoose (16); humans (122); white-faced capuchin (47); squirrel monkey (27); gray-cheeked mangabey (33); yellow baboon (45); chimpanzee (60); orangutan (59)

Table 1. (continued).

Selection Factors[1] / Taxonomic Group	Examples[2]
Birds	African grey parrot (73); golden-naped parrot (49); red and blue macaw (64); trumpeter swan (33); mute swan (27); ring-billed gull (32); scrub jay (16); Royal albatross (58); northern fulmar (48); Manx shearwater (30)
Reptiles & Amphibians[3]	Rosenberg's tree frog (3.5)
Fish[4]	Basking shark (32); dusky shark (30); hound shark (28); nurse shark (25); whale shark (70)

[1]The two general categories of 'Environmentally-selected' and 'Socially-selected' are not mutually exclusive. Environmentally-selected life-span extension may allow overlapping generations and sociality; sociality may allow expansion into otherwise inhospitable environments.
[2]Scientific names given in Carey (2001b) and Carey and Judge (2000).
[3]Care of the mass of developing eggs and/or the hatchlings is exhibited in some members of all three major groups of amphibians (Wake, 1998); however no species of either amphibian or reptile are truly social and only a small number of reptilian species such as crocodilians and pythons exhibit any level of parental care (protection).
[4]The example shark species are all live-bearers.

Smith and Szathmary 1999) which, in turn, is linked to extended life span. And intensive parental care is linked to flight capability in birds and bats[6] which, in turn, is also linked to extended life span. No system of classification is perfect and the one presented in Table 1 is no exception—the categories are not mutually exclusive and therefore some species could be placed in either or both categories.[7] However, this classification serves as a practical and heuristic tool for considering the evolution of animal life spans. In particular this system provides a general background for closer examination of specific human attributes and sets the stage for addressing questions of process.

EVOLUTION OF EXTENDED LONGEVITY IN WASPS: THE INTERACTIVE ROLE OF SOCIALITY

Classifying long-lived species by life-history characteristics is important because it suggests that the evolution of extended longevity is fundamentally different in the social versus

[6] Most bird species are socially monogamous with both sexes helping in rearing young (e.g. one can incubate or protect the nest while the other collects food). If one of the pair dies, the chances that the surviving individual can rear the brood by itself are drastically reduced (Gill 1995). The majority of bat species produce a single altricial (naked and helpless), relatively large offspring at a time. Flight constraints may limit the ability of females to forage for food while gestating multiple young (Wilson 1997), and thus bat parental investment in a single offspring is substantial.

[7] The sociality and extreme longevity of African mole-rats have led comparative biologists to develop a "food-aridity" hypothesis to explain the spectrum of sociality seen in the family (Faulkes 1998). Constraints imposed by ecological factors (unpredictable rainfall) causing widely distributed roots led to living in large social groups with cooperation and reproductive suppression to better exploit an ecological niche where solitary animals would be unlikely to survive. The extended longevity of mole-rats is first a response to environment and then augmented by its sociality.

Table 2. Evolutionary changes in wasp longevity and social complexity.

Stage	Description	Key concepts and/or events	Life span (days)
I[a]	Solitary	Parasitoids; host as incubator of parasitoid larvae	14–60
II[b]	Nest as locus	Nest provides a protected microenvironment for female and brood; thus different selective factors operate; selection reduces senescence rates and increases life span	30–90
III[c]	Extensive parental care	Extensive parental care increases life span to one year; larval and pupal mortality reduced to near zero; this fosters reduction in birth rate; allows females to invest more resource for their own maintenance and for rearing of their offspring	60–365
IV[d]	Colony and queen concepts	Female's life further prolonged and overlaps with progeny which remain in nest to form extended family (helpers); colony rather than the individuals within it begins to become the unit of selection with the fate of the queen inextricably tied to fate of colony; a new level of individualism emerges (colony) and thus life of queen becomes adaptive to the long-term colony needs	180–1,000

[a] Example: spider wasp, *Natocyphus*
[b] Example: sand nesting wasps, *Haploneurion; Amophila*
[c] Example: progressive provisioning *Gorytes* spp.; and primitive paper wasps, *Stenogaster spp.*
[d] Example: advanced eusocial wasps including yellow jacket,*Vespula spp.*
Sources: Carey 2001a; Carey 2001b; Carey and Gruenfelder 1997; Evans 1958; Frank 1998; Holldobler and Wilson 1990; Michod 1999; Turner 2000; Wilson 1971; Wilson 1977.

solitary species (Table 1); the extended longevity of species in these different categories was a response to different types of environmental and socio-ecological problems. In this section, we consider the co-evolution of longevity extension and sociality in social wasps in a sequence of grades (Carey 2001a; Carey and Gruenfelder 1997; Evans 1958) that can be seen logically as evolutionary steps (Holldobler and Wilson 1990; Wilson 1971). Understanding this evolutionary progression from short-lived, solitary species to long-lived, eusocial species provides important perspective fostering understanding of the process of longevity extension in a broad array of social species.

This schema is summarized in Table 2. Basically, nesting behaviour and sociality result in improved micro-environmental conditions that foster greater survival; and that survival improves conditions for increased provisioning and more intensive social organization,

creating a positive feed back and longevity self-reinforcement. Incipient sociality creates conditions for the evolution of incremental increases in longevity that, in turn, create conditions for the evolution of more complex and innovative social structure. This positive feedback relationship is based on the demographic relationship between increased offspring survival and reduced birth rate, *ceteris paribus*. Because of the reduced costs of reproduction and parental care, female wasps with fewer offspring remained healthier longer, raised healthier offspring with higher survival rates that, in turn, fostered yet further reductions in mortality and reproduction. Greater longevity of parents also increased the likelihood that they can contribute as grandparents to the fitness of both their offspring and grand-offspring. Inasmuch as the principles of social evolution are general (Wilson 1977), it follows that the same pattern of evolution of longevity extension in social species will also be general. The main point is that the on-going process of longevity extension in social species adds age classes that increase the fitness of other age classes. This creates a dynamic that changes the rhythm and synchrony of life cycle events that alters the qualitative properties of the life history.

Foundational Principles: Longevity Extension in Social Systems

The purpose of this section is to describe three basic principles concerning longevity that emerge from the wasp example and will serve as the foundation for our theory that longevity extension is self-reinforcing in social animals. The underlying concept is that sociality initially evolved through natural selection to increase survival and/or reproduction through sharing and helping (Bonner 1980; Wilson 1977); that, as Wilson notes (Wilson 1998), the proximate rewards of cooperation (including status, power, sex, access, comfort, and health) are reflected in the universal bottom line of fitness including greater longevity and reproduction. However, these conditions then became both cause and consequence of extended adult longevity as an outcome of natural and kin selection. The evolutionary theory of ageing (Principle #1) serves as the basis by which adult longevity is initially extended, which then sets the stage for intergenerational transfer (Principle #2) and division of labour (Principle #3)—both of which underlie the self-reinforcing dynamic of prolonged life span.

PRINCIPLE #1: EVOLUTIONARY THEORY OF AGEING

Medawar (1957) proposed that if deleterious hereditary factors are expressed at some intermediate age and if the age of this expression is both variable and heritable, then selection will weed out earlier expressions more effectively than later expressions delaying the average age of expression and increasing longevity. As the force of selection is reduced by the declining reproductive value of increasingly older individuals, those deleterious traits will accumulate resulting in a mosaic and variable pattern of age-specific infirmity and thus senescence (Kirkwood 1997). This argument requires that reproductive value (Frank 1998) decreases with age and this will generally be true due to stochastic sources of mortality even in the absence of physiological deterioration. As more individuals live longer (especially due to reductions in early life mortality), the force of selection increases at later ages—weeding out later-expressing deleterious alleles—selection for somatic maintenance is prolonged and senescence is delayed (Charlesworth 1994; Medawar 1957; Roff 1992),

resulting in extended life spans.[8] Williams extended this line of thinking by noting that pleiotropic genes may have both beneficial and deleterious effects and, to the extent that beneficial effects precede deleterious, the genes may be selected for even in the face of their positive effect on mortality later in life (Williams 1957).

PRINCIPLE #2: INTERGENERATIONAL TRANSFERS

Investment of resources in reproduction can be extended to investment of resources in offspring and other relatives after birth. Increased per capita investment in offspring *decreases* juvenile mortality, *increases* the health and well-being of offspring and thus *improves* adult health and survival. At the extreme, older parents can 'bankroll' reproductive offspring and thus increase their production of grandchildren (Hill and Kaplan 1999; Kaplan *et al*. 2000). In systems where different age classes interact, natural selection will favour net transfers from old to young because the reproductive value of young individuals is greater (Frank 1998). However, intergenerational transfers can flow up as well as down generations (Lee 1997). If investment from older to younger individuals decreases mortality, then selection for increased longevity results and that investment can flow for a longer period. Selection for longevity also increases the return on higher levels or prolonged periods of investment. Intergenerational transfers are most prolonged in highly social species (Wilson 1971; Wilson 1977). While transfers of genetic information and resources from parents to offspring contribute to the evolution of longevity, additional forms and pathways of intergenerational transfer can elaborate and increase the rate of impact on longevity extension. Social learning and community level organization increase the pathways and volume of intergenerational transfers of information and the benefits that accrue from innovation (Boyd and Richerson 1985) and should be associated with more extreme longevity extension compared to related species with fewer transmission paths. In humans the transmission of longevity promoting genes and resources are augmented by culturally transmitted information ("memes," Dawkins 1976).

PRINCIPLE #3: DIVISION OF LABOUR

Division of labour distributes related tasks among members of a population in a coherent system of symbiotic relationships (Petersen 1986; Smith 1937). It is based on specialization of function—individuals use their differences in skill and/or resources to best advantage (Abramovitz 1989) and the energy returns per unit of labour increase.[9] The concept is fundamental to economics and business, as well as biology and anthropology, because it is the basis for increasing efficiency at all levels of organization—from enzymes and cells to organisms and societies. In addition to increased efficiency, division of labour:

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[8] Evolutionary theory of ageing postulates that the force of natural selection will decrease with age when populations are steady or increasing in size. It provides the conceptual foundation for two population genetic hypotheses to explain ageing: 1) *negative pleiotropy*—alleles that have beneficial effects in early components of fitness can also have deleterious effects on later components of fitness (Williams 1957); and 2) *mutation accumulation*—decrease in the force of natural selection with age results in little selection on deleterious mutations with effects confined to late life.

[9] Three principles emerged from Adam Smith's *Wealth of Nations* (Smith, 1776) Division of labour (i) is worthwhile when there is increased efficiency of production, (ii) pays only if the market is sufficiently large, and (iii) the extent depends on the ease of communication within a market of a given size (Smith 1999).

(1) accentuates individual differences; (2) produces new specialization through finer and finer task division; and (3) increases interdependencies—the entire colony will die if the queen dies, families are at great risk if a parent is lost (Wilson 1971). All of these outcomes have a direct bearing on longevity extension because they reduce innovation costs, increase the efficiency and thus the net resource return to the (kin) group, and increase the behavioural repertoire of the colony or community as a whole. The concept of a complex, integrated society is inextricably linked to the dual concepts of division of labour and individual continuity, and so, with individual specialization and longevity.

Model of Longevity Extension

Our objective in this section is to describe a general model of longevity extension in social species that builds on the three fundamental principles described in the previous section and on basic demographic and life-history tenets. A primary tenet is the cost of reproduction (Bell and Koufopanou 1986; Partridge and Harvey 1988; Reznick 1985); allocation of energy to reproduction removes its availability for somatic growth and repair and thus is reflected in increased mortality. The second tenet is that demographic/epidemiologic transition theory is based on declines in mortality that precede declines in fertility (Caldwell 1976; Demeny 1968; Keyfitz 1985; Notestein 1945). Changes in patterns of disease result in shifts in ages of deaths as well as changes in the age–sex structure of the population (Omran 1971; Preston *et al*. 1978; Ross 1982). Three principles presented in the previous section serve as the foundation for demographic shifts including mortality reduction in infants, reduction in numbers of births, improvement in parental health, and increase in offspring quality. All of these factors both contribute to, and interact with, longevity. Although we draw many of the concepts from the demographic literature, we believe that the model is general and applies to a wide range of both vertebrate and invertebrate species.

I: REDUCED INFANT MORTALITY

All else equal, increased survival from birth to sexual maturity improves energetic efficiency to the parent by decreasing reproductive waste (offspring who die prior to adulthood but after parental investment), and allows parents to either produce more young or to invest more per capita in existing young (Clutton-Brock 1991; Preston and Haines 1991; Szirmai 1997). Inasmuch as early reproduction in increasing populations will have a greater effect on fitness than later reproduction (Futuyma 1998), the former will out-compete the latter. But, even in increasing populations, increased *per capita* investment can be selected for if the age-specific increase in fitness of those offspring more than offsets losses due to numbers of young foregone. Increased resources available for reproduction can have any of the following effects depending on which age classes can access them: (1) increase number of young, (2) increase survival of young, (3) delay maturity of young by allowing the parental generation to support overlapping sets of offspring, and/or (4) reduce the cost of reproduction to mothers—"grandmothering" (Hawkes *et al*. 1998). The first will have no necessary effect on longevity while the latter three outcomes are conducive to longevity reinforcement through increased size, improved health, and better developed resource acquisition skills.

II: DEMOGRAPHIC TRANSITION

A general observation from studies on the comparative life histories of both invertebrate and vertebrate species is that an increase in offspring survival is followed by a decrease in fecundity (Clutton-Brock 1991; Ricklefs 1979). Most demographers and sociologists agree that one of the basic causes of a general decline in fertility is a reduction in mortality that reduces the number of births necessary to have any "desired" number of children (Montgomery and Cohen 1998; Preston 1978; Becker, 1991:135–154). Parents (especially mothers) with fewer offspring remain healthier due to reduced energy allocation to early stage parental effort (especially pregnancy and lactation in contrast to effort expended on older children), and healthier young with even higher survival rates at both young and old ages result (Walle 1986). The decline in fertility may also be understood as a balance between growing family size and declining economic advantage of family (Buikstra and Konigsberg 1985). The transition from simple agriculture to industrial economies devalues children as early producers. Whereas a young person on a farm becomes a useful member of the labour force at an early age (Cain 1977; Kaplan 1996), the young person in industrial or post-industrial society requires an extensive and expensive education (Ryder 1959). Kaplan's model of embodied human capital provides important insights into the trade-offs inherent in providing necessary skills to offspring versus producing additional offspring, and suggests that the inherent mechanisms of demographic transition characterized pre-transition humans as well (Kaplan *et al*. 2002). There is some empirical evidence that mothers in traditional horticultural/pastoral societies appear to produce optimal numbers of offspring to maximize their subsequent reproductive success (Borgerhoff Mulder 2000). Where heritable resources influence reproductive success there appears to be some trade-off between numbers of offspring produced and the per capita wealth that is inherited (Borgerhoff Mulder 1998).

III: IMPROVEMENT IN PARENTAL HEALTH AND SURVIVAL

Parents experiencing fewer births but unchanged reproduction remain healthier. Consequently they experience higher survival and can invest more of their resources in a smaller number of 'high quality' offspring—healthier, larger, more competitive (Clutton-Brock 1994), skilled and innovative (Preston and Haines 1991; Richard 2001). That healthier mothers produce healthier infants (Wood 1994) and that excessive maternity demands deplete maternal health is well documented (Hrdy 1999). In addition to intergenerational effects, reducing numbers of reproductive attempts without sacrificing reproductive output will improve the health and survivorship of first-generation mothers. The fitness benefits of this trajectory are even greater in species with long and costly post-infancy dependency. For example, improving the health and nutrition of girls and women and reducing maternal depletion improves the health of subsequent generations—because healthy, better educated mothers can provide high-quality care over an extended period including investments such as prolonged breast-feeding, increased vigilance, and longer education. Improved survivorship and competitive ability increases the number of productive adult (parent and grandparent) years relative to the number of juvenile/sub-adult years as well as the per year return—years of additional productivity that can further expand intergenerational transfers (Hawkes *et al*. 1998; Kaplan *et al*. 2000).

IV: INCREASE IN OFFSPRING QUALITY

A second result of a decrease in the number of offspring can be an increase in the average quality of a smaller number of offspring because the per capita amount of both depreciable (e.g. food, nutrients) and non-depreciable (e.g. vigilance, teaching) care will increase (Clutton-Brock 1991). For example, in humans a decrease in the number of children will increase the average quality of a smaller number of offspring in two respects. First, the nourishment a baby receives from its mother mediates its mortality risk due to infectious diseases early, and nutrition and exposure to infection after birth determine its susceptibility to disease in later life (Barker 1994; Elo and Preston 1992). Thus healthy mothers may prevent the early onset of the degenerative diseases of old age that are linked to inadequate cellular development early in life. The increase in childhood survival then fosters even further reductions in fertility and improvements in offspring quality. Second, parents can invest heavily in one or a small number of offspring for a longer period. Development of the brain, of language as a means of transmitting social learning, and of group size are characteristic of hominid evolution (Hammer and Foley 1996). Language as a mechanism for social (and therefore less hazardous) learning allowed humans to transmit information not only across generations via reproduction with variations that arise independent of real world problems, but also to transmit information directed toward solving ecological problems. Cultural transmission increased the production of innovation, the rate at which innovations dispersed, and allowed innovations to be directly targeted toward hazards of the environment that threatened survival.

Contemporary studies, demonstrating that family size is negatively related to high school graduation (Blake 1989a, 1989b), but this effect is mediated through resources (SES). These are modern incarnations of processes ongoing since the first information revolution in early *Homo sapiens*. Education is a measure of offspring 'quality' that impacts longevity in two respects. At the individual level, the relationship between educational attainment and longevity is well documented (Hoyert *et al*. 1999). Even if the correlation between these two is mediated by intelligence (as measured by IQ which is susceptible to poor prenatal and post natal environments including nutrition and social environment). At the societal level, economic growth can be attributed to advances in science and technology that are only possible through education and training of highly skilled specialists.[10] The focus of contemporary specialists on biomedical research (Cruse 1999; Nutton 1996; Szirmai 1997; Thomas 1977) is as natural as was the focus of *Homo erectus* on the use of fire to cook, warm, and deter predators.

INCREMENTAL INCREASE IN LONGEVITY AS CAUSE AND CONSEQUENCE

The culmination of the effects of Phases I–IV yields an overall increase in longevity that is related to the extent and speed of the resource, quality, and productivity changes noted

[10] Just as highly-trained industrial workers in the 19th and 20th centuries replaced untrained agrarian workers, highly educated technologists (someone who works with both their hands and theoretical knowledge such as X-ray technicians and computer workers) of the 21st century "Knowledge Society" will replace the industrial workers (Drucker 1993).

above. Reduced litter size, mortality, and increased parental investment are associated with a broad array of organisms with prolonged life spans. As generational overlap extends, healthy adults are longer-lived and thus become healthy grandparents who can contribute to offspring rearing and further increase the subsidies discussed above. In humans this process is exaggerated through the ability to transmit symbolic information across and within generations and at a tempo substantially faster than generation times. Solutions to environmental or physiological hazards are transmitted broad band across all age classes of the population rather than solely to younger age classes through genetic modes. Incremental increases in longevity increases survival at early ages through increased subsidization of development. This is a new and expanded way of viewing the "contract between the generations" that is invoked for economic transactions across age classes by economists (Szirmai 1997). When intergenerational transfers occur at the pace of generation times (via natural selection) the process is self-promoting but at a slower rate of increase than when multiple means and directions of information and resource flow are possible (Boyd and Richerson 1985). In humans the cognitive ability to target innovation to specific problems can result in technologies that further improve health and do so much more rapidly than could be accomplished by natural selection on random variation (Bonner 1980; Durham 1991). Better-educated, more innovative children then increase the rate of technological innovations (Chant 1989) that contribute to health and longevity (Cruse 1999; Nutton 1996) and higher adult survival to older and older ages. Innovation is spurred by the increased return through prolonged later life[11] to the increased number of surviving older adults who can benefit. Furthermore, expectations of increased benefits accrued through longer life may promote longevity itself (Becker 1998).

Model Application

HUMAN LONGEVITY IN BIODEMOGRAPHIC CONTEXT

A graphical perspective of the primate life span relative to life spans of other mammalian orders reveals two relationships that provide important context. First, the life spans of nearly all primate species are greater than those predicted by body mass alone. Chiroptera (bats) are the only other major (that is with more than a few species) group that uniformly exhibit greater life spans than those predicted from body mass alone (Figure 1). Primates are long-lived mammals with life spans of most species ranging from 1.25 to 1.5-fold greater than that predicted from body mass alone (Judge and Carey 2000). Humans, in turn, are long lived for a primate (Figure 2) with a life span over 2-fold greater than that predicted from body mass. Including primate brain mass in predictive regressions increased the human predicted life span into the region of eight to nine decades (depending on comparison group (Judge and Carey 2000). Anthropoid primates are relatively large brained, social, and have complex forms of communication. Language, as the co-evolutionary product

[11] Long life expectancy is one of the most important explanatory factors proposed by historians of technology to explain why technological developments accelerate. Long life gives prospective inventors the years necessary to accumulate technical knowledge, as well as the security to embark on long development programs yielding delayed rewards (Diamond 1998). Thus increases in life expectancy brought by modern medicine may have contributed to the recently accelerating pace of biomedical innovation and invention.

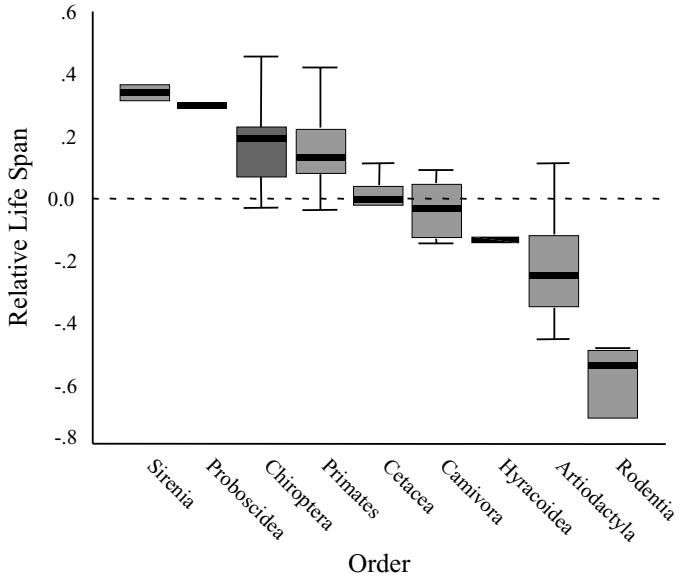

Figure 1. Relative life span (life span controlled for body size) for nine mammalian orders. Relative life-span is the record life span less the life-span value predicted from mammalian regression of life span on body mass. Predictions were calculated using ordinary least squares regression with log transformed values and case deletion. Sample comprises average logged values of species for 62 families of mammals in nine orders. Means are indicated within boxes. Source: Carey and Judge 2001.

of social and biological processes, changed the nature of information transfer across and within generations (Deacon 1997:349–365). Potential life span appears to have increased rapidly in *Homo* with predicted life spans into seven decades for *Homo erectus*, between eight and ten decades for *Homo sapiens*, and with a current record of 122 years (Allard *et al*. 1998)—over twice the life span of any other documented primate. Evidence of extensive intergenerational subsidization is widespread and has given rise to hypotheses regarding the role of grandmothers (Hawkes 1997; Hawkes *et al*. 1998) for which corroborative data are mixed (Hill and Hurtado 1991) and for parental investment more generally (Kaplan 1996). We believe that this model helps to explain the role of intergenerational transfers in the evolution of longevity and suggests that the specific transfer pathways may differ under varying ecologies.

PRIMATE ORIGINS OF LONGEVITY EXTENSION

Judge and Carey (2000) combined the primate life-span and body-mass data presented in Figure 2 with brain size to develop a regression equation for predicting the evolved life span of both modern humans and ancestral hominids (Table 3). The analysis revealed that humans, both archaic and modern, have a primate morphology that predicts a life span

Table 3. Estimates of longevity for fossil hominids (Judge and Carey 2000) based on hominoid body size relationships range from 42–44 years for *Australopithecus* to 50 years for *Homo erectus* (McHenry 1994). Incorporation of brain mass increased estimates for *Homo habilis* from 43 years to 52–56 years and for *Homo erectus* from 50 years to 60–63 years.

Hominid species	Life span (years)	Incremental change	Cumulative change
Australopithecus afarensis	46.6	8.4	8.4
Homo habilis	55.0	7.0	15.4
H. erectus	62.0	10.9	26.3
H. sapiens (pre-historical)	72.9	49.1	75.4
H. sapiens (contemporary)	122.0		

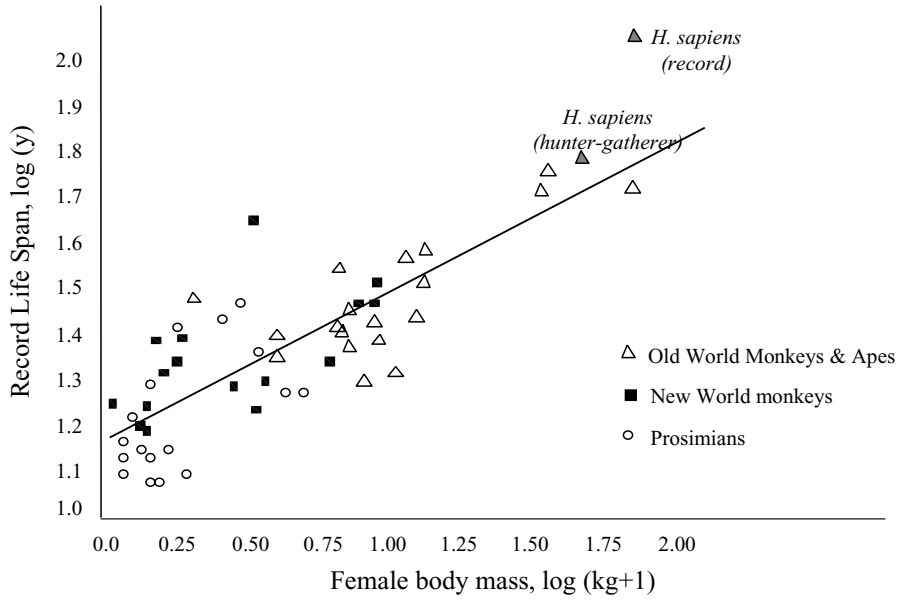

Figure 2. Record captive life spans by body size for primate genera. Mean record captive life spans (years) by female body mass (kg + 1) for 53 genera of primates. The left axis and abscissa are the log-transformed values used in ordinary least-squares regressions yielding a positive relationship with $r = 0.817$, $p < 0.001$, R^2 adjusted = .660); the right axis provides values in years. The statistical outlier in the midrange of body mass is the New World monkey, genus, *Cebus*, with a mean life span record of 46 years (Carey and Judge 2001).

of 72 to 90 years—well beyond the age of menopause in modern females.[12] These predictions also exceed other estimates (Angel 1969; Buikstra and Konigsberg 1985; Washburn 1981). With a primate longevity advantage, reduction of litter size to one, and shifts to a higher quality diet that required more skill to obtain (Kaplan 1996), hominids appear to have broken into the longevity feedback loop. Fossil evidence indicates that *H. erectus* demonstrated larger stature (McHenry 1994) and slower dental development, suggesting longer inter-birth intervals than earlier hominoids. This suggests overall increases in per offspring parental investment rather than translation of higher quality diet into more offspring. Greater adult life expectancy and generational overlap is required for the intergenerational transfers of resources, knowledge and skills in later *Homo.* Reductions in juvenile and sub-adult mortality, through adult subsidization of juvenile diet, probably increased life expectancy at birth as well as the age at sexual maturity. Thus, additional investment in individual young by parents was more likely to have a fitness payoff (Kaplan *et al*. 2000).

PREHISTORIC AND HISTORICAL PATTERNS OF LONGEVITY CHANGE

Human life spans that approach and sometimes exceed the "design capacity" indicated from primate allometry are not unusual in contemporary Western societies and may have been more common in early hunter-gatherer societies than is generally realized.[13] Studies of extant hunter-gatherers find that a significant proportion of those reaching adulthood live into their seventh decades (Hill and Kaplan 1999). As more people reach older ages, investments in health and well-being were more likely to yield returns, in terms of prolonged working life span, to more individuals. Historical developments substantially reduced early mortality—revealing design capacity longevity—and subsequently allowed technological attenuation of early senescing systems (e.g. eye glasses, dentures) (Fogel 1997; Landes 1998). Only with the last quarter century have humans pressed beyond the "design capacity for longevity" and extended that capacity with large scale systemic innovations such as joint replacement and organ transplants (Nutton 1996; Smith 1993; Thomas 1977). The self-reinforcing process of increasing life expectancy increasing age-specific productivity and thus both demand and resources for health improvements should occur only to the extent that productive life span is increased along with absolute life span.

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[12] We find it useful to deconstruct contemporary human life span (with a recorded maximum of 120 years; Robine 1998:174) into two segments: (1) the Darwinian or 'evolved' segment of 72–90 years; and (2) the post-Darwinian segment which is the component that emerged due to improved living conditions of modern society. The argument that human life span has not changed in 100,000 years (Fries 1980; Hayflick 2000) can be considered substantially correct when the 'evolved' life span is considered and is likely to include a post-reproductive period in females prior to the origin of *Homo sapiens* (Judge 2000). The argument is incorrect when the non-evolved segment of human life span is considered (Wilmoth 2000).

[13] Advent of sophisticated tool culture around 40,000 years ago led to efficiencies in hunting and food preparation but no major change in nomadic/hunter-gather life style until 12,000 years ago at end of last ice age with the emergence of agriculture. It is not at all clear that human health and longevity improved with the invention of agriculture since the settlement associated with agriculture also cultivated disease (Larsen 1995:153).

HEALTH, WEALTH AND LONGEVITY

It is intuitively obvious that wealth is conducive to longevity—wealthier nations have higher life expectancies and larger proportions of very elderly citizens (Bloom and WIlliamson 1998). However, at the population level, improvements in longevity are also conducive to improvements in wealth and thus create a so-called "virtuous spiral". Four main categories of relationships may account for this relationship (Bloom and Canning 2000): (1) *Productivity*. Longer-lived populations tend to be healthier and thus have higher labour productivity because workers are physically more energetic and mentally more robust for longer. Societies in which a large fraction of the population attains older ages can have a greater division of labour. (2) *Teaching, learning and education*. Long-lived people are repositories of knowledge, wisdom, and technical expertise and are therefore teachers and educators. Healthier people who live longer have stronger incentives to invest in developing their skills because they expect to reap those benefits over a longer period. Increased technical training and schooling promotes greater productivity and higher quality output and thus increases income. (3) *Investment in physical capital*. Improvements in health and longevity create an incentive to plan for the future, including the need for saving which, in turn, promotes greater investment. Investment promotes employment and workers will thus have access to more resources as their incomes rise. A healthy, long-lived, and educated workforce acts as a strong magnet for foreign investment. (4) *Demographic dividend*. The transition from high to low mortality rates, particularly in the young, typically trigger declines in fertility rates. This, in turn, increases the proportion of the population of working age that increases productivity. In addition, populations with large cohorts of older (retired) persons actually stimulate economic growth, presumably because they work or enable others to work by minding their children, and many continue to impart their accumulated knowledge to others.[14]

Implications of Longevity-Oriented Theory

We believe that the theory we describe in this paper has several important implications. First, expansion of the theoretical foundations of the finitude of life provides a new framework for discussing the future of human life span (Hayflick 2000; Manton and Stallard 1996; Vaupel *et al*. 1998; Wilmoth *et al*. 2000). In particular, it shifts discussion from the issue of mortality reduction based on putative limits imposed by the evolutionary theory of ageing, to discussion of a more inclusive process of longevity extension of which reduction in ageing rate is one component.

Second, a theory of longevity raises questions about the interpretation of results of studies on the biological mechanisms of ageing using model species such as fruit flies, laboratory rodents, and nematode worms, all of which are solitary (non-social) species. Inasmuch

[14] But as Hillman (1999) notes, common definitions of productivity are too narrow a measure of usefulness. Older parents may provide social support, information, etc. that is not captured in economic definitions. New York real estate developer Donald Trump once stated "Oftentimes, I will still pick up the phone to dial them (my parents) only to realize they're no longer there. I still want to share my successes and failures with them" (*New York Times*, February 7, 2001).

as our theory suggests that extended longevity in solitary species evolved under different ecological contexts than in social species, the underlying mechanisms of ageing between animals in these two broad categories may be different, and assumptions about age-specific reproductive value are certainly different. For example, the ageing response to caloric restriction (Sohal and Weindruch 1996; Weindruch 1996) in solitary species which must survive independent of a social group may be fundamentally different than the mechanisms in social species with evolved behaviours for helping, sharing, and food storage. Whereas ageing-oriented research necessarily focuses on lower levels of biological organization such as the molecule and cell, longevity-oriented theory focuses on the level of organization considered by many biologists to be the quintessence of biological relevance—the whole organism. All discoveries related to the rate of ageing at lower levels of biological organization must ultimately be tested at the level of the individual.

Third, our theory suggests that life span as a measure of length of life should be considered more central to life-history theory than has hitherto been the case. Life span as a concept is either absent from essentially all of the mainstream texts in ecology (Begon *et al*. 1996), evolution (Futuyma 1998), and population biology, or is discussed as an outcome variable of size and mortality (Roff 1992:120–121). Classic life-history theory treats life span as an outcome of the relative mortality of juvenile and adult stages and trade-offs between early and late reproduction (Stearns 1992). Evolution of life span per se is considered only in the context of the evolution of repeated reproduction (Stearns 1992:186). Inasmuch as life history theory is concerned with trade-offs, questions concerning trade-offs between extraordinary longevity and other traits must certainly constitute issues central to this area of inquiry.[15]

Fourth, a longevity-oriented theory concerns human longevity in the broader context of its life history (Hill and Kaplan 1999) and culture (Durham 1991). Whereas most anthropologists consider many traits such as covert ovulation, menopause, and speech as unique, and bipedalism, brain size, and the use of tools as exceptional, extended longevity remains unappreciated. Human life span should be considered nearly as extraordinary as human brain size. Life span receives scant attention in life history context and yet is 2.5-fold greater than would be predicted from body size alone (Judge and Carey 2000); whereas the brain, which receives considerable attention, is 3-fold greater than is predicted from body size alone (Diamond 1992).

Human Life Span Extension: a Framework for the Future

The extensions of human longevity occur through the same basic processes as in other organisms. The difference is not in the relationships of reproductive value, intergenerational transfer, or specialization, but in the mechanisms by which those processes are implemented. Intergenerational transfers are expanded beyond genetic and immediate resources

[15] For example, Moyle and Herbold (1987) found that there is a slightly higher percentage of fishes that either hide their brood or are live-bearers in western North America where stream and lake levels are less predictable than in eastern North America or Europe. More parental care is associated with greater longevity.

to include the information necessary to increase the production of resources, highly transferable and partible symbols of resources, and information about ecological problems that allow targeted adaptive responses. Specialization is developed beyond that in other species through these same unusual mechanisms.

The theory presented here extends Fogel and colleagues' concept of techno-physio evolution (Fogel 1994; Fogel 1997; Fogel and Costa 1997) which states that mortality reductions in human populations occur because our species has a level of control over our environment that is unprecedented among animals. The model demonstrates the link between the Fogel model and Becker's "demand for children," human capital and specialization (Becker 1991: 135–154; Becker and Murphy 1992). We argue then that advances in human longevity are the result of some special conditions within a broader evolutionary model applicable to animals more generally. This self-reinforcement model of longevity extension in humans integrates evolutionary (sociobiological) and economic processes that collectively apply to longevity extension in many social species. In other words, sociality evolved in many groups in response to the advantages of controlling the physical and biological environment. Advantages include protection from predators, temperature and humidity controls, and food acquisition, storage and production (Hill and Kaplan 1999; Turner 2000). Generalizing the concept reveals that humans are simply one of a number of social species in which longevity extension has occurred and is continuing to occur as a result of basic principles linking sociality and longevity extension. Our theory expands Fogel's time horizon from 300 years of modern technological development to the entire history of human technological development. Early technological developments influenced longevity through environmental modifications including the use of stone tools, control of fire, shelter construction, invention of farming, and the emergence of bureaucracies (Foley 1992; Zvelebil 1994). Subsequent technological changes in communication and organizational efficiency included the invention of writing and improvements in information transfer, improvements in transportation, industry, and sanitation (Cruse 1999; DeGregor 1985), and continuing scientific specialization such as cloning, genomics, and molecular techniques in biomedicine (Collins 1998; Gurdon and Colman 1999; Silver 1997). The cost of coordinating specialized workers may constrain the division of labour and specialization (Becker and Murphy 1992). The declining costs of coordination associated with the explosion of information technology over the past century may have contributed to increased specialization, increased rates of scientific progress and, we suggest, contributed to the vast increases in observed human life spans over the same period.

We believe that one of the most important contributions of a longevity-oriented theory is to re-frame the way scientists consider the future of human life expectancy. The more conventional ageing-oriented question is "How low do mortality rates have to go to substantially increase longevity in the future?" (Fries 1980; Olshansky *et al*. 2001), whereas the longevity-oriented question is "To what extent will future gains in longevity (or improvements in mortality) extend life expectancy further?" Whereas the ageing-oriented question assumes the age-specific improvements in survival impact only older ages, the self-reinforcing model argues that age-specific decrements in late life mortality can also have a positive effect on early survival and productivity through selection, intergenerational transfers of resources and information, and increasing innovation from specialization. The

longevity-oriented question recognizes a built-in dynamic whereby the effects of reducing mortality at one age are spread across multiple ages and thus amplify longevity extension effects. The longevity-oriented approach also suggests that the present trajectory of science and technology, including organ cloning, xenotransplantation, and molecular medicine will lead to 1) sweeping transformations in health, and 2) to what Wilson (1998) refers to as 'volitional evolution'—the decommissioning of natural selection so that individuals can make choices conducive to engineering a long life for themselves and their children (Baltimore 2001). As De Grey notes (2000), it is certain that human scientific knowledge and consequent technological prowess will continue to advance at a non-negligible rate for as long as civilization survives. It is thus likely that human longevity will continue to advance, and to have lasting and transformational effects on society.[16]

Conclusions

To understand human longevity we must look not only to our ability to control our environment, but also to our phylogenetic and historical legacy (Coe 1990; Foley 1995). Parental care is part of our mammalian heritage as is the tendency for females to be more risk-averse and males to be more risk-prone. Our anthropoid heritage produced long gestation times, single infant births, and long inter-birth intervals consonant with high levels of maternal effort; and sociality is a firmly established core heritage. Brain expansion and use of manufactured tools was linked to increased longevity in the genus *Homo.* With the fully modern brain, anatomy, and behavioural repertoire of *Homo sapiens* came an awareness of our own mortality and directed attempts to escape it. Our modern human heritage includes living in larger groups through the development of agriculture and subsequent sophistication (Diamond 1998). The outcome of these transitions is to "... we find less talk of life as an exercise in endurance, and of death in a hopeless cause; and we hear more of life as a seeking and a journeying." (Southern 1953). We are now in the era of emerging ability to control our actuarial destiny in response to the desire in humans throughout history to live comfortably and to delay death (Holliday 2001; Preston *et al*. 1978).

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[16] To borrow a metaphor from Peter Drucker in reference to long-term social change, like "... ocean currents deep below the hurricane-tormented surface of the seas..."(Drucker, 1993).

References

Abramovitz, M. (1989) "Manpower, capital, and technology". In: Abramovitz, M. (ed.), *Thinking About Growth: And Other Essays on Economic Growth and Welfare*. Cambridge: Cambridge University Press, pp. 173–186.

Allard, M., Lebre, V., and Robine, J.-M. (1998) *Jeanne Calment: From Van Bogh's time to ours, 122 extraordinary years*. New York: W. H. Freeman.

Angel, J. L. (1969) "The bases of paleodemography", *American Journal Physical Anthropology*, 30:427–438.

Austad, S. N. (1997) *Why We Age.* New York: John Wiley.

Baltimore, D. (2001) "Our genome unveiled", *Nature*, 409:814–816.

Barker, D. J. P. (1994) *Mothers, Babies, and Disease in Later Life.* Vol. 311, London: BMJ Publishing Group.

Becker, G. (1991) *A Treatise on the Family.* Cambridge, MA: Harvard University Press.

Becker, G., and Murphy, K. (1992) "The division of labor, coordination costs, and knowledge", *Quarterly Journal of Economics*, 107:1137–1160.

Begon, M., Harper, J. L., and Townsend, C. R. (1996) *Ecology.* London: Blackwell Science Ltd.

Bell, G., and Koufopanou, V. (1986) "The cost of reproduction". In: Dawkins, R. Ridley, M. (eds.), *Oxford Surveys in Evolutionary Biology*, Oxford: Oxford University Press, pp. 83–131.

Beshers, S. N., and Fewell, J. H. (2001) "Models of division of labor in social insects", *Annual Review of Entomology*, 46:413–440.

Blake, J. (1989a) *Family Size and Achievement.* Berkeley: University of California Press.

Blake, J. (1989b) "Number of siblings and educational attainment", *Science*, 245:32–36.

Bloom, D. E., and Canning, D. (2000) "The health and wealth of nations", *Science*, 287:1207–1209.

Bloom, D. E., and WIlliamson, J. G. (1998) "Demographic transitions and economic miracles in emerging Asia", *World Bank Economic Review*, 12:419–455.

Bonner, J. T. (1980) *The Evolution of Culture in Animals.* Princeton: Princeton University Press.

Borgerhoff Mulder, M. (1998) "The demographic transition: Are we any closer to an evolutionary explanation?", *Trends in Ecology and Evolution*, 13:266–270.

Borgerhoff Mulder, M. (2000) "Optimizing offspring: The quantity-quality tradeoff in agropastoral Kipsigis", *Evolution and Human Behavior*, 21:391–410.

Boyd, R., and Richerson, P. (1985) *Culture and the Evolutionary Process.* Chicago, IL: University of Chicago Press.

Bronson, F. H. (1998) "Global zones and reproduction". In: Knobil, E., Neill, J. D. (eds.), *Encyclopedia of Reproduction*. San Diego: Academic Press, pp. 452–460.

Buikstra, J. E., and Konigsberg, L. W. (1985) "Paleodemography: Critiques and controversies", *American Anthropologist*, 87:316–333.

Cain, M. (1977) "The economic activities of children in a village in Bangladesh", *Population and Development Review*, 3:201–208.

Caldwell, J. C. (1976) “Toward a restatement of demographic transition theory”, *Population Development and Review*, 2:321–366.

Carey, J. R. (2001a) “Demographic mechanisms for the evolution of long life in social insects”, *Experimental Gerontology*, 36:713–722.

Carey, J. R. (2001b) “Insect biodemography”, *Annual Review of Entomology*, 43:79–110.

Carey, J. R., and Gruenfelder, C. A. (1997) “Population biology of the elderly”. In: Wachter, K., Finch, C. (eds.), *From Zeus to the Salmon: The Biodemography of Aging*. Washington, DC: National Academy Press, pp. 127–160.

Carey, J. R., and Judge, D. S. (2000) *Longevity Records: Life Spans of Mammals, Birds, Amphibians, Reptiles and Fish.* Odense, Denmark: Odense University Press.

Carey, J. R., and Judge, D. S. (2001) “Principles of biodemography with special emphasis on human longevity”, *Population*, 13(1):9–40.

Chant, C. (1989) *Science, Technology, and Everyday Life 1870–1950*. New York: The Open University.

Charlesworth, B. (1994) *Evolution in Age-structured Populations.* Cambridge: Cambridge University Press.

Clutton-Brock, T. H. (1991) *The Evolution of Parental Care.* Princeton: Princeton University Press.

Clutton-Brock, T. H. (1994) “The costs of sex”. In: Short, R. V., Balaban, E. (eds.), *The Differences Between the Sexes*. Cambridge: Cambridge University Press, pp. 347–362.

Coe, C. L. (1990) “Psychobiology of maternal behavior in nonhuman primates”. In: Krasnegor, N. A., Bridges, R. S. (eds.), *Mammalian Parenting*. New York: Oxford University Press, pp. 157–183.

Collins, F. S. (1998) “New goals for the U.S. human genome project: 1998–2003”, *Science*, 282:682–689.

Comfort, A. (1961) “The life span of animals”, *Scientific American*, 205:108–119.

Cruse, J. M. (1999) “History of medicine: The metamorphosis of scientific medicine in the ever-present past”, *American Journal of the Medical Sciences*, 318:171–180.

Dawkins, R. (1976) *The Selfish Gene*, 2nd edn. Oxford, UK: Oxford University Press.

Deacon, T. (1997) *The Symbolic Species: The Co-evolution of Language and the Brain.* New York: WW Norton & Co.

DeGregor, T. R. (1985) *A Theory of Technology*. Ames: Iowa State University Press.

deGrey, A. D. N. J. (2000) “Gerontologists and the media: The dangers of over-pessimism”, *Biogerontology*, 1:369–370.

Demeny, P. (1968) “Early fertility decline in Austria-Hungary: A lesson in demographic transition”, *Daedalus*, 97:502–522.

Diamond, J. (1992) *The Third Chimpanzee.* New York: HarperPerennial.

Diamond, J. (1998) *Guns, Germs and Steel.* New York: W. W. Norton & Company.

Drucker, P. F. (1993) “The age of social transformation”, *Atlantic Monthly*, 272:53–80.

Dunbar, R. I. M. (1992) “Neocortex size as a constraint on group size in primates”, *Journal of Human Evolution*, 20:469–493.

Durham, W. H. (1991) *Coevolution*. Stanford: Stanford University Press.

Elo, I. T., and Preston, S. H. (1992) "Effects of early-life conditions on adult mortality: A review", *Population Index*, 58:186–212.

Evans, H. E. (1958) "The evolution of social life in wasps", *Proceedings of the 10th International Congress of Entomology*, 2:449–457.

Faulkes, C. G. (1998) "Naked mole-rats". In: Knobil, E., Neill, J. D. (eds.), *Encyclopedia of Reproduction*. San Diego: Academic Press, pp. 321–326.

Finch, C. E. (1990) *Longevity, Senescence, and the Genome.* Chicago: University of Chicago Press.

Fogel, R. W. (1993) "New sources and new techniques for the study of secular trends in nutritional status, health, mortality and the process of aging", *Historical Methods*, 26:5–43.

Fogel, R. W. (1994) "Economic growth, population theory, and physiology: The bearing of long-term processes on the making of economic policy", *American Economic Review*, 84:369–395.

Fogel, R. W. (1997) "Economic and social structure for an ageing population", *Philosophical Transactions of the Royal Society of London B*, 352:1905–1917.

Fogel, R. W., and Costa, D. L. (1997) "A theory of technophysio evolution, with some implications for forecasting population, health care costs, and pension costs", *Demography*, 34:49–66.

Foley, R. (1992) "Evolutionary ecology of fossil hominids". In: Smith, E. A., Winterhalder, B. (eds.), *Evolutionary Ecology and Human Behavior*. New York: Aldine de Gruyter, pp. 131–164.

Foley, R. (1995) *Humans Before Humanity.* Cambridge, Massachusetts: Blackwell Publishers Ltd.

Frank, S. A. (1998) *Foundations of Social Evolution.* Princeton: Princeton University Press.

Fries, J. F. (1980) "Aging, natural death, and the compression of morbidity", *The New England Journal of Medicine*, 303:130–135.

Futuyma, D. J. (1998) *Evolutionary Biology.* 3rd edn. Sunderland, Massachusetts: Sinauer Associates, Inc.

Gill, F. B. (1995) *Ornithology*. New York: W. H. Freeman and Company.

Goldwasser, L. (2001) "The biodemography of life span: Resources, allocation and metabolism", *Trends in Ecology and Evolution*, 16:536–538.

Gurdon, J. B., and Colman, A. (1999) "The future of cloning", *Nature*, 402:743–746.

Hakeem, A., Sandoval, R., Jones, M., and Allman, J. (1996) "Brain and life span in primates". In: Birren, J. (ed.), *Handbook of the Psychology of Aging,* NY: Academic Press, pp. 78–104.

Hammer, M., and Foley, R. (1996) "Longevity, life history and allometry: How long did hominids live?", *Human Evolution*, 11:61–66.

Hauser, P. M., and Duncan, O. D. (1959) *The Study of Population*. Chicago: University of Chicago Press.

Hawkes, K., O'Connell, J. F., and Blurton Jones, N. (1997) "Hadza women's time allocation, offspring provisioning, and the evolution of long postmenopausal life spans", *Current Anthropology*, 38:551–577 (with commentary).

Hawkes, K., O'Connell, J. F., Blurton Jones, N. G., Alvarez, H., and Charnov, E. L. (1998) "Grandmothering, menopause, and the evolution of human life histories", *Proceedings of the National Academy of Science*, 95:1336–1339.

Hayflick, L. (2000) "The future of ageing", *Nature*, 408:267–269.

Hill, K., and Hurtado, A. M. (1991) "The evolution of premature reproductive senescence and menopause in human females: An evaluation of the 'Grandmother hypothesis', ". *Human Nature*, 2:313–350.

Hill, K., and Kaplan, H. (1999) "Life history traits in humans: Theory and empirical studies", *Annual Review of Anthropology*, 28:397–430.

Hillman, J. (1999) *The Force of Character.* New York: Ballantine Books.

Holldobler, B., and Wilson, E. O. (1990) *The Ants.* Cambridge, Massachusetts: Harvard University Press.

Holliday, R. (2001) "Human ageing and the origins of religion", *Biogerontology*, 2:73–77.

Hoyert, D. L., Kochanek, K. D., and Murphy, S. L. (1999) "Deaths: Final data for 1997", *Center for Disease Control*, Atlanta.

Hrdy, S. B. (1999) *Mother Nature: A History of Mothers, Infants, and Natural Selection.* New York: Pantheon Books.

Judge, D. S., and Carey, J. R. (2000) "Postreproductive life predicted by primate patterns", *Journal of Gerontology: Biological Sciences*, 55A:B201–B209.

Kannisto, V., Lauritsen, J., Thatcher, A. R., and Vaupel, J. W. (1994) "Reductions in mortality at advanced ages: Several decades of evidence from 27 countries", *Population and Development Review*, 20:793–810.

Kaplan, H. (1996) "A theory of fertility and parental investment in traditional and modern human societies", *Yearbook of Physical Anthropology*, 39:91–135.

Kaplan, H., Hill, K., Lancaster, J., and Hurtado, A. M. (2000) "A theory of human life history evolution: Diet, intelligence, and longevity", *Evolutionary Anthropology*, 9:156–185.

Kaplan, H., Lancaster, J., Tucker, W. T., and Anderson, K. G. (2002) "Evolutionary approach to below replacement fertility", *American Journal of Human Biology*, 14:233–256.

Keyfitz, N. (1985) *Applied Mathematical Demography*, 2nd edn. New York: Springer-Verlag.

Kirkwood, T. B. L. (1992) "Comparative life spans of species: Why do species have the life spans they do?", *American Journal of Clinical Nutrition*, 55:1191S–1195S.

Kirkwood, T. B. L. (1997) "The origins of human ageing", *Philosophical Transactions of the Royal Society of London, Series B*, 353:1763–1772.

Landes, D. S. (1998) *The Wealth and Poverty of Nations*. New York: W. W. Norton & Company.

Larsen, C. S. (1995) "Biological changes in human populations with agriculture", *Annual Review of Anthropology*, 24:185–213.

Lee, R. D. (1997) "Intergenerational relations and the elderly". In: Wachter, K. W., Finch, C. E. (eds.), *Between Zeus and the Salmon. The Biodemography of Longevity*. Washington, D.C.: National Academy Press, pp. 213–233.

Manton, K. G., and Stallard, E. (1996) "Longevity in the United States: Age and sex-specific evidence on life span limits from mortality patterns 1960–1990". *Journal of Gerontology*, 51A:B362–B375.

McHenry, H. M. (1994) "Behavioral ecological implications of early hominid body size", *Journal of Human Evolution*, 27:77–87.

Medawar, P. B. (1955) "The definition and measurement of senescence". In: Wolstenholme, G. E. W., Cameron, M. P., Etherington, J. (eds.), *CIBA Foundation Colloquia on Ageing*. Boston: Little, Brown and Co.

Medawar, P. B. (1957) *The Uniqueness of the Individual.* New York: Dover Publications, Inc.

Michod, R. E. (1999) “Individuality, immortality, and sex”. In: Keller, L. (ed.), *Levels of Selection in Evolution*. Princeton: Princeton University Press, pp. 53–74.

Montgomery, M. R., and Cohen, B. (1998) *From Death to Birth: Mortality Decline and Reproductive Change*. Washington, D.C.: National Academy Press.

Moyle, P. B., and Herbold, B. (1987) “Life-history patterns and community structure in stream fishes of Western North America: Comparisons with Eastern North America and Europe”. In: Matthews, W. J., Heins, D. C. (eds.), *Community and Evolutionary Ecology of North American Stream Fishes*. Norman, Oklahoma: University of Oklahoma Press, pp. 25–34.

Notestein, F. (1945) “Population—the long view”. In: Schultz, T. W. (ed.), *Food for the World*. Chicago: University of Chicago Press.

Nutton, V. (1996) “The rise of medicine”. In: Porter, R. (ed.), *The Cambridge Illustrated History of Medicine*, Cambridge: Cambridge University Press, pp. 52–81.

Olshansky, S. J., Carnes, B. A., and Desesquelles, A. (2001) “Prospects for human longevity”, *Science*, 291:1491–1492.

Omran, A. R. (1971) “The epidemiologic transition: A theory of the epidemiology of population change”, *Milbank Memorial Fund Quarterly*, 49:509–538.

Partridge, L., and Harvey, P. H. (1988) “The ecological context of life history evolution”, *Science*, 241:1449–1455.

Petersen, W. (1986) *Dictionary of Demography.* Westport, Connecticut: Greenwood Press, Inc.

Philipson, T., and Becker, G. (1998) “Old-age longevity and mortality-contingent claims”, *Journal of Political Economy*, 106:551–573.

Preston, S. H. (1978) *The Effects of Infant and Child Mortality on Fertility*. New York: Academic Press.

Preston, S. H., and Haines, M. R. (1991) *Fatal Years: Child Mortality in Late Nineteenth-Century America.* Princeton: Princeton University Press.

Preston, S. H., Keyfitz, N., and Schoen, R. (1978) *Causes of Death: Life Tables for National Populations.* New York: Seminar Press.

Reznick, D. (1985) “Costs of reproduction: An evaluation of the empirical evidence”, *Oikos*, 44:257–267.

Richards, M., Hardy, R., Kuh, D., and Wadsworth, M.E.J. (2001) “Birth weight and cognitive function in the British 1946 birth cohort: Longitudinal population based study”, *British Medical Journal*, 322:199–203.

Ricklefs, R. E. (1979) *Ecology*, 2nd edn. New York: Chiron Press Incorporated.

Robine, J.-M., and Allard, M. (1998) “The oldest human”, *Science*, 279:1834–1835.

Roff, D. A. (1992) *The Evolution of Life Histories.* New York: Chapman & Hall.

Ross, J. A. (1982) *International Encyclopedia of Population*. New York: The Free Press.

Ryder, N. B. (1959) “Fertility”. In: Hauser, P. M., Duncan, O. D. (eds.), *The Study of Population*. Chicago: University of Chicago Press, pp. 400–426.

Sacher, G. A. (1978) “Longevity and aging in vertebrate evolution”, *Bioscience*, 28:497–501.

Silver, L. (1997) *Remaking Eden.* New York: Avon Books.

Smith, A. (1776) *The Wealth of Nations.* New York: Modern Library.

Smith, D. W. E. (1993) *Human Longevity.* New York: Oxford University Press.

Smith, J. M., and Szathmary, E. (1999) *The Major Transitions in Evolution.* Oxford: Oxford University Press.

Sohal, R. S., and Weindruch, R. (1996) "Oxidative stress, caloric restriction, and aging", *Science*, 273:59–63.

Southern, R. W. (1953) *The Making of the Middle Ages.* New Haven: Yale University Press.

Stearns, S. (1992) *The Evolution of Life Histories.* Oxford, UK: Oxford University Press.

Szirmai, A. (1997) *Economic and Social Development.* London: Prentice Hall.

Thomas, L. (1977) "On the science and technology of medicine", *Daedalus*, 106:35–46.

Tuljapurkar, S., Li, N., and Boe, C. (2000) "A universal pattern of mortality decline in the G7 countries", *Nature*, 405:789–792.

Turner, J. S. (2000) *The Extended Organism: The Physiology of Animal-built Structures.* Cambridge, Massachusetts: Harvard University Press.

Vaupel, J. W., Carey, J. R., Christensen, K., Johnson, T. E., and al., A. I. Y. e. (1998) "Biodemographic trajectories of longevity", *Science*, 280:855–860.

Wake, M. H. (1998) "Amphibian reproduction, overview". In: Knobil, E., Neill, J. D. (eds.), *Encyclopedia of Reproduction*. San Diego: Academic Press, pp. 161–166.

Walle, F. v. d. (1986) "Infant mortality and the European demographic transition". In: Coale, A. J., Watkins, S. C. (eds.), *The Decline of Fertility in Europe*. Princeton: Princeton University Press, pp. 201–233.

Washburn, S. L. (1981) "Longevity in primates". In: McGaugh, J. L., Kiesler, S. B. (eds.), *Aging: Biology and Behavior*. New York: Academic Press, pp. 11–29.

Weindruch, R. (1996) "Caloric restriction and aging", *Scientific American*, 274:46–52.

Williams, G. C. (1957) "Pleiotropy, natural selection, and the evolution of senescence", *Evolution*, 11:398–411.

Wilmoth, J. R., Deegan, L. J., Lundstrom, H., and Horiuchi, S. (2000) "Increase of maximum life-span in Sweden, 1861–1999", *Science*, 289:2366–2368.

Wilson, D. E. (1997) *Bats in Question.* Washington, D.C.: Smithsonian Institution Press.

Wilson, E. O. (1971) *The Insect Societies.* Cambridge, Massachusetts: Harvard University Press.

Wilson, E. O. (1977) *Sociobiology: The New Synthesis.* Cambridge, Massachusetts: Harvard University Press.

Wilson, E. O. (1998) *Consilience.* New York: Alfred A. Knopf.

Wood, J. W. (1994) *Dynamics of Human Reproduction.* New York: Aldine de Gruyter.

Zvelebil, M. (1994) "Plant use in the Mesolithic and the transition to farming", *Proceedings of the Prehistoric Society*, 60:35–74.

Section 2

Empirical and Analytical Studies of Ageing and Oldest-Old Populations

SECTION 2. EMPIRICAL AND ANALYTICAL STUDIES OF AGEING AND OLDEST-OLD POPULATIONS

Evidence from low mortality countries shows that the age-related mortality increase decelerates at old ages. In Chapter 4, Zeng Yi and James Vaupel show that this is also the case for China. The Kannisto two-parameter logistic model fits Han Chinese death rates at oldest-old ages better than the Gompertz and four other alternative models. Chinese death rates appear to be roughly similar to Swedish and Japanese rates after age 97 for both males and females. The authors think that reports of age appear to be reliable up to age 100 and perhaps age 105 in China, and that this convergence may be mainly due to mortality selection in the heterogeneous Chinese population. This convergence supports the hypothesis that the level of the mortality plateau, suggested by the logistic trajectory, may be quite independent of current environmental conditions. In this case, it can be quite difficult to forecast future changes in the oldest-old mortality. New data should confirm the accuracy of the age reporting for the oldest-old in China.

Despite a heated controversy on the compression of mortality, the distribution of the ages at death has been poorly examined. In Chapter 5, after a review of the existing central and dispersion indicators of individual life durations, Väinö Kannisto proposes new indicators, especially designed to tackle the question of the compression of mortality and the question of the rectangularization of the survival curve. For measuring the dispersion of individual life durations and the compression of mortality, the author proposes the C-family indicators—C10, C25, C50, and C90—which give the shortest age-interval in which a given percentage of all deaths takes place, and compares them with existing indicators such as the inter-quartile range of age at death (IQR). Kannisto also proposes a new index, R, to better monitor the phenomenon of rectangularization of the survival curve. Therefore this chapter provides new tools for the study of human longevity, to better describe the distribution of adult life durations and the shape of the survival curve.

Using more usual indicators, Wilma Nusselder examines in Chapter 6 these questions of compression of mortality and rectangularization of the survival curve for the Netherlands. The author analyses recent trends, from the early 1970s to the late 1990s, of old-age mortality—which follows in that country an unusual pattern for a Western country. Whereas life expectancy at age 60 increased during the whole period, since the 1980s life expectancy at age 85 actually declined in men although it remained constant in women. Nusselder explores the consequences of this trend for the compression of mortality and the rectangularization of the survival curve, showing that rectangularization of the survival curve occurred both in a relative sense and an absolute sense since 1980/84; and that despite the lack of increase in life expectancy at advanced ages, compression of mortality and tendency towards rectangularization continued during the late 1990s. This work shows

that, contrary to common sense, compression of mortality and rectangularization of the survival curve are not necessarily linked to increase in life expecatncy.

Age validation is not only a problem for developing countries but concerns all studies dealing with exceptional longevity. There is now a long list of "fairy tales" or rumours about supercentenarians in remote mountainous areas and isolated islands. Are Okinawa and Sardinia the modern versions of these tales? In Chapter 7, Michel Poulain and his colleagues discuss the age validation process used in the Sardinian study of centenarians. Sardinia is an area of exceptional interest because of the large reported proportion of male centenarians within the population. In many places, claims for exceptional numbers of centenarians and other unusual features, such as exceptional ages, have almost always been found to be based upon defective data. Therefore age validation is of tremendous importance for the Sardinian study of healthy longevity (AKEA), which found an unexpectedly low femininity ratio (female to male) among the centenarians. The chapter describes the validation process implemented during the years 2000 and 2001 and presents the main results of the validation.

Data quality is also the principal topic of Chapter 8, by Robert Bourbeau and Bertrand Desjardins, who review the most recent data on mortality of the very old in Canada. The chapter examines the precision of the reported ages at death. It presents the results of a linkage study and the corresponding mortality measures. While age validation is the main concern when studying exceptional longevity, study of mortality at extreme ages raises more questions about data quality. At extreme ages, the number of observations is ineluctably small and a few errors can have a substantial impact in the estimation of the mortality pattern. However, different methods such as the extinct generation method, using only observed deaths for cohorts which have been completely eliminated by mortality to reconstruct them, allow the authors to estimate with great accuracy the mortality pattern at extreme age for Canada and to compare it for a selection of low mortality countries, including France, Sweden, Japan and the United States.

CHAPTER 4. OLDEST-OLD MORTALITY IN CHINA

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Abstract

At very old ages mortality decelerates in developed countries. We show that this is also the case for China. We find that the Kannisto model, a two-parameter logistic formula, fits Han Chinese death rates at oldest-old ages better than the Gompertz and four other models. Chinese death rates appear to be roughly similar to Swedish and Japanese rates after age 97 for both males and females. Since reports of age appear to be serviceably reliable up to age 100 and perhaps age 105 in China, we think that this convergence may be mainly due to mortality selection in the heterogeneous Chinese population.

Introduction

Mounting evidence from developed countries indicates that at advanced ages death rates do not continue to rise exponentially. Instead, the increase in death rates decelerates (i.e. death rates rise more slowly than predicted by an exponential Gompertz curve) at the oldest ages (e.g. Vaupel *et al.* 1998; Kannisto, Lauritsen, Thatcher, and Vaupel 1994; Thatcher, Kannisto, and Vaupel 1998; Human Mortality Database 2002). Does mortality deceleration also occur in developing countries? More generally, what does the trajectory of mortality at advanced ages in a developing country look like? What are the similarities and differences compared with developed countries? Previous studies have not answered such questions because of data limitations.

China offers an unparalleled opportunity for studies in a developing country of the mortality of the very old—for two key reasons. First, the Chinese population is huge, totalling about 1.3 billion. Despite past high mortality, there are large numbers of the oldest-old today. The population of China is ageing rapidly (e.g. Banister 1990; Ogarwa 1988; Poston and Duan 2000). In particular, the number of octogenarians, nonagenarians and centenarians is growing at an extraordinarily rapid rate (Zeng and Vaupel 1989; Zeng and George 2000). Second, age reporting among very old Han Chinese appears to be acceptably reliable, as discussed below. This is important because misreporting of age bedevils demographic

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analyses of the very old in most developing countries as well as in the United States and some other developed countries (Coale and Kisker 1986; Preston *et al.* 1996; Elo and Preston 1994; Preston *et al.* 1998; Kannisto 1990).

Based on serviceably reliable data on Han Chinese mortality derived from the 1990 census, this article analyses the Han Chinese mortality trajectory at advanced ages and discusses the convergence of Han Chinese death rates with Japanese and Swedish rates after age 97. We also present the first Chinese life table for advanced ages, with a comparison to Japanese and Swedish life tables.

Data Resources

Coale and Li (1991) studied the mortality data from the 1982 Chinese census. This census not only obtained information on the living but also about those who had died in the previous year and a half. In these mortality data however, Han and ethnic minority populations are not distinguished and the last age category is 100+. Coale and Li found that death rates at very old ages are subject to serious distortion from mis-reported ages in the Xinjiang autonomous region. In Xinjiang, Han Chinese account for less than 40 percent of the total population. The majority belongs to the Uygur and other ethnic groups for which age is not reported reliably. At least up to age 100, however, Coale and Li concluded that Chinese death rates escape severe distortion if the data from Xinjiang are omitted (Coale and Li 1991:298–300).

The data we were able to use from the 1990 census include information about the ethnicity of those who had died in the previous year. Furthermore, data are available by single year of age up to the highest ages reported. Therefore, we were able to study mortality past age 100 and we were able to focus on the Han Chinese population.[1]

The population data from this census are by single year of age and refer to people alive on July 1, 1990. The 1990 Chinese census asked each household whether any household member had died in 1989 or in the first half of 1990. Information on the basic demographic characteristics, including ethnicity, of the deceased was collected. Previous studies have shown that the enumeration of deaths is more complete for the six-month period immediately prior to the census than for the preceding year (see, for example, Coale 1993). Adopting the approach suggested by Coale (1993), we estimated the age-specific number of deaths in the whole year of 1990 by doubling the death counts in the first half of 1990.

The data for the populations of people 80-years-old and older in Sweden and Japan are taken from the Kannisto–Thatcher Oldest-Old Mortality Database, which is available at www.demogr.mpg.de.

[1] There are 56 officially recognised ethnic groups in China. Some minority groups are well integrated with the Han Chinese and have shared Han culture for hundreds or thousands of years; the accuracy of their age reports is similar to that of the Han Chinese. However, the ethnic-specific sub-sample sizes are too small to allow us to distinguish the minority groups whose oldest-old accurately reported their ages from those who did not. We therefore exclusively use Han Chinese data to estimate the mortality trajectory at oldest-old ages. The Han accounted for about 92 percent of the total population in 1990.

The Quality of Age Reports for Very Old Han Chinese

The population age distribution and sex ratios at advanced ages for Han Chinese appear reasonable, as compared with those of Sweden and Japan (Wang *et al.* 1998:131, Table 2). Coale and Li (1991) proposed an index[2] for measuring the degree of digit preference at ages divisible by five or ten for older people. Wang *et al.* (1998) computed this index for the Han Chinese as well as for the populations of Sweden, Japan, France, Italy, and Germany from age 85 to 105, from age 95 to 105, and from age 100 to 105. The indices for the Han Chinese match the Swedish indices about as closely as the indices for the other populations (Wang *et al.* 1998:133, Table 3). Sweden is considered to be the country with the most reliable demographic data in the world, so it may indicate that the age reporting of the Han Chinese is serviceably reliable.

Whipple's index is a classic measurement for evaluating age heaping (Newell 1988:24–25). We compared Whipple's index for the Han Chinese vs. Sweden for male and female population counts and death counts at ages 65, 70, 75, 80, 85, 90, and 95. The United Nations recommends that if Whipple's index deviates by less than 5% from a perfect standard, then age reporting can be considered very accurate (United Nations 1955; Newell 1988). We used the Swedish data to establish a perfect standard and found that almost all of the Whipple indices we calculated using the Han Chinese data deviated by less than 5% from the standard.[3]

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[2] The index is defined as a mean of the ratios of the number at each age to a two-stage moving average (the five-term average of a five-term average).

[3] Whipple's Index for evaluating the general degree of age heaping in a population of all ages is usually calculated as:

$$\text{Whipple's Index} = \frac{(\text{sum of number at ages } 25,30,\ldots,55,60) * 100 * 5}{\text{Total number between ages 23 and 62}}$$

The value of Whipple's Index in a population with perfect age reporting as well as no large changes in fertility, mortality, and migration for a long time would be 100. The United Nations recommended a standard for measuring the age heaping as follows:

Whipple's Index	*Quality of data*	*Deviation from perfect*
<105	Very accurate	<5%
105–110	Relatively accurate	5–9.99%
110–125	OK	10–24.9%
125–175	Bad	25–74.99%
>175	Very bad	>=75%

The choice of 23 and 62 as the age-band limits to be examined in the classic Whipple's Index calculation is arbitrary but has been found most suitable for the practical purpose of measuring age heaping in general in a population of all ages (United Nations, 1955:39–45). However, this age band cannot be used for the oldest-old since it excludes persons above age 62. We therefore define Whipple's Index for the oldest-old survivors or deaths at age x and over as follows:

$$\text{Whipple's Index for the oldest-old} = \frac{(\text{sum of number at ages } 65,70,\ldots,90,95) * 100 * 5}{\text{Total number between ages 63 and 97}}$$

Wang *et al.* (1998) evaluated Han Chinese centenarians' age reporting by comparing its Whipple Index with ages 93 and 107 as the age band limits to the Swedish WI. They found that the WI for the Han Chinese centenarians deviated by less than 5% from the Swedish standard.

The above analysis shows the lack of severe age heaping for the Han Chinese elderly population. The absence of significant digit preference at ages divisible by five or ten, however, is not necessarily proof of data accuracy, since other kinds of errors in age misreporting may also distort the data quality. One way of addressing this issue is to examine the reported population at very old ages relative to the total elderly population. As shown by Coale and Kisker (1986), the proportion of those aged 95 or over among people aged 70 or over in 23 countries with accurate data was always less than six per thousand. This proportion in 28 countries with poor data ranged from one percent to ten percent (Coale and Kisker 1986). The proportions of those male and female Han Chinese aged 95 or over among those aged 70 or over in 1990 is 0.76 per thousand and 2.18 per thousand respectively, which are almost exactly the same as the values for Sweden in the period 1985–1994. The male and female proportions of those aged 100 or over among those aged 75 or over for the Han Chinese in 1990 were 0.128 and 0.388 per thousand. The corresponding proportions for the Swedish population in 1985–1994 were 0.127 and 0.386 per thousand. The close correspondence of these values for Han Chinese and Swedes is undoubtedly a coincidence because the measure is determined by a complicated interplay of the number of births in cohorts that are now very old and the survivorship of these cohorts. Nonetheless, the low values of the measure for the Han Chinese suggests that age may be reported fairly reliably, even at very old ages.

Coale and Kisker (1986:389–390) plotted the ratio of e_{70} (life expectation at age 70) against l_{70}/l_5 (conditional survival probability from age 5 to age 70) for the female populations in countries or regions with good data.[4] They found a close relationship between e_{70} and l_{70}/l_5 among countries or regions with good data; they captured the relationship by a third-degree polynomial curve fitted by least squares (Coale and Kisker 1986:389, Figure 1). Plots of e_{70} against l_{70}/l_5 for the female populations in countries with poor data[5] all lie far above this curve (Coale and Kisker 1986:390, Figure 2). We computed the ratio of e_{70} to l_{70}/l_5 for the Han Chinese female population in 1990. The Han Chinese ratio is almost exactly on Coale and Kisker's curve.

The evidence discussed above shows that the age reporting of Han Chinese people, who account for 92 percent of the total population, is probably acceptably reliable. Almost all Han Chinese, however, even if illiterate, can supply a precise date of birth. Younger, educated Han can supply their birth date according to the Western calendar. Older, illiterate Han can supply a birth date according to the traditional Chinese calendar combined with the animal year of birth.[6] Such a date can be easily translated to the Western calendar by census enumerators using a standard coding form (Coale and Li 1991:294).

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[4] Countries or regions with good data include Sweden, Austria, Belgium, Czechoslovakia, Denmark, England, Finland, France, Germany, Hungary, Ireland, Italy, Japan, Luxembourg, Netherlands, Norway, New Zealand, Scotland, Switzerland and Taiwan.

[5] Countries with poor data include Bolivia, Costa Rica, El Salvador, Guatemala, Honduras, Malaysia, Mexico, Panama, Peru, Philippines, Sri Lanka and Thailand.

[6] The precise date of birth is significant when deciding important life events—such as marriage matchmaking, date of marriage, starting to build a house, date of travelling, etc., according to the Han Chinese cultural tradition.

Reports, however, of ages of 106 and above seem to us to be too questionable to be useable. Even if only a tiny proportion of younger elderly misreport their age, serious distortions can occur at age 106 and over when these younger elderly falsely "survive" to age, 106+, since most other younger elderly who report their age correctly cannot survive to age 106+. (Wang *et al.* 1998). Furthermore, population sizes are so small at these extreme ages that the estimated death rates fluctuate widely. Therefore, we limit our analysis to ages 105 and younger in this article, and we are cautious about the possibility that age misreporting may affect estimated values beyond age 97 or so. We present 95% confidence intervals for estimated age-specific death rates to show how much small population size affects the estimates.

Age Trajectory of Han Chinese Mortality at Oldest-Old Ages

Male central death rates rise from 0.14 at age 80 to about 0.45 at age 96 and then start to fluctuate substantially. Female central death rates increase from 0.10 at age 80 to about 0.42 at age 100; they tend to moderately increase up to age 105 (see Tables 3a and 3b). After age 96, Han Chinese age-specific mortality probabilities show sizeable irregularities and a widening 95% confidence interval (see Figures 1a and 1b). The likelihood ratio test shows that the overall difference between male and female Han Chinese death rates after age 80 is statistically significant[7]. The gender differentials of the death rates at oldest-old ages tend to decrease with age: female death rates at ages 80–84 are 26 percent lower than male rates, but by ages 100–105 the female advantage is only 16 percent, as shown in Table 1.

Using maximum likelihood estimation procedures as implemented in JMP Software (SAS Institute 2002), we fit Gompertz, Weibull, Heligman and Pollard, Quadratic, Logistic, and Kannisto mortality models to observed single-year age-specific numbers of death counts and persons alive for the Han Chinese. Detailed description and discussion of these models, which are summarized in Appendix Table A-1, can be found in Thatcher, Kannisto, and Vaupel (1998). We fitted the six models to the observed data at ages 80 up to and including 96. The age 96 was chosen as the upper limit because there are only small fluctuations in the observed rates up to this age for both males and females; but considerable fluctuations exist after age 96, as shown in Figures 1a and 1b. Furthermore, we wanted to be cautious in using

[7] The results of the likelihood ratio test on the gender differentials of Han Chinese mortality at oldest-old ages are as follows:

	Log of Maximum Likelihood
Male and female separately (B)	Male: −7898766.3; Female: −7494039.6
Male and female combined (A)	−15463396
The statistics: −2*log(LA/LB)	1411802
$X^2_{1.95} = 0.004$	

Therefore, the H_0 hypothesis of no differences between males and females is rejected: i.e. there is a significant difference between the male and female mortality of Han Chinese at oldest-old ages.

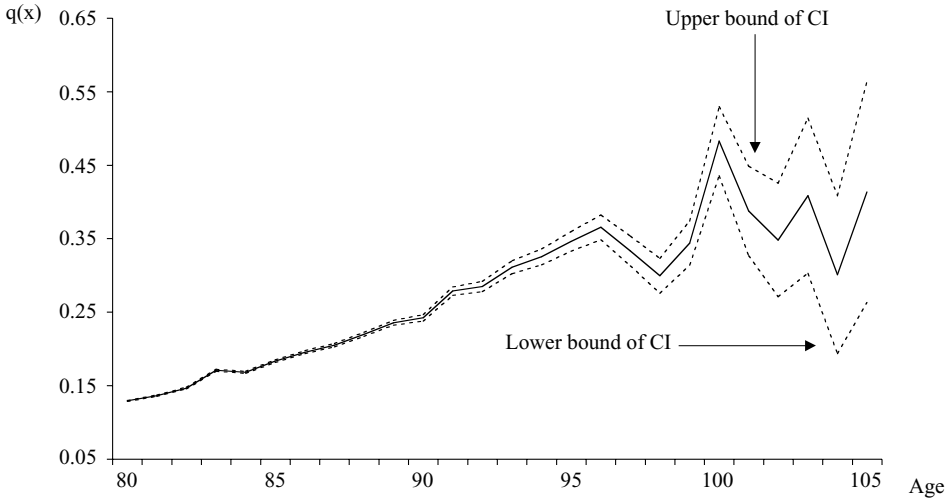

Figure 1a. Single Age-specific Probability of Death and 95% Confidence Interval Han Chinese, 1990, Males.

age-specific data pertaining to advanced ages greater than 96. The estimated parameters of the models fit to the Chinese oldest-old mortality data at ages 80–96 are given in Appendix Table A-1. These parameters were used to calculate predicted values of q(x) from ages 80 to 105, assuming that the models continue to hold after age 96.

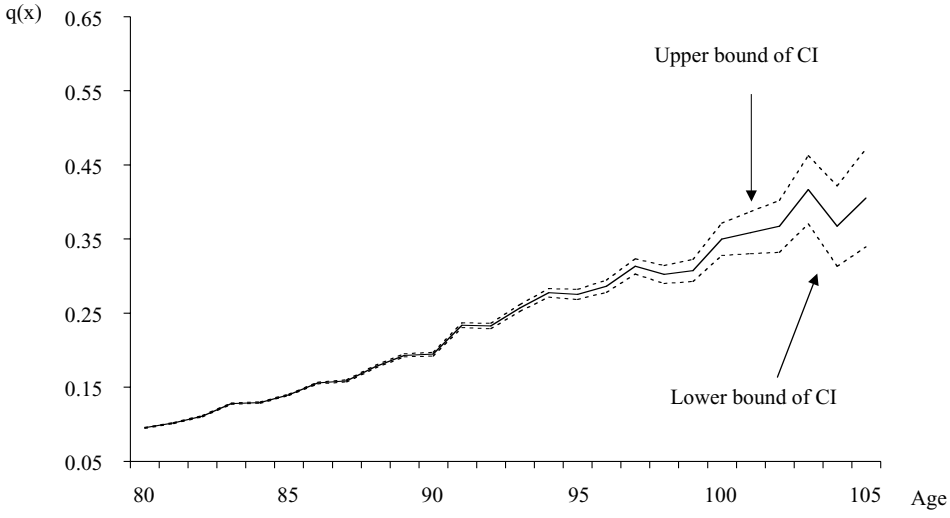

Figure 1b. Single Age-specific Probability of Death and 95% Confidence Interval Han Chinese, 1990, Females.

Table 1. Five-year age specific death rates at oldest-old ages for Han Chinese, 1990.

Age	Male	Female	(Female-male)/Male
80–84	0.1571 (0.1566–0.1576)	0.1165 (0.1161–0.1168)	−25.8%
85–89	0.2232 (0.2221–0.2243)	0.1727 (0.1720–0.1733)	−22.6%
90–94	0.3151 (0.3120–0.3183)	0.2541 (0.2524–0.2559)	−19.4%
95–99	0.4146 (0.4051–0.4241)	0.3396 (0.3349–0.3443)	−18.1%
100–105	0.5290 (0.4945–0.5646)	0.4459 (0.4268–0.4592)	−15.7%

Note: Figures in parentheses are 95% Confidence Interval.

The predicted values of q(x) at ages 80–105 are compared with the observed ones in Figures 2a and 2b (and listed in Appendix Tables A-2 and A-3). The predicted values of q(x) at ages 97–105 are entirely based on the observed data at ages 80–96 and thus independent of the observed values with which they are being compared. Thatcher *et al.* (1998) followed a similar procedure of fitting models to data at "younger" ages and extrapolating the fits to the oldest ages. One of the main purposes of our model fitting is to test whether the parameter estimates of a model based on the good data at ages 80–96 can be used to reasonably predict the observed rates after age 96.

On the scales used in depicting the model fits to the data at ages 80–96, the six models are practically indistinguishable up to age 96 and all remarkably close to the observed data. The various models then start to diverge, as shown in Figures 2a and 2b. After age 96, the highest predictions of mortality are given by Gompertz model. The lowest predictions are provided by the Kannisto model, which is a simplified two-parameter logistic model. The other four models are in between. The predictions of the Kannisto model tend to be closest to the empirical observations at most ages above 96 for both males and females; and these predictions are generally within the 95% confidence bounds on the data. The model tends, however, to yield predictions that are above the observed death rates at the highest ages.

Thatcher *et al.* (1998) conclude that the Kannisto model provides the best two-parameter fit to the data for the developed countries they analysed. It is possible that age misreporting or perhaps underreporting of deaths resulted in some underestimation of Han Chinese death rates after age 96 in the 1990 census. If so, the projected values of the Kannisto model might provide an approximate depiction of Chinese mortality at advanced ages. On the other hand, it is also possible that the Han Chinese data are serviceably accurate after age 96, perhaps up to age 100 or so and perhaps even up to age 105. If so, then the pattern of Chinese death rates at the highest ages might reflect not only current conditions but also the legacy of very high mortality at younger ages at earlier dates. That is, the relatively low level of Chinese mortality after age 96 might be a result of mortality selection (i.e., the death of the frail) in the cohorts that have reached extreme old age.

There is certainly some age misreporting and death underreporting among the oldest-old in China but it is not clear how much. Mortality selection undoubtedly affects the trajectory

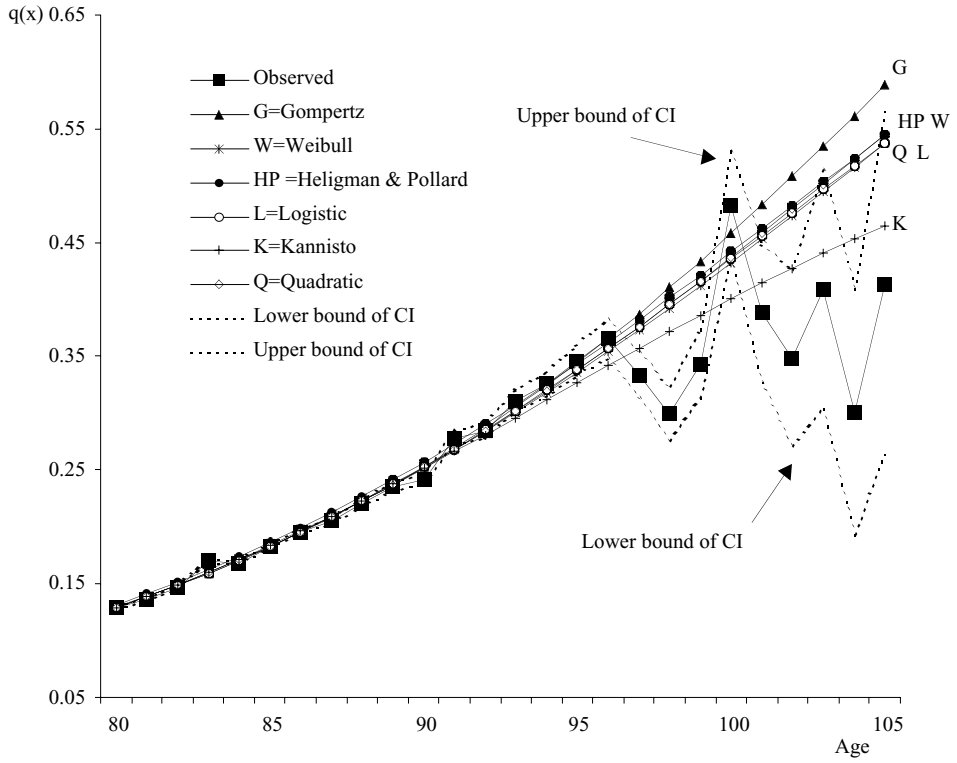

Figure 2a. Observed q(x) and the model fittings to the data at ages 80–96, and the extrapolated q(x) from age 97 to age 105 based on the model prediction, Han Chinese, 1990, Males.

of mortality at advanced ages, but whether such selection would pull death rates below the projected values of the Kannisto model in China (but not for the 13 developed countries studied by Thatcher *et al.* (1998)) is questionable. We conjecture that the Kannisto model may provide a rough mid-to-upper bound to the trajectory of Chinese mortality after age 96 and that the empirical data may provide an approximate and rather erratic mid-to-lower bound. Whenever appropriate in the rest of this article, we present and discuss both trajectories.

We also fitted Gompertz, Weibull, Heligman and Pollard, Quadratic, Logistic, and Kannisto mortality models to observed age-specific numbers of death counts and persons alive from ages 80 to 105 for the Han Chinese, following maximum likelihood estimation procedures. The male and female curves of the Kannisto model fit to data at ages 80–105 are almost identical to those fit to data at ages 80–96. Compared with the other five models, the fits of the Kannisto model based on either data at ages 80–105 or data at ages 80–96 tend to

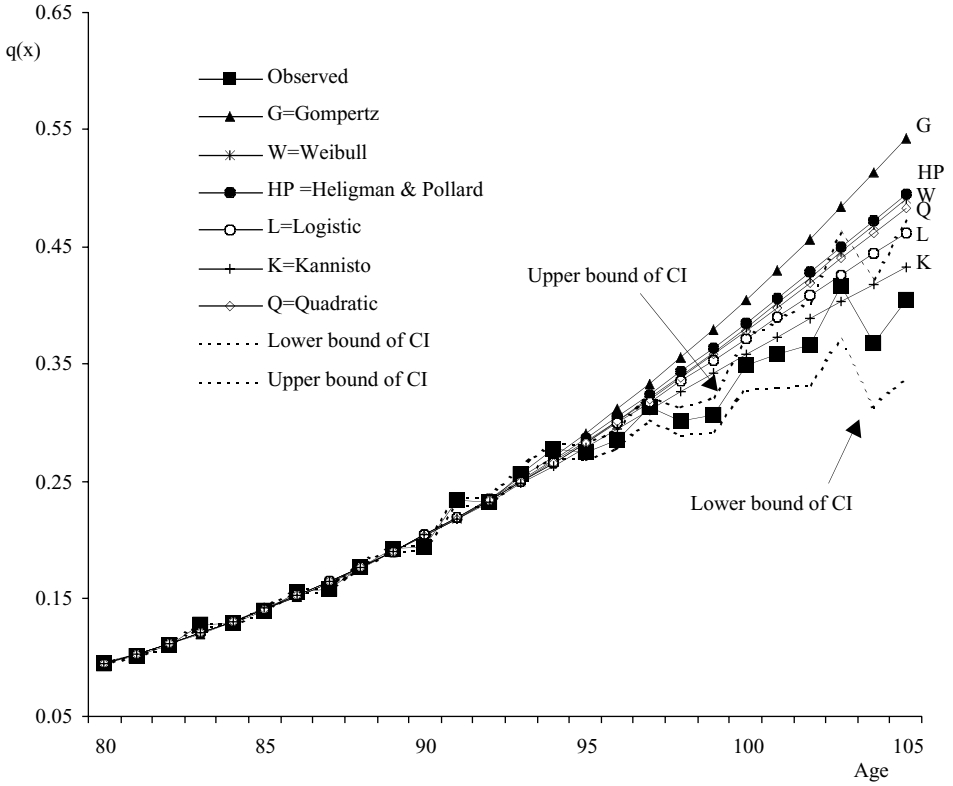

Figure 2b. Observed q(x) and the model fittings to the data at ages 80–96, and the extrapolated q(x) from age 97 to age 105 based on the model prediction, Han Chinese, 1990, Females.

be closer to the observed values at advanced ages. These additional model-fitting efforts (see Figures 3a and 3b) further support our earlier argument that the Kannisto model may provide a rough mid-to-upper bound to the trajectory of Chinese mortality after age 96.

In any case, it seems clear from Figures 2a, 2b, 3a, and 3b that a Gompertz curve fails to capture the trajectory of Chinese mortality at the highest ages. Unless there is very severe age misreporting or underreporting of deaths, which seems unlikely, death rates rise more slowly than predicted by an exponential Gompertz curve fit to the data at ages 80–96 and ages 80–105. In contrast, the Kannisto, Logistic, and Quadratic models (especially the Kannisto model) fit the data much better than the exponential Gompertz model. These results indicate that mortality deceleration appears to hold in the developing country of China as well as in developed countries.

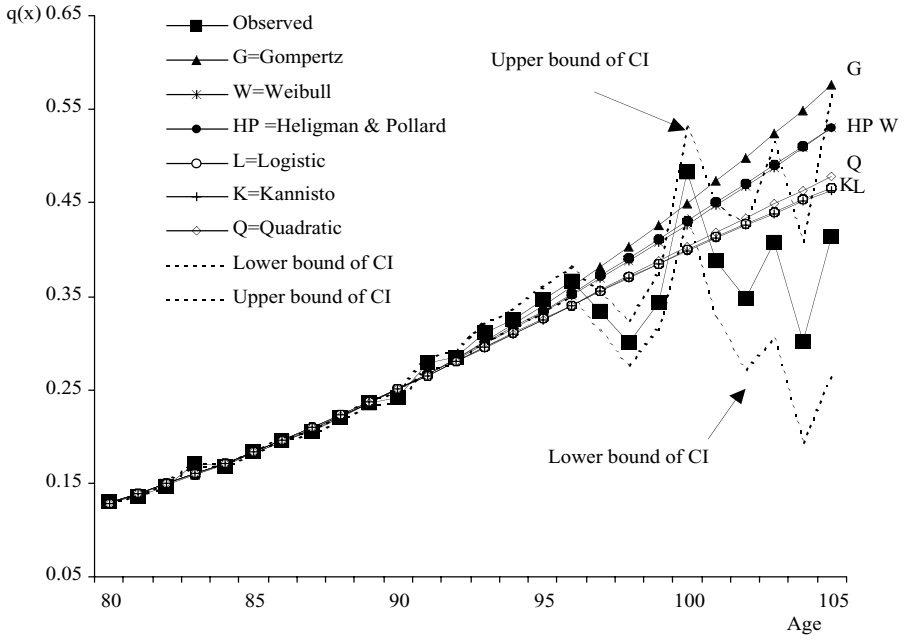

Figure 3a. Observed q(x) and the model fittings to the data at ages 80–105 Han Chinese, 1990, Males.

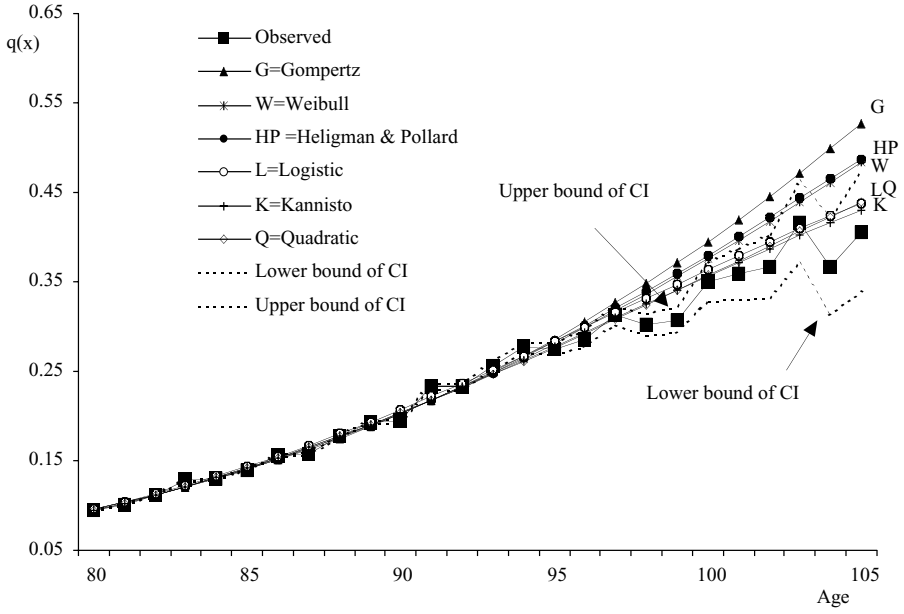

Figure 3b. Observed q(x) and the model fittings to the data at ages 80–105 Han Chinese, 1990, Females.

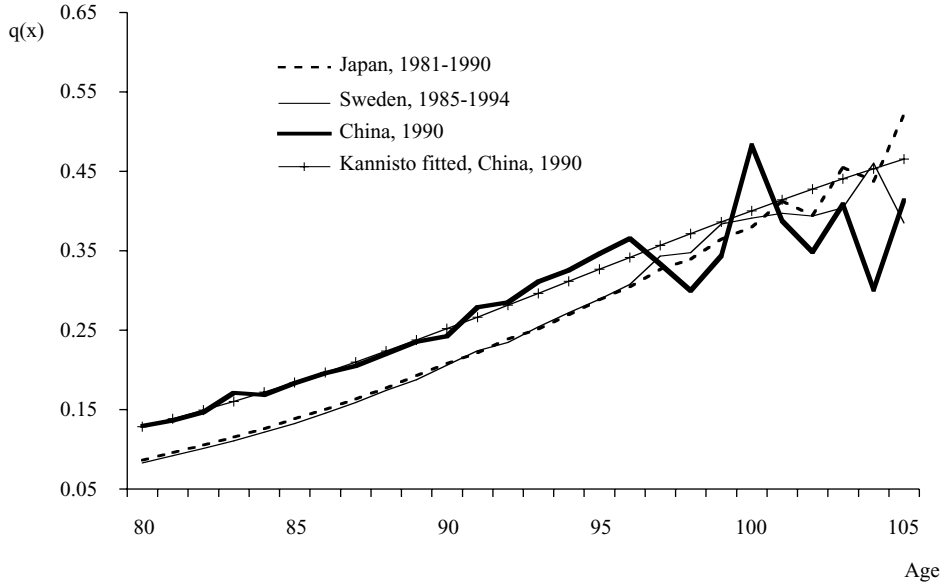

Figure 4a. Comparison of death probabilities, observed Han Chinese 1990, Kannsito model Fitted Han Chinese 1990, Japanese 1981–1990, and Swedish 1985–1994, males.

Convergence of Han Chinese Mortality with Japanese and Swedish Mortality

In Figures 4a and 4b we plot age-specific probabilities of death for Han Chinese, Swedish and Japanese males and females from ages 80 to 105. For the Han Chinese the empirical data is plotted as well as the projected values of the Kannisto model. The likelihood ratio test shows that the overall difference between the magnitudes of Chinese vs. Japanese and Swedish mortality at ages 80 and over is statistically significant.[8] The general age

[8] The results of the likelihood ratio test on the difference between the Han Chinese and Japanese/Swedish death rates at oldest-old ages are as follows:

	Log of Maximum Likelihood				
	Han Chinese	Japanese	Swedish	Han Chinese & Japanese	Han Chinese & Swedish
Male	−7898766.3	−6098723	−1335918	−13922471	9246201
Female	−7494039.6	−6108900	−1347457	−13695912	8886068

Statistics	Han Chinese & Japanese	Han Chinese & Swedish
Male	150036	23034
Females	185946	44572

$X^2_{1,95} = 0.004$

Therefore, the H_0 hypothesis of no differences between the male and female Han Chinese and Japanese death rates at oldest-old ages is rejected, as well as for the Han Chinese and Swedish death rates.

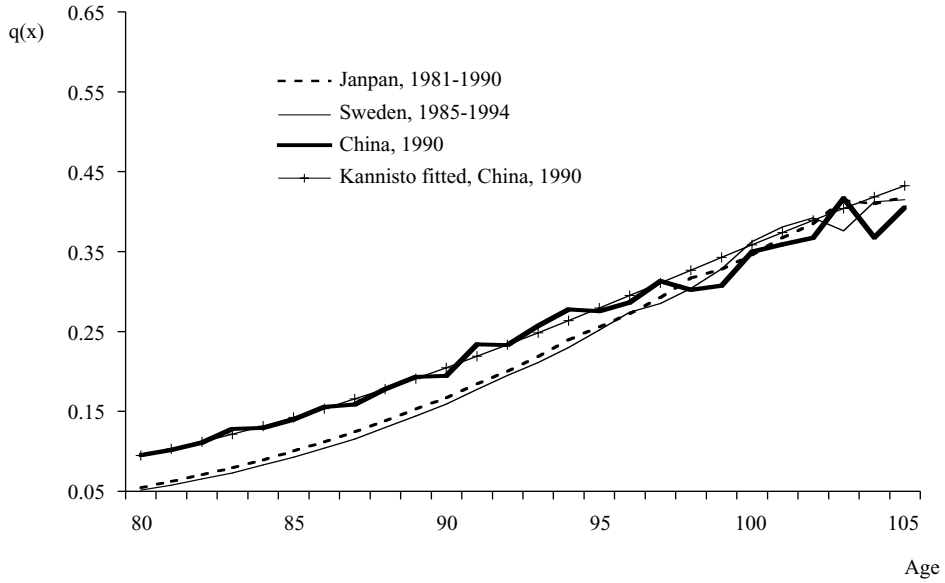

Figure 4b. Comparison of death probabilities, observed Han Chinese 1990, Kannisto model fitted Han Chinese 1990, Japanese 1981–1990, and Swedish 1985–1994, females.

patterns of the mortality are, however, roughly similar, with some evidence of convergence of the Han Chinese probabilities toward the Swedish and Japanese ones at the oldest ages. Note that the Han Chinese mortality trajectories shown in Figures 4a and 4b are based on data for one year—1990—only. The Japanese and Swedish curves shown in the same figures are based on data covering 10 years, since too many random fluctuations (due to small population sizes) would be present if they were based on the data for a single year. This fact concretely demonstrates the advantage of using data for China, with its huge population, to study mortality at advanced ages.

For both males and females, Han Chinese death probabilities are higher than the corresponding Japanese and Swedish ones before age 97. The empirical data after this age suggest a possible crossover; the Kannisto model suggests rough convergence. How can one explain this convergence or modest crossover after age 97? Some age misreporting and death underreporting could account for the pattern. On the other hand, the convergence or crossover could be real and could reflect the impact of mortality selection in heterogeneous populations. In this regard, a brief discussion of black–white mortality crossover in the United States is informative.

A crossover of the age trajectories of black vs. white death rates in the U.S. at ages over 75 has been observed in both cross-sectional and cohort studies. The death rates of black Americans were substantially lower than the white rates after the crossover, especially at

the oldest-old ages over 85 (see, e.g., Kitagawa and Hauser 1973; Nam and Okay 1977; Thornton and Nam 1972). Black Americans were subject to more adverse health conditions during childhood and adulthood, as compared to white Americans. Some scholars, therefore, believe that the more vulnerable members of a cohort die at high rates, leaving behind an exceptionally hardy group of survivors at older ages. The crossover has provided empirical underpinnings for a "survival of the fittest" mechanism operating on old-age mortality (Manton, Stallard, and Vaupel 1981; McCord and Feeman 1990; Otten *et al.* 1990; Zopf 1992). Other scholars suggest, however, that cohorts subject to severe health conditions in early life also experience elevated mortality in later life (Elo and Preston 1992; Mosley and Gray 1993). Coale and Kisker (1986) use indirect evidence to suggest that most instances of mortality crossovers simply reflect inaccurate data at older ages.

The age at which the black death rates start to fall below white levels, the crossover age, has been increasing over time: from ages 75 or so to 88 or more in various studies over the past a few decades. The increase in the crossover age is probably due to the improvement in the quality of black (and white) mortality data (Markides and Black 1996; Corti *et al.* 1999; Lynch, Brown, and Harmsen 2000). Preston and his colleagues recently carried out a rigorous investigation on the quality of age reporting by blacks and whites at old ages. They linked a sample of death certificates of persons aged 65+ in 1985 to records for the same individuals in the U.S. censuses of 1900, 1910, and 1920 and to records of the Social Security Administration. When corrected ages at death are used to estimate age-specific death rates, the death rates of blacks above age 85 increase substantially (Preston *et al.*, 1996). Nonetheless, a crossover appears to exist—at around age 95 for males and in the age range of 90–94 for females, suggesting that black Americans may indeed enjoy lower mortality than whites do at extreme ages (Hill, Preston, and Rosenwaike 2000:194).[9]

Han Chinese mortality curves converge toward or slightly crossover those of their Swedish and Japanese counterparts at an even higher age. Furthermore, the extent of the crossover is less than for blacks vs. whites in the United States. The level of black mortality at ages 95+, corrected for age misreporting by Preston and his colleagues, is 10.0 percent lower for males and 10.7 percent lower for females than the corresponding white rates. (Hill *et al.* 2000:194; see also Table 2 in this article). In contrast, the level of Han Chinese mortality at age 95 and above is 8 or 9 percent *higher* for males and 2 to 4 percent *higher* for females compared with Japanese or Swedish levels. Furthermore, the average death rate at ages 100–105 is also higher for Han Chinese males than for Japanese or Swedish males and the average death rates at these ages for Han Chinese females is only 4 or 5 percent lower, as shown in Table 2.

We believe that the mortality convergence or slight crossover after age 97 of Han Chinese vs. Swedish or Japanese age-trajectories of mortality is probably mainly due to differential

[9] Hill *et al.* (2000:1994) also noted that this is not fully conclusive, however, since the corrected black rates are based on a small number of deaths at ages 90+ and on the questionable accuracy of the census data.

Table 2. Comparisons of death rates at very old ages between the U.S. whites vs. blacks (corrected for age-misreporting by Preston *et al.* (1996) and Hill et al. (2000)), and between the Han Chinese versus Japanese and Swedish populations.

	Males		Females	
	Ages 95+	**Ages 100+**	**Ages 95+**	**Ages 100+**
U.S. White	0.3587	NA	0.3257	NA
U.S. Black	0.3232	NA	0.2908	NA
Black vs. White	−10.0%	NA	−10.7%	NA
Han Chinese	0.4274	0.5376	0.3546	0.4464
Japanese	0.3891	0.5181	0.3472	0.4651
Swedish	0.3906	0.5025	0.3413	0.4717
Chinese vs. Japanese	+9.8%	+3.8%	+2.1%	−4.0%
Chinese vs. Swedish	+9.4%	+7.0%	+3.9%	−5.4%

Sources: The death rates for U.S. white and black are estimated by Preston and his colleagues through correcting age-misreporting errors (Preston *et al.* 1996:205, Table 10; Hill *et al*. 2000: 184, Table 10). The death rates for Han Chinese are based on the 1990 census data. The death rates for Japanese and Swedish refer to 1981–1990 and 1985–1994, respectively, and all based on the Kannisto–Thatcher oldest-old mortality data base, available online at www.demogr.mpg.de.

mortality selection in heterogeneous populations. Very old people in China have suffered major civil wars, the Second World War, very poor living conditions, and inadequate medical care in the past few decades. Their misery has been much worse than that in Sweden and somewhat worse than that in Japan. Furthermore, even among people in their 80s and early 90s, death rates in China are higher than in Sweden and Japan. As a result, centenarians are much rarer in China than in Sweden or Japan: in 1990 there were about 5 centenarians per million Han Chinese compared with about 60 per million in Sweden and 25 per million in Japan. Deprivation early in life can result in debilitation of survivors as well as death of the frail, but such debilitation increases mortality among the debilitated as a cohort ages, resulting in mortality selection. Even though current living conditions and medical care are poor, Chinese death rates around age 100 may be similar to Swedish and Japanese levels because the Chinese who endured to age 100 may tend to be more robust with respect to various genetic and non-genetic characteristics.[10] This

[10] It is also interesting to note that the Japanese male and female oldest-old death rates are either slightly higher than or almost identical to the Swedish ones before ages 96 and 99, respectively. But the Japanese and Swedish male and female death rates slightly crossover at ages 96 and 99. The Japanese male and female death rates are lower than the Swedish ones at ages 97–100 and 100–102; both fluctuate a lot after age 100 and 102, respectively. The number of centenarians in Japan (about 25 per million in 1990) was much smaller than that in Sweden (about 60 per million in 1990). Centenarians in Japan are more selected than their Swedish counterparts. The stronger selection of Japanese oldest-old may explain why male and female Japanese and Swedish mortality rates slightly crossover at ages 96 and 99.

may produce mortality convergence or slight crossover after age 97 of Han Chinese vs. Swedish or Japanese age-trajectories of mortality. It is, however, also possible that for a small proportion of elderly Han Chinese, age of the living or age at death might not be accurately reported. Furthermore, in any comparison of death rates at advanced ages, analysts must bear in mind the rapidly widening 95% confidence bands that surround the observed estimates. Given these data limitations, it would be injudicious to draw any conclusions from the data except that mortality appears to decelerate in China as well as in Sweden and Japan and that death rates around age 100 appear to be roughly similar in China, Sweden, and Japan.

Life Tables for the Han Chinese Oldest-Old with a Comparison to Sweden and Japan

Tables 3a and 3b present the population at risk (N(x)), number of deaths (D(x)), central death rates, probability of death (q(x)) and their confidence interval, probability of surviving from age 80 to age x (l(x)), and remaining life expectancy (e(x)) from age 80 to 105. These are the first life tables for the Chinese oldest-old population. The l(x) and e(x) for Swedish and Japanese populations are also presented in Tables 3a and 3b for purposes of comparison. On average, Han Chinese males aged 80, 90, and 100 could expect to survive 5.3, 3.0, and 1.9 more years, respectively, if the observed age-specific death rates in 1990 applied to the rest of their life span. The corresponding figures are 6.5, 3.6, and 2.2 years for females.[11]

Han Chinese male and female life expectancies at age 80 in 1990 are 22–25 percent lower than those of their Japanese and Swedish counterparts. At age 95, the male and female Han Chinese life expectancies are only about 4% and 7% lower, respectively, than the Swedish and Japanese ones. At age 100 and above, Han Chinese life expectancies are slightly higher than those in Sweden and Japan. This is consistent with the convergence or slight crossover after age 97 discussed above.

The observed female Han Chinese life expectancies at ages 80, 90, and 100 are 23, 21, and 20 percent higher than those of male Han Chinese. Using estimates based on the Kannisto model, the estimated female Chinese life expectancies at ages 80, 90, and 100 are 23, 21, and 17 percent higher than those of the males. The female Swedish life expectancies at ages 80, 90, and 100 are 26, 19, and 7 percent higher than the male Swedish life expectancies, and the corresponding figures for the Japanese oldest-old are 24, 16, and 11 percent. That is, there is a convergence of remaining male vs. female life expectancy in Sweden and Japan but not in China: in China, the female advantage persists. Based on data

[11] The number of Han Chinese oldest-old male and female life table survivors (l(x)) of age 106 and above account for only 3.9 and 4.9 percent of the male and female life table total numbers of survivors aged 100 and above. Therefore, the questionable data quality at age 106 and above may not seriously distort the estimates of life expectancy at age 100.

Table 3a. Life table measurements at oldest-old ages for Han Chinese 1990, Japanese 1981–1990, and Swedes 1985–1994, Males.

	Han Chinese						Japanese		Swedish	
Age	N(x)	D(x)	m(x)	q(x)	l(x)	e(x)	l(x)	e(x)	l(x)	e(x)
80	537494	74158	0.1380	0.1291 (0.1282, 0.1300)	1.0000	5.29	1.0000	6.68	1.0000	6.85
81	437320	63976	0.1463	0.1363 (0.1353, 0.1373)	0.8709	4.99	0.9139	6.26	0.9176	6.42
82	353525	55940	0.1582	0.1466 (0.1455, 0.1477)	0.7522	4.70	0.8266	5.87	0.8335	6.02
83	282440	52700	0.1866	0.1707 (0.1694, 0.1720)	0.6419	4.43	0.7396	5.51	0.7494	5.63
84	235098	43168	0.1836	0.1682 (0.1668, 0.1696)	0.5323	4.23	0.6544	5.16	0.6666	5.27
85	181174	36548	0.2017	0.1832 (0.1815, 0.1849)	0.4428	3.99	0.5720	4.83	0.5856	4.93
86	137214	29740	0.2167	0.1955 (0.1935, 0.1975)	0.3617	3.77	0.4929	4.53	0.5082	4.61
87	104567	23876	0.2283	0.2049 (0.2026, 0.2072)	0.2910	3.57	0.4189	4.25	0.4343	4.31
88	77393	19110	0.2469	0.2198 (0.2170, 0.2226)	0.2314	3.36	0.3506	3.98	0.3654	4.03
89	54869	14630	0.2666	0.2353 (0.2320, 0.2386)	0.1805	3.16	0.2886	3.73	0.3018	3.77
90	33786	9310	0.2756	0.2422 (0.2379, 0.2465)	0.1380	2.98	0.2330	3.50	0.2453	3.52
91	19778	6402	0.3237	0.2786 (0.2728, 0.2844)	0.1046	2.77	0.1846	3.30	0.1949	3.30
92	14076	4671	0.3319	0.2846 (0.2777, 0.2915)	0.0755	2.65	0.1438	3.10	0.1512	3.11
93	9288	3420	0.3682	0.3110 (0.3023, 0.3197)	0.0540	2.51	0.1094	2.92	0.1158	2.91
94	5992	2327	0.3884	0.3252 (0.3143, 0.3361)	0.0372	2.42	0.0819	2.74	0.0864	2.73
95	4011	1679	0.4186	0.3461 (0.3327, 0.3595)	0.0251	2.34	0.0599	2.57	0.0629	2.56
96	2583	1155	0.4471	0.3654 (0.3486, 0.3822)	0.0164	2.31	0.0426	2.42	0.0447	2.40
97	1701	680	0.3999	0.3332 (0.3127, 0.3537)	0.0104	2.36	0.0296	2.28	0.0310	2.24
98	1209	426	0.3521	0.2994 (0.2756, 0.3232)	0.0069	2.29	0.0200	2.16	0.0204	2.15
99	799	332	0.4149	0.3436 (0.3137, 0.3735)	0.0049	2.05	0.0132	2.03	0.0133	2.03
100	329	210	0.6363	0.4827 (0.4357, 0.5297)	0.0032	1.86	0.0084	1.93	0.0082	1.99
101	200	96	0.4808	0.3876 (0.3269, 0.4483)	0.0017	2.13	0.0052	1.82	0.0050	1.94
102	122	51	0.4214	0.3481 (0.2710, 0.4252)	0.0010	2.15	0.0031	1.78	0.0030	1.89
103	67	34	0.5128	0.4082 (0.3026, 0.5138)	0.0007	2.04	0.0019	1.64	0.0018	1.79
104	60	21	0.3542	0.3009 (0.1933, 0.4085)	0.0004	2.10	0.0010	1.64	0.0011	1.67
105	33	17	0.5211	0.4134 (0.2629, 0.5639)	0.0003	1.78	0.0006	1.57	0.0006	1.67

Figures in parentheses give the 95% confidence interval for q(x).

Table 3b. Life table measurements at oldest-old ages for Han Chinese 1990, Japanese 1981–1990, and Swedes 1985–1994, Females.

	Han Chinese						Japanese		Swedish	
Age	N(x)	D(x)	m(x)	q(x)	l(x)	e(x)	l(x)	e(x)	l(x)	e(x)
80	845425	84458	0.0999	0.0951 (0.0945, 0.0957)	1.0000	6.51	0.9454	8.29	1.0000	8.63
81	723076	77334	0.1070	0.1015 (0.1008, 0.1022)	0.9049	6.15	0.8866	7.74	0.9486	8.07
82	610891	71706	0.1174	0.1109 (0.1101, 0.1117)	0.8131	5.78	0.8241	7.22	0.8940	7.53
83	517081	70634	0.1366	0.1279 (0.1270, 0.1288)	0.7229	5.44	0.7587	6.73	0.8358	7.02
84	458746	63406	0.1382	0.1293 (0.1284, 0.1302)	0.6304	5.17	0.6911	6.26	0.7750	6.53
85	373009	56034	0.1502	0.1397 (0.1386, 0.1408)	0.5489	4.86	0.6219	5.83	0.7108	6.08
86	299409	50516	0.1687	0.1556 (0.1544, 0.1568)	0.4722	4.57	0.5524	5.42	0.6449	5.65
87	235086	40422	0.1719	0.1583 (0.1569, 0.1597)	0.3988	4.32	0.4838	5.04	0.5781	5.25
88	182539	35610	0.1951	0.1777 (0.1760, 0.1794)	0.3356	4.04	0.4170	4.69	0.5114	4.86
89	137683	29406	0.2136	0.1930 (0.1910, 0.1950)	0.2760	3.80	0.3533	4.36	0.4450	4.51
90	92002	19814	0.2154	0.1944 (0.1920, 0.1968)	0.2227	3.59	0.2944	4.06	0.3809	4.19
91	56065	14827	0.2645	0.2336 (0.2303, 0.2369)	0.1794	3.34	0.2401	3.78	0.3204	3.89
92	42688	11244	0.2634	0.2327 (0.2289, 0.2365)	0.1375	3.20	0.1921	3.52	0.2636	3.62
93	29603	8721	0.2946	0.2568 (0.2522, 0.2614)	0.1055	3.02	0.1501	3.28	0.2122	3.37
94	20591	6631	0.3221	0.2774 (0.2717, 0.2831)	0.0784	2.90	0.1142	3.06	0.1674	3.14
95	14490	4623	0.3191	0.2752 (0.2684, 0.2820)	0.0567	2.82	0.0850	2.88	0.1289	2.93
96	9757	3258	0.3339	0.2861 (0.2778, 0.2944)	0.0411	2.70	0.0619	2.70	0.0965	2.74
97	6518	2418	0.3710	0.3130 (0.3027, 0.3233)	0.0293	2.58	0.0438	2.53	0.0701	2.59
98	4692	1669	0.3557	0.3020 (0.2899, 0.3141)	0.0201	2.52	0.0299	2.38	0.0501	2.42
99	3149	1143	0.3631	0.3073 (0.2925, 0.3221)	0.0141	2.40	0.0201	2.27	0.0349	2.26
100	1517	643	0.4237	0.3497 (0.3279, 0.3715)	0.0097	2.24	0.0132	2.15	0.0234	2.12
101	906	396	0.4370	0.3586 (0.3303, 0.3869)	0.0063	2.17	0.0083	2.03	0.0149	2.05
102	592	266	0.4494	0.3670 (0.3319, 0.4021)	0.0041	2.10	0.0051	1.95	0.0093	2.00
103	350	184	0.5261	0.4165 (0.3705, 0.4625)	0.0026	2.04	0.0030	1.88	0.0056	1.96
104	247	111	0.4500	0.3673 (0.3129, 0.4217)	0.0015	2.13	0.0018	1.88	0.0035	1.84
105	169	86	0.5083	0.4053 (0.3392, 0.4714)	0.0009	2.08	0.0010	1.86	0.0021	1.78

Figures in parentheses give the 95% Confidence Interval for q(x).

from the 1998 healthy longevity survey, Zeng, Liu, and George (2002) found that very old Chinese females suffer from substantially disadvantageous status compared with males with respect to education, marital status, living arrangement, retirement pensions, overall income, and medical services, as well as physical and mental health. Gender differentials in socio-economic status and access to medical services are much smaller in Sweden and Japan than in China. The poor relative status of very old females vs. males in China may imply that there is less mortality selection among frailer males than frailer females. This might account for the lack of convergence in the male and females mortality trajectories. This is speculative, however, and further research is needed on this question.

Conclusions

Based on 1990 census data, we estimated age-specific death rates and the first life table for very old Han Chinese aged 80–105. We fit different mortality models to the Han Chinese death rates at ages 80–96. We extrapolated the models to predict the rates up to age 105, and compared them with the observed ones. We found that a simplified, two-parameter logistic model, the Kannisto model, performed better than the other models. This is consistent with a study based on European and Japanese data (Thatcher, Kannisto, and Vaupel 1998). A Gompertz curve fails to capture the trajectory of Chinese mortality at high ages. Chinese death rates rise considerably more slowly after age 97 than predicted by a Gompertz curve fit to the data at ages 80–96 or 80–105. Our estimates confirm that the pace of increase in death rates decelerates at advanced ages not only in the developed world, but also in China, a developing country.

While male and female Han Chinese death rates at older ages are generally higher than Swedish and Japanese rates, the curves converge or slightly crossover after age 97. Based on studies of the crossover of U.S. black vs. white death rates and based on analyses of the validity of age reporting among the Han Chinese, we believe that the convergence or slight crossover of the Chinese mortality rates with Japanese and Swedish ones after age 97 is due mainly to the effects of mortality selection in heterogeneous populations. It is also possible, however, that small errors in age or death reporting among the Han Chinese may partially contribute to the mortality convergence or slight crossover.

Life tables for the oldest-old Han Chinese show a persistent female advantage in remaining life expectancy. In contrast, in Sweden and Japan the gap between the remaining life expectancies of males vs. females tends to diminish with increasing age. It seems possible, if at first glance paradoxical, that the relatively disadvantaged condition of women vs. men at all ages in China contributes to more mortality selection and thus the persistent female life-expectancy advantage. In any case, further study of living conditions of males vs. females in China seems warranted.

Appendix

Table A1. Estimates of the parameters and Log Likelihood of goodness of the fittings to the single-year age-specific probabilities of death at ages 80–96.

Models	Function	-Log Likelihood
Males		
Logistic	$\mu(x) = 9.25 * 10^{-4} + \frac{2.048 * 10^{-4} e^{0.082x}}{1 + 8.29 * 10^{-5}(e^{0.082x} - 1)}$	1194628.1
Kannisto	$\mu(x) = \frac{8.19 * 10^{-5} e^{0.094x}}{1 + 8.19 * 10^{-5}(e^{0.094x} - 1)}$	1194638.3
Quadratic	$\mu(x) = \exp(-10.32 + 0.13x - 0.00032x^2)$	1194626.3
Gompertz	$\mu(x) = 3.54 * 10^{-4} e^{0.074x}$	1194631.3
Weibull	$\mu(x) = 1.027 * 10^{-13} x^{6.36}$	1194626.0
Heligman & Pollard	$q(x) = \frac{2.039 * 10^{-4} e^{0.082}}{1 + 2.039 * 10^{-4} e^{0.082}}$	1194627.7
Females		
Logistic	$\mu(x) = 6.13 * 10^{-4} + \frac{5.64 * 10^{-5} e^{0.094x}}{1 + 4.038 * 10^{-5}(e^{0.094x} - 1)}$	1898353.8
Kannisto	$\mu(x) = \frac{3.88 * 10^{-5} e^{0.099x}}{1 + 3.88 * 10^{-5}(e^{0.099x} - 1)}$	1898364.0
Quadratic	$\mu(x) = \exp(-12.53 + 0.17x - 0.00049x^2)$	1898352.0
Gompertz	$\mu(x) = 1.37 * 10^{-4} e^{0.082x}$	1898357.0
Weibull	$\mu(x) = 3.24 * 10^{-15} x^{7.077}$	1898351.7
Heligman & Pollard	$q(x) = \frac{8.402 * 10^{-5} e^{0.089}}{1 + 8.402 * 10^{-5} e^{0.089}}$	1898353.4

Note: Although the deviations from the other five models are very small, the Weibull model has the lowest value of the negative of the log likelihood, which implies that it is the best-fitting model in terms of maximum likelihood. We, however, use "fits best" in our discussion in this paper in a different way—we mean that the curves capture the trajectory of mortality at the highest ages.

Table A2. Comparisons between the observed and fitted values of the single-year age-specific probabilities of death at ages 80–96 and extrapolated from age 97 to age 105, Males.

Age	Observed	Logistic	Kannisto	Quadratic	Gompertz	Weibull	Heligman & Pollard
80	0.1291	0.1292	0.1284	0.1290	0.1296	0.1288	0.1316
81	0.1363	0.1387	0.1384	0.1387	0.1389	0.1386	0.1413
82	0.1466	0.1488	0.1490	0.1489	0.1488	0.1489	0.1516
83	0.1707	0.1595	0.1601	0.1596	0.1593	0.1598	0.1626
84	0.1682	0.1708	0.1717	0.1710	0.1704	0.1712	0.1741
85	0.1832	0.1828	0.1839	0.1830	0.1823	0.1832	0.1863
86	0.1955	0.1955	0.1966	0.1956	0.1948	0.1958	0.1992
87	0.2049	0.2088	0.2097	0.2088	0.2082	0.2090	0.2127
88	0.2198	0.2227	0.2233	0.2227	0.2223	0.2228	0.2269
89	0.2353	0.2373	0.2373	0.2372	0.2372	0.2372	0.2417
90	0.2422	0.2526	0.2516	0.2524	0.2529	0.2522	0.2572
91	0.2786	0.2686	0.2662	0.2682	0.2695	0.2677	0.2733
92	0.2846	0.2851	0.2811	0.2847	0.2870	0.2839	0.2900
93	0.3110	0.3023	0.2961	0.3017	0.3053	0.3006	0.3073
94	0.3252	0.3200	0.3113	0.3194	0.3245	0.3179	0.3251
95	0.3461	0.3383	0.3264	0.3377	0.3447	0.3358	0.3435
96	0.3654	0.3571	0.3415	0.3565	0.3656	0.3542	0.3624
97	0.3332	0.3763	0.3565	0.3759	0.3875	0.3730	0.3817
98	0.2994	0.3958	0.3713	0.3958	0.4102	0.3924	0.4014
99	0.3436	0.4157	0.3859	0.4161	0.4337	0.4121	0.4214
100	0.4827	0.4358	0.4002	0.4369	0.4580	0.4323	0.4416
101	0.3876	0.4561	0.4141	0.4580	0.4829	0.4528	0.4621
102	0.3481	0.4765	0.4276	0.4795	0.5085	0.4736	0.4827
103	0.4082	0.4968	0.4406	0.5012	0.5347	0.4947	0.5033
104	0.3009	0.5171	0.4532	0.5231	0.5613	0.5160	0.5240
105	0.4134	0.5372	0.4652	0.5451	0.5883	0.5375	0.5445

Table A3. Comparisons between the observed and fitted values of the single-year age-specific probabilities of death at ages 80–96 and extrapolated from age 97 to age 105, Females.

Age	Observed	Logistic	Kannisto	Quadratic	Gompertz	Weibull	Heligman & Pollard
80	0.0951	0.0950	0.0946	0.0949	0.0958	0.0949	0.0953
81	0.1015	0.1031	0.1029	0.1031	0.1036	0.1031	0.1033
82	0.1109	0.1118	0.1118	0.1119	0.1119	0.1119	0.1118
83	0.1279	0.1211	0.1213	0.1212	0.1208	0.1212	0.1210
84	0.1293	0.1311	0.1314	0.1312	0.1305	0.1312	0.1308
85	0.1397	0.1416	0.1421	0.1417	0.1408	0.1417	0.1413
86	0.1556	0.1529	0.1534	0.1529	0.1518	0.1529	0.1525
87	0.1583	0.1648	0.1653	0.1648	0.1637	0.1647	0.1644
88	0.1777	0.1774	0.1778	0.1773	0.1764	0.1772	0.1770
89	0.1930	0.1906	0.1908	0.1904	0.1899	0.1904	0.1903
90	0.1944	0.2045	0.2045	0.2043	0.2043	0.2042	0.2045
91	0.2336	0.2191	0.2186	0.2188	0.2197	0.2188	0.2194
92	0.2327	0.2343	0.2331	0.2340	0.2361	0.2341	0.2350
93	0.2568	0.2500	0.2481	0.2499	0.2534	0.2501	0.2514
94	0.2774	0.2663	0.2634	0.2664	0.2718	0.2668	0.2686
95	0.2752	0.2831	0.2790	0.2836	0.2913	0.2841	0.2864
96	0.2861	0.3003	0.2947	0.3014	0.3118	0.3022	0.3050
97	0.3130	0.3179	0.3106	0.3198	0.3335	0.3210	0.3242
98	0.3020	0.3358	0.3265	0.3387	0.3562	0.3404	0.3441
99	0.3073	0.3539	0.3424	0.3582	0.3799	0.3604	0.3645
100	0.3497	0.3721	0.3581	0.3781	0.4047	0.3810	0.3854
101	0.3586	0.3904	0.3737	0.3985	0.4305	0.4022	0.4067
102	0.3670	0.4086	0.3889	0.4193	0.4573	0.4239	0.4284
103	0.4165	0.4267	0.4038	0.4404	0.4849	0.4461	0.4503
104	0.3673	0.4445	0.4183	0.4617	0.5132	0.4686	0.4725
105	0.4053	0.4621	0.4324	0.4833	0.5422	0.4915	0.4948

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References

Banister, J. (1990) "Implications of aging of China's population". In: Zeng, Yi., Zhang, C., Peng, S. (eds.), *Changing Family Structure and Population Aging in China: A Comparative Approach*. Beijing: Peking University Press, published in English. [Also in Dedley, L., Jr. Poston, D. Yaukey (eds.), *The Population of Modern China*. New York: Plenum Press].

Coale, A. (1993) "Estimation of the Chinese mortality rates based on the 1990 census data", *Manuscript.*

Coale, A., and Shaomin, Li. (1991) "The effect of age misreporting in China on the calculation of mortality rates at very high ages", *Demography*, 28(2):293–301.

Coale, A., and Kisker, E. E. (1986) "Mortality crossovers: Reality or bad data?", *Population Studies*, 40:389–401.

Corti, M. C., Guralnik, J. M., Ferucci, L., Izmirlian, G., Leville, S. G., Pahor, M., Cohen, H. J., Pieper, C., and Havlik, R. J. (1999) "Evidence for a Black-White crossover in all-cause and coronary heart disease mortality in and older population: The North Carolina EPESE", *American Journal of Public Health*, 89:308–314.

Elo, I. T., and Preston, S. H. (1994) "Estimating African-American mortality from inaccurate data", *Demography*, 31(3):427–458.

Elo, I., and Preston, S. (1992) "The effect of early life conditions on adult mortality: A review", *Population Index*, 58:186–212.

Hill, M. E., Preston, S. H., and Rosenwaike, I. (2000) "Age reporting among white Americans aged 85+: Results of a record linkage study", *Demography*, 37:175–186.

Human Mortality Database (2002) Online at www.humanmortality.de

Jeune, B., and Kannisto, V. (1997) "Emergence of centenarians and super-centenarians". In: Robine, J.-M., *et al*. (eds.), *Longevity: To the Limits and Beyond*. Berlin, Heidelgerg, New York: Springer-Verlag, pp. 77–89.

Jeune, B., and Vaupel, J. W. (1995) *Exceptional Longevity: From Prehistory to the Present*. Odense: Odense University Press, p. 169.

Kannisto, V., Lauritsen, J., Thatcher, A. R., and Vaupel, J. W. (1994) "Reductions in mortality at advanced ages: Several decades of evidence from 27 countries", *Population and Develoment Review*, 20:793–870.

Kannisto, V. (1990) *Mortality of the Elderly in Late 19th and Early 20th Century Finland*. Helsinki: Tilastokeskus, 49.

Kitagawa, I. M., and Hauser, P. M. (1973) *Differential Mortality in the U.S.*: *A Study in Socioeconomic Epidemiology*. Cambridge, MA: Harvard University Press.

Lynch, S. M., Brown, J. S., and Harmsen, K. G. (2000) *Black-White Differences in Mortality Deceleration and Compression and the Mortality Crossover Reconsidered*. Paper presented at the annual meeting of the Population Association of America, Los Angeles, CA, March 2000.

Manton, K. G., Stallard, E., and Vaupel, J. W. (1981) "Methods for comparing the mortality experience of heterogeneous population", *Demography*, 18:389–410.

Markides, K. S., and Black, S. A. (1996) "Race, ethnicity, and aging: The impact of inequality". In: Binstock, R. H., George, L. K. (eds.), *Handbook of Aging in the Social Sciences*, (4th ed.) San Diego, CA: San Diego Academic Press, 153–170.

McCord, C., and Freeman, H.P. (1990) "Excess mortality in Harlem", *New England Journal of Medicine*, 322: 173–177.

Mosley, W. H., and Gray, R. (1993) "Childhood precursors of adult morbidity and mortality in developing countries: Implications for health programs". In: Gribble, J. Preston, S. (eds.), *The Epidemiological Transition: Policy and Planning Implications for Developing Countries*. Washington, DC: National Academy Press, 69–100.

Nam, C. B., and Okay, K. A. (1977) *Factors Contributing to the Mortality Crossover Pattern*. Mexico City: XVIII General Conference of the International Union for the Scientific Study of Population.

Newell, C. (1988) *Methods and Models in Demography*. New York: The Guilford Press.

Ogawa, N. (1988) "Aging in China: Demographic alternatives", *Asian-Pacific Population Journal*, 3(3):21–64.

Otten, M. W., Teutsch, S. M., Williamson, D. F., and Marks, J. S. (1990) "The effect of known risk factors on the excess mortality of black adults in the United States", *Journal of the American Medical Association*, 263:845–850.

Poston, D. L., and Duan, C. C. (2000) "The current and projected distribution of the elderly and eldercare in the People's Republic of China", *Journal of Family Issues*, 21:714–732.

Preston, S. H., Elo, I. T., Foster, A., and Fu, H. (1998) "Reconstruction the size of the African American population by age and sex, 1930–1990", *Demography,* 35(1):1–21.

Preston, S. H., Elo, I. T., Rosenwaike, I., and Hill, M. (1996) "African-American mortality at older ages: Results of a matching study", *Demography*, 33:193–209.

SAS Institute (2002) JMP the Statistical Discovery Software. www.jmpdiscovery.com.

Thatcher, A. R., Kannisto, V., and Vaupel, J. W. (1998) *The Force of Mortality at Ages 80 to 120*. Odense: Odense University Press. Online at http://www.demogr.mpg.de/Papers/Books/Monograph5/ForMort.htm.

Thornton, R. G., and Nam, C. B. (1972) "The lower mortality rates of non-Whites at the old ages: an enigma in demographic analysis", *Research Reports in Social Science*, 11:1–8.

United Nations (1955) "Methods of appraisal of quality of basic data for population estimates, manual II", *Population Studies*, No. 23.

Vaupel, J. W., Carey, J. R., Christensen, K., Johnson, T. E., Yashin, A. I., Holm, N. V., Iachine, I. A., Kannisto, V., Khazaeli, A. A., Liedo, P., Longo, V. D., Zeng, Y., Manton, K. G., and Curtsinger, J. W. (1998) "Biodemographic trajectories of longevity", *Science*, 280:855–860.

Voland, E., and C. Engel. (1986) "Ist das postmenopausale sterbealter variable einer fitness-maximierenden reproduktionsstrategie?", *Anthropologischer Anzeiger*, 44(1):10–34.

Wang, Z., Zeng, Y., Jeune, B., and Vaupel, J. W. (1998) "Age validation of Han Chinese centenarians", *GENUS—An International Journal of Demography,* LIV:123–141.

Zeng, Y., Vaupel, J. W., Xiao, Z., Zhang, C., and Liu, Y. (2001) "The healthy longevity survey and the active life expectancy of the oldest-old in China", *Population*: *An English Selection*, 13(1):95–116.

Zeng, Y., Liu, Y., and George, L. (2003) "Gender differentials of oldest-old in China". *Research on Aging*, 25:65–80.

Zeng, Y., and George, L. (2000) "Family dynamics of 63 million (in 1990) to more than 330 million (in 2050) elders in China", *Demographic Research*, 2(5):1–48.

Zeng, Yi., and Vaupel, J. W. (1989) "Impact of urbanization and delayed childbearing on population growth and aging in China", *Population and Development Review*, 15(3):425–445.

Zopf, P. E. (1992) *Mortality Patterns and Trends in the United States*. Westport, CT: Greenwood Press.

CHAPTER 5. CENTRAL AND DISPERSON INDICATORS OF INDIVIDUAL LIFE DURATIONS: NEW METHODS

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1. Introduction

The secular transition from high to low mortality, and particularly its course during the last decades, has caused profound changes in the length of life. Both the average lifetime and its individual variability have been affected, and this process is still continuing. In this paper, the duration of human life is observed in the light of both central and dispersion indicators. Some new methods are proposed and applied to past and on-going developments.

As to central indicators, we find the three classical statistical averages—mean, median and mode—sufficient and do not propose any others. However, we do consider that the mode deserves more attention than it has been getting because it has properties which contribute to a more balanced understanding of the length of life.

During the period before the great mortality transition, Lexis paid much attention to the mode in late life and observed that if the form of the age-at-death distribution, observed after the modal age, is replicated as a mirror image on the left side, the result is a normal curve representing normal lifetime with its variability. Deaths further left or above the normal curve represented premature mortality, ascribed to a person's abnormal constitution or to external influences (Lexis 1877).

When the mortality transition is essentially completed, the mode in early life is reduced to a very small size but it still exists in a relatively even sharper form. Lives saved in childhood, youth and middle age now end closer to the late-life mode which has grown to large proportions. The views of Lexis about the normal curve astride the mode are, however, equally applicable today and stand or fall together.

Changes in the variability of individual life duration have been no less important than the gains in longevity. To measure this variability, we propose first of all two indicators which quantify it at advanced ages: the standard deviation above the mode and the standard deviation in the highest quartile. For an indicator covering a wider age span, we consider first the inter- quartile range and find that while it serves the purpose to some extent, it also has serious shortcomings.

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An important concept in the individual variability of the length of life is the compression of mortality, first developed by Fries as compression of *morbidity* between a delayed onset of chronic diseases and a fixed limit to life (Fries 1980). This idea was soon considered equally applicable to *mortality* which would likewise be compressed into a narrower age interval. According to Fries, the process is completed when mortality from exogenous causes is eliminated and the remaining variability of the age at death is caused by genetic factors (Fries 1980).

As mortality is compressed, the survival curve takes on an increasingly rectangular form. The concepts of compression of mortality and rectangularization of the survival curve are so interdependent that they are sometimes considered a single issue. We see no advantage in equating the two while we are still far from the theoretical end result—and may never reach it. We propose instead to measure both: compression of mortality by a family of C-indicators, and rectangularity by a set of R-indexes.

In the following, we shall apply all measures to a life table, the prime domain of analysis of all-cause mortality. This can be done equally well in period and cohort tables but we shall use here only the first-mentioned which are of greater practical interest. An examination of mortality in old age between 1950 and 1985 in five countries of low mortality showed that every stage in the development—onset of decline, acceleration, deceleration, stagnation or reversal—occurred in each country simultaneously in all old age groups, proving that the transition was caused by period factors and not by supposedly healthier cohorts advancing in age (Kannisto 1994: 55–59).

2. Central Indicators

2.1. MEAN LIFETIME

This is the arithmetic mean of the age at death, or *life expectancy at birth*, denoted e (0). Its development during the secular mortality transition is illustrated, together with that of other central indicators, by the series for French females in Figure 1.

Of all measures of the length of life, this is the most fundamental and by far the most often used. Though apparently equitable, this average is very strongly affected by child

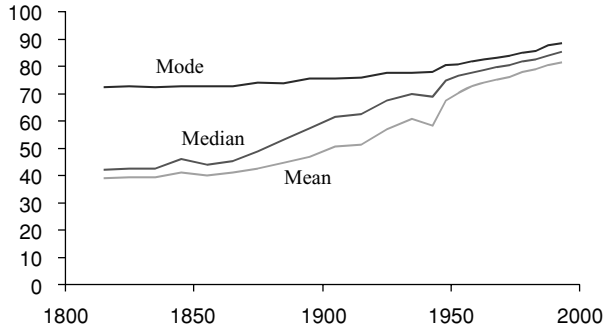

Figure 1. Mean, median, and mode of the length of life. France, female.

mortality. When a small child dies, some 60–80 years are lost to the numerator but when the child's parent dies, the loss is likely only half as great. To e (0), therefore, a young adult life is worth only half of that of a child—an absurd appraisal. Health policies since 1950 have been largely geared to increase e (0) which is widely seen by decision-makers as a good indicator of health conditions. Consequently, health policies have been largely biased in favour of reducing child mortality and neglecting adult health problems. In the U.N.-sponsored Symposium on Health and Mortality in Brussels in 1997, many participants stressed that mortality in childhood had been drastically reduced even in countries where the mortality of adults had declined little or not at all (United Nations 1999).

2.2. MEDIAN LIFETIME

The median lifetime is the age at which half of all children born are still alive. This measure is obtained readily in a life table at the exact point where l (x) = 1 (0)/2. The median is not very useful as an analytical measure of human life and is little used for that purpose. On the other hand, it is a practical, descriptive indicator of any contingent of deaths outside of a life table. It is often calculated for a particular cause of death and is used as such in medicine and public health to which it may impart valuable information. Its level may indicate universality and effectiveness of immunization or treatment. As an example, the median age at death from pulmonary tuberculosis used to be in the neighbourhood of 20–30 years but with a good case-finding program and chemotherapy may now exceed 75 years.

2.3. MODAL LIFETIME

The distribution of the length of life (age at death) is typically bimodal with one mode immediately after birth and the other in late life. Occasionally there is a third mode in young adult age, sometimes caused by accidents and violence for males and maternal deaths for females.

It is the late life mode which is of principal interest demographically as it represents the most common duration of adult life and is often considered the normal lifetime in the given circumstances. The late life mode is unique in the sense that there is no known and proven case of there having been more than one of them. When the data have shown more than one, it has been caused by age heaping or some other inaccuracy in the basic data or by random variation in insufficient data.

The mode is calculated from the d (x) column of a life table which for the purpose has to be relatively smooth, the values descending on both sides of a maximum. If the series is not smooth, a moving average may be applied to q (x), the remainder of the table being modified accordingly. Alternatively, smoothing may be applied only to the highest part of the d (x) column for the single purpose of determining the mode, the table itself remaining unchanged. The exact mode can then be calculated as:

$$M = x + \frac{d(x) - d(x-1)}{[d(x) - d(x-1)] + [d(x) - d(x+1)]} \tag{1}$$

where x is the age with the highest d in late life (Kannisto 2001).

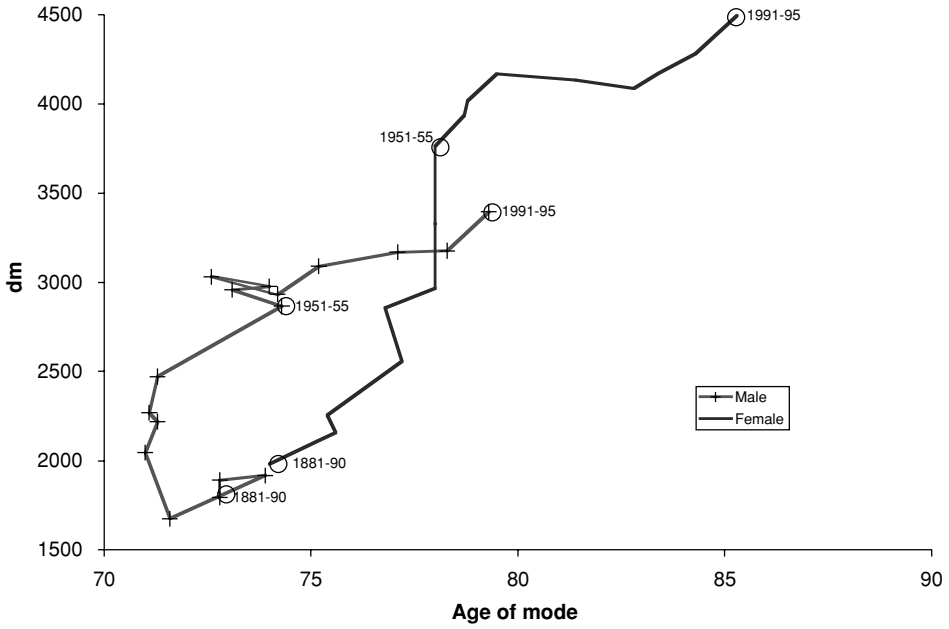

Figure 2. Age and height of mode. Finland 1881–1995.

As is evident in Figure 1, the mode is the most stable of the three central indicators of life duration. During the great mortality transition, as large numbers of lives were saved from premature death, they were extended to a fuller lifetime, reaching what was the most common age at death in the circumstances. This is shown for Finnish males and females in Figure 2. During a long period of mortality decline, the mode moved only slowly to a higher age but grew in height as ever more deaths occurred at the same approximate age. This pattern changed significantly and rather abruptly in the 1960s when the mode virtually stopped growing and began instead to move to higher age.

The same happened, though at slightly varying times, in most low-mortality countries due to an unprecedented decline in death rates at advanced ages.

3. Dispersion Indicators

3.1. STANDARD DEVIATION ABOVE MODE

The usual statistical measures of dispersion are the mean deviation and the standard deviation of individual values from an average. When the mode is the measure of the most common length of life, then the standard deviation in relation to it is a logical measure of dispersion. The negative deviations, however, are an amalgam of cases totally different in nature, ranging from neonatal deaths over youthful mortality to middle age. An indicator based on all of them is not likely to be very meaningful.

Table 1. Selected mortality indicators. Females.

Country and period	Mode	SD (M+)	Highest quartile		IQR Years	C50 Years
			Mean	SD		
1	2	3	4	5	6	7
England						
1841	72.9	9.1	78.8	5.47	65.1	44.4
1891–1900	73.6	8.9	79.9	4.61	55.8	31.7
1950–52	80.1	7.1	87.4	3.10	16.6	14.8
1990–92	86.2	7.0	93.0	3.12	15.9	14.8
Finland						
1881–90	74.0	8.3	79.1	4.46	67.2	36.7
1921–30	77.2	7.6	82.9	3.75	42.9	24.5
1951–55	79.0	7.0	85.0	3.05	16.4	14.8
1991–95	85.3	6.5	92.1	2.76	13.5	12.5
Netherlands						
1850–60	72.8	8.5	76.1	5.24	65.3	49.7
1900–10	76.5	8.0	84.2	4.18	47.0	25.3
1950–60	80.8	7.0	88.5	2.97	15.0	13.8
1990–95	86.7	6.5	93.2	2.74	14.4	13.1
Switzerland						
1876–80	70.8	8.8	76.8	4.69	63.2	35.3
1910–11	75.0	7.4	80.7	3.70	38.6	23.5
1948–53	79.9	7.0	87.0	3.17	16.6	15.0
1988–93	87.6	6.0	98.7	2.54	13.6	12.4

The positive deviations, on the other hand, can be understood as individual variation in lifetime which tends to the mode. This variability can be measured by the standard deviation above the mode, expressed as SD(M+) and being the root-mean-square of the positive deviations. If we accept the notion of Lexis of a symmetrical distribution on the left side, this measure is valid also for the entire mode-centered distribution.

Historical and recent values of the mode and the standard deviation above it are given in Table 1 (col. 2–3), based on life tables from four countries with reliable data. The development has been roughly similar in all four countries, the mode tending to increase and the standard deviation above it tending to decline. This means that the increase in life expectancy has not resulted in the mode simply sliding to the right, maintaining its form intact, but undergoing at the same time a considerable transformation in which the right hand slope has become steeper. Results of less systematic historical comparisons for Australia, Austria, Denmark, France, Italy, Japan, Sweden, and the United States are in line with these findings.

The arithmetic mean of the positive deviation from the mode equals the life expectancy at mode, denoted e(M) .

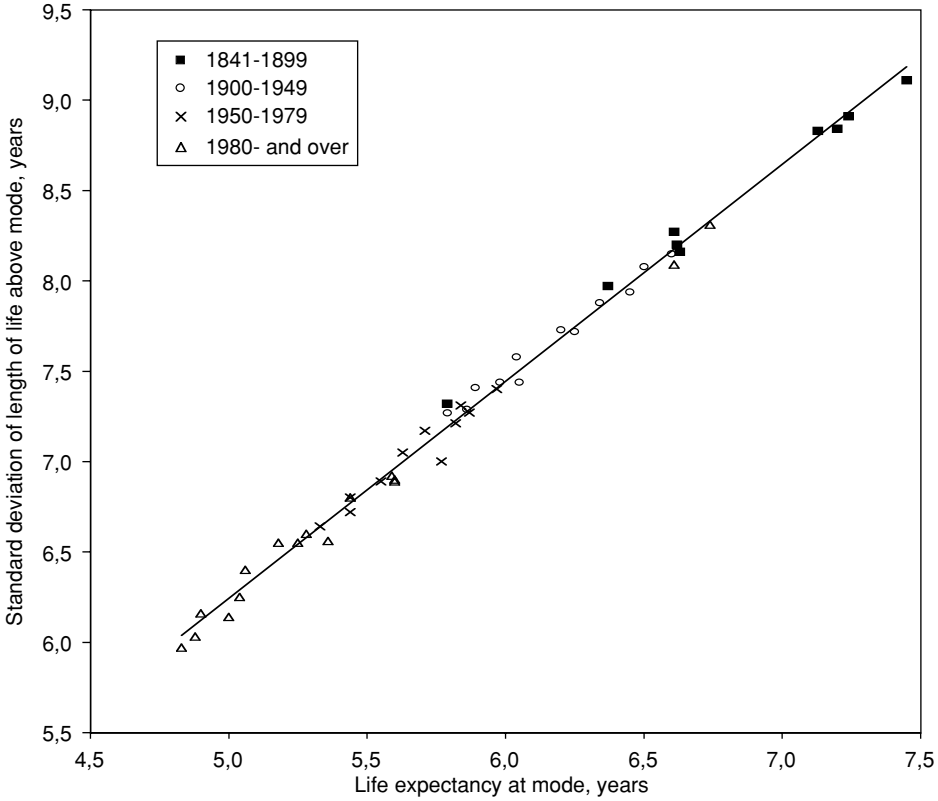

Figure 3. Life expectancy at mode and standard deviation of length of life above mode. Female in 16 countries at various periods.

When we plot SD(M+) against e(M), we find an extremely tight correlation illustrated in Figure 3. In 16 countries and for all periods combined, $r = +0.995$. The ratio SD(M+)/e(M) varied generally within the narrow limits of 1.22 and 1.25. It is interesting to recall that in a normal curve, the ratio of standard deviation to mean deviation equals $\sqrt{\pi/2} = 1.253$. Our empirical distributions—which may include observation errors—conform thus very well to normal curves, giving strong support to the views of Lexis.

3.2. STANDARD DEVIATION IN THE HIGHEST QUARTILE

The dispersion of individual life durations at high ages can also be measured in the highest quartile, i.e. above Q3, for which the mean age at death and its standard deviation are given in Table 1 (col. 4–5).

The mean age at death in this quartile has been historically several years higher than the mode, and increasing over time. Its standard deviation has declined relatively even more

than that above mode: 39–48% vs. 21–31%. These findings support those made in relation to the mode that relative compression tends to increase at high ages, even though the greatest absolute concentration of deaths is always situated around the mode.

3.3. INTER-QUARTILE RANGE

Another dispersion indicator often used in statistical distributions is the inter-quartile range

$$\mathrm{IQR} = \mathrm{Q3} - \mathrm{Q1}$$

It can be applied to the length of life and is readily obtained in a life table as the age interval, in years, between points 1 (x) = 75,000 and 1 (x) = 25,000.

Its historical development is given in Table 1 (col. 6) where its massive and consistent long-term decline is evidence that significant compression of mortality has taken place. However, IQR has shortcomings which are discussed further below and which lessen its value as a dispersion indicator.

3.4. C-FAMILY OF COMPRESSION INDICATORS

We propose to measure the dispersion of life duration by a compression indicator C which gives the shortest age interval in which a given proportion of all deaths take place, the chosen percentage given after the letter C. We have found use for indicators C10, C25, C50, and C90. Free from both the age scale and the percentile scale, they point out the ages where deaths are most heavily concentrated. A decline in their value means compression of mortality. Compression at certain ages always implies decompression at some other ages. The calculation of C10, C25, and C50 is shown in Table 2.

The historical development of C10, C25 and C50 in five countries is illustrated in Figure 4. All three indicators show in all countries a consistent and rapid long-term decline which has more recently slowed down. Though the development has been approximately similar in all countries, significant differences between them can be noted in certain periods, most of all in the last few decades when the value has stabilized in the U.S. and turned into a tentative increase in England, while continuing to decline in the others. As the three indicators give a roughly similar account of the course of events, it may be appropriate to select only one of them for recommended use. It would seem that C50 is the most expressive of the rapid fall, the ensuing slowdown and the current differences. It also has the merit of representing a larger segment of deaths. The development of C50 is therefore shown in the last column of Table 1.

We shall conclude the presentation of C-indicators by introducing C90 which would be the ultimate touchstone of compression. It is only realistic to grant that even a completed demographic cycle may be less than absolutely so. Fries himself made allowance for a certain number of cases which would not conform to the rule but die at different ages.

Table 2. Calculation of C_{10}, C_{25} and C_{50}. Example: France, female, 1991–95.

A. Part of d (x) distribution around mode			B. Ranking of d (x) values		
x	**d (x)**	**Rank**	**Rank**	**d(x)**	**Σd(x)**
79	2,652	16	1	4,561	4,561
80	2,954	15	2	4,540	9,101
81	3,207	13	3	4,510	**13,611**
82	3,482	12	4	4,421	18,032
83	3,788	10	5	4,386	22,418
84	4,044	8	6	4,218	**26,636**
85	4,218	6	7	4,207	30,843
86	4,386	5	8	4,044	34,887
87	4,510	3	9	3,903	38,790
88	4,561	1	10	3,788	42,578
89	4,540	2	11	3,505	46,083
90	4,421	4	12	3,482	49,565
91	4,207	7	13	3,207	**52,772**
92	3,903	9			
93	3,505	11			
94	3,044	14			
95	2,543	17			

Each indicator equals the number of years needed to reach the resp. total, less the fraction of the last-added year which exceeds the total.
Solution: $C_{10} = 3 - 3{,}611/4{,}510 = 2.20$ years; $C_{25} = 6 - 1{,}636/4{,}218 = 5.61$ years; $C_{50} = 13 - 2{,}772/3{,}207 = 12.14$ years

If it is judged that this residual variability in the age at death should not comprise more than ten percent of all cases, it follows that the compression of mortality is not essentially completed until C90, together with the lower order indicators, is reduced to one year.

It should be noted that C90 becomes meaningful only when early childhood mortality is small enough to be excluded from it. Until then, C90 simply indicates the age to which 90 percent of the newborn survive. As early deaths become fewer, this age grows. Once the early mortality is excluded from it, C90 begins to decline with declining mortality and shows compression. For the time being this decline is going on quite vigorously and shows hardly any sign of slowdown in the countries given in Figure 5.

Table 3 summarizes the present level of compression in 22 countries at 10, 50, and 90 percent levels. In a very general way, countries most advanced in compression—at the top of the Table—are those with lowest mortality; while many of those with relatively high mortality are found at the bottom of the table, affected as they still are by frequent premature deaths. Exceptions, however, abound, and the situation varies depending on each particular indicator. Besides, C90 is in some cases affected by volatility.

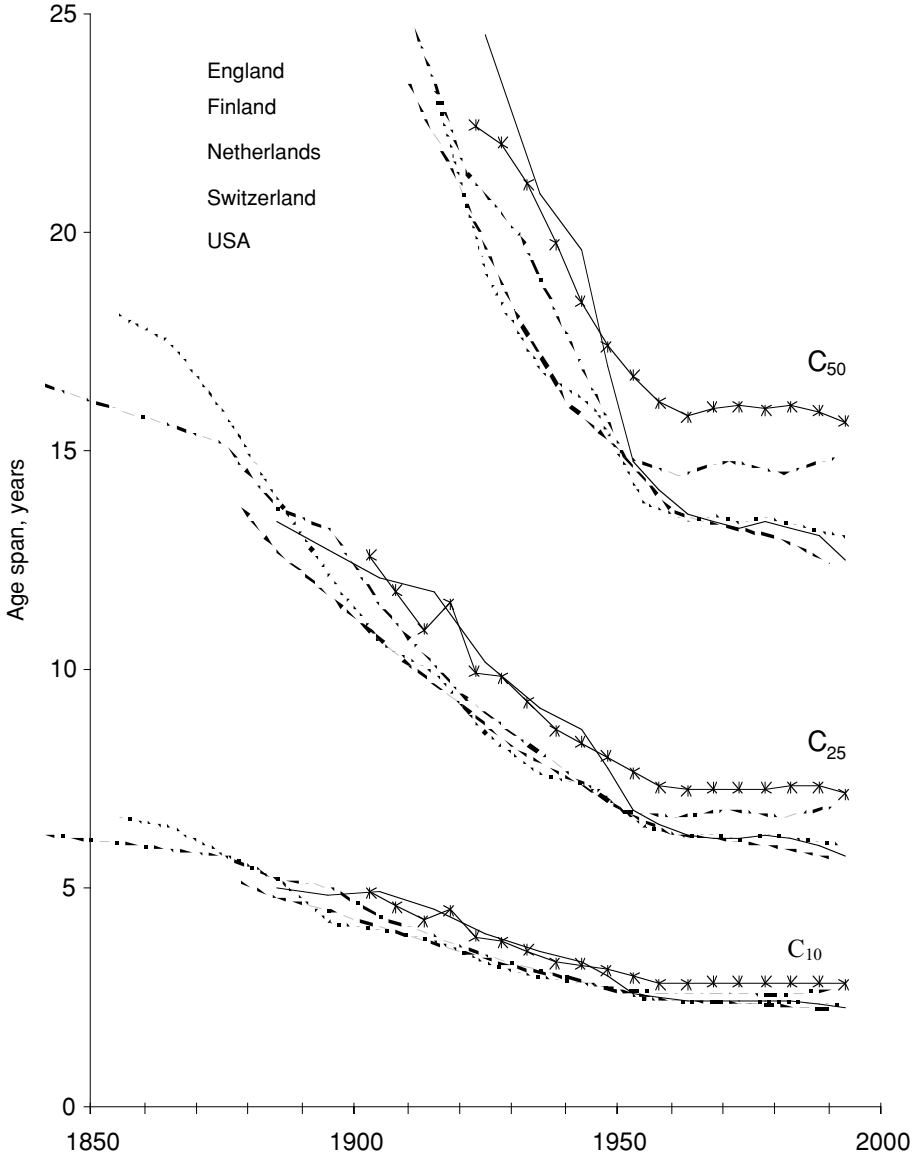

Figure 4. Compression of mortality, female.

With two minor exceptions in C90, all data in Table 3 show that the mortality of females is on every level of measurement more compressed than that of males. This difference is particularly pronounced in the case of France, Hungary and Slovenia and less so in Japan, Sweden and the Netherlands—a situation which is in line with sex differentials in life expectancy in these countries.

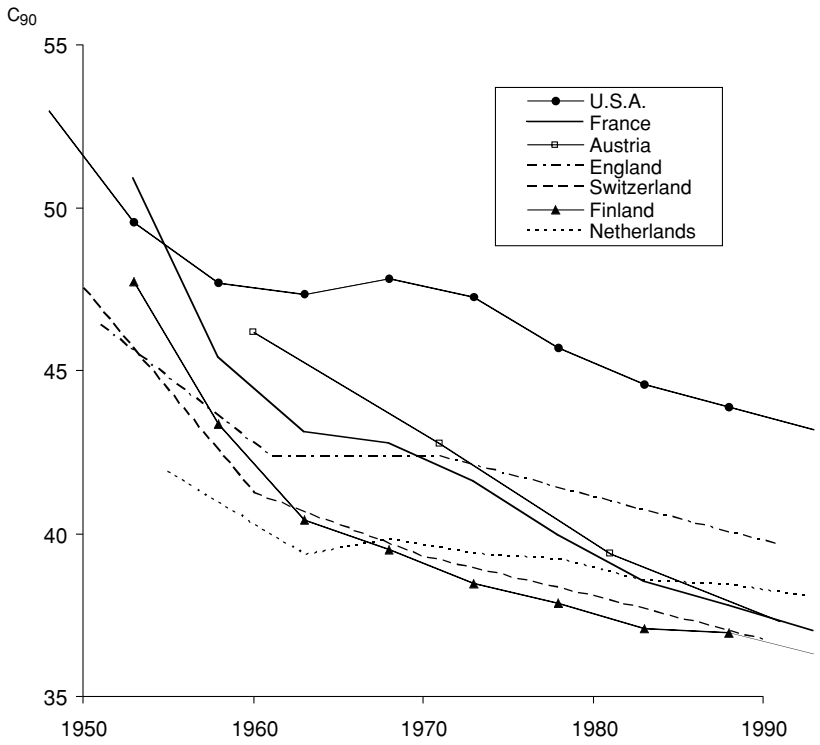

Figure 5. Shortest age interval for 90 percent of deaths. Female.

In a recent article, Wilmoth and Horiuchi analysed ten possible indicators for the compression of mortality and concluded that the inter-quartile range was the best choice for general use, being highly correlated with most of the other nine as well as being convenient and easy to interpret (Wilmoth and Horiuchi 1999). As both IQR and C50 are measures of an age interval in which half of all deaths occur, it is of interest to compare the results they give. By definition, C50 cannot have a larger value than IQR; and, in fact, in all the approximately 30 countries which we have studied, C50 gives without exception a lower value than IQR, thus pointing to the existence of a greater concentration of deaths. For different proportions of deaths, the other C-indicators locate similarly the greatest concentrations.

In order to study more closely the wide differences between IQR and C50 in high- and medium-mortality populations, we give in Figure 6 the age-at-death distribution of Swedish males before and after the mortality transition.

In 1861–70, C50 measured an age span of 38 years in the mature ages from 47 to 85. While undoubtedly long, this range nevertheless corresponds to the greatest concentration of deaths in late life in the epoch. In sharp contrast with this, IQR fails to catch any concentration of deaths which existed and falls flat between the two modes into an age

Table 3. Recent compression indicators for various countries. In ascending order of C50 for females.

		C_{10}		C_{50}		C_{90}	
Country	**Period**	**M**	**F**	**M**	**F**	**M**	**F**
France	1991–95	3.02	2.20	17.1	12.1	47.6	37.0
Japan	1995	2.63	2.20	14.6	12.3	40.6	36.5
Switzerland	1988–93	2.83	2.24	15.5	12.4	45.1	36.7
Italy	1993	2.86	2.24	15.7	12.4	42.8	36.0
Sweden	1992–96	2.64	2.29	14.4	12.6	39.7	36.8
Austria	1990–92	2.92	2.22	16.2	12.6	44.5	37.3
Finland	1991–92	3.01	2.25	16.4	12.6	45.8	36.3
Netherlands	1990–95	2.74	2.35	15.0	13.1	40.0	38.0
Germany, W.	1986–88	2.85	2.37	15.8	13.1	43.2	38.2
Slovenia	1993–95	3.25	2.39	17.7	13.1	47.0	37.6
Ireland	1990–92	2.81	2.46	15.1	13.8	40.2	38.0
Australia	1994–96	2.75	2.42	15.2	13.9	42.4	39.6
England	1990–92	2.86	2.70	15.6	14.8	41.2	39.6
Hungary	1990	3.79	2.72	20.5	14.8	50.8	42.7
Greece	1980	3.00	2.75	16.3	14.9	46.5	39.9
New Zealand	1985–87	2.98	2.76	16.3	15.0	45.1	49.8
Denmark	1994–95	3.03	2.77	16.3	15.5	43.7	41.1
Scotland	1980–82	3.03	2.82	16.6	15.6	43.9	42.4
Korea, S.	1985–87	3.14	2.87	17.0	15.7	44.0	42.3
USA	1991–95	3.21	2.82	17.7	15.7	50.7	43.2
Chile	1986–89	3.39	2.89	18.5	15.8	49.5	43.4
China	1981	3.12	2.90	16.9	16.8	57.3	61.1

range where deaths were actually *least* concentrated. This results in an IQR of 64.7 years. When this is used as a starting point, the magnitude of the ensuing compression is vastly exaggerated.

In the fundamentally transformed d-distribution of 1991–95, the two indicators are much closer together and partly overlap. However, a visual inspection is sufficient to show that C50 covers in a more balanced manner the greatest concentration of deaths while IQR remains slightly out of focus in a somewhat wider age interval (Kannisto 2000).

As a rule, C50 is situated at an older age than IQR. It would, however, be a mistake to conclude from this that it is by nature an indicator of compression in old age while IQR is one for the entire age range. C50 is so constructed that it is entirely neutral regarding both age and survival ranking. In the Egyptian life table 1944–46 for males, IQR was 64.78 years between ages 1.74 and 66.51, while C50 was 35.40 years between ages 0.00 an 35.40. This is a typical situation in high-mortality populations.

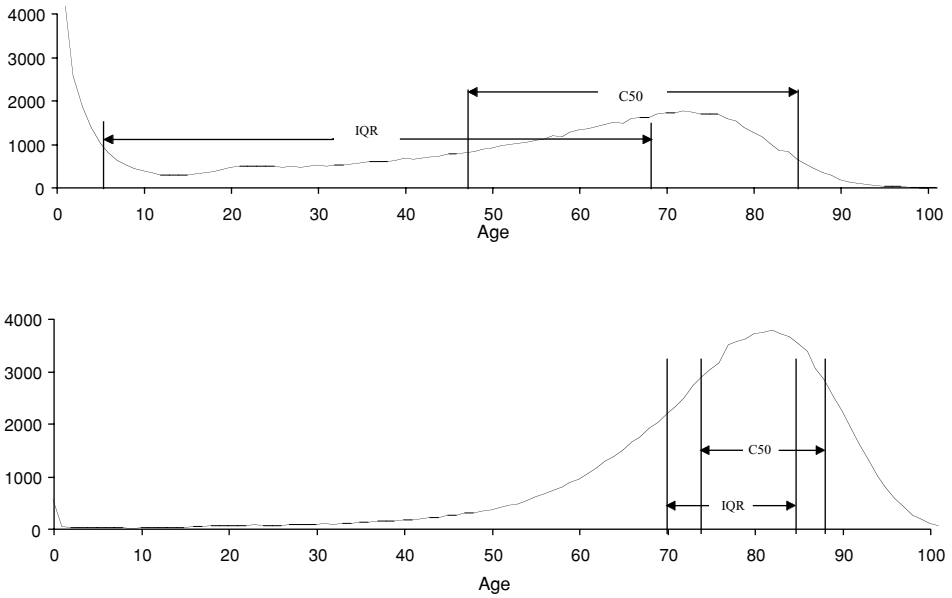

Figure 6. Distribution of deaths by age. IQR and C50. Sweden, male, 1861–70 and 1991–95.

To conclude, we find C50 a better compression indicator than IQR because it consistently points out a narrower age interval for the same number of deaths—in other words, a greater concentration. IQR is particularly ill-suited to measure compression in high-mortality populations. C50 has the additional advantage that it can be supplemented by other C-indicators which together give a more complete and many-sided picture of compression. Robine ends his thorough analysis of the two indicators by concluding that while C50 is more complicated to calculate than IQR, it is better adapted to measuring the development of the concentration of lifetimes and that it points directly to the age segment where this concentration is greatest (Robine 2001).

3.5. INDEX OF RECTANGULARITY

A lively and so-far inconclusive discussion has been going on among demographers as to whether the survival curve has undergone and/or is undergoing *rectangularization*, which would mean that it increasingly resembles a rectangle. In order to measure the process, if any, of rectangularization, it will be helpful if there is a suitable indicator of the degree of *rectangularity*.

We began to study the measurement of rectangularity at the Max Planck Institute in 1999 and opted for an *index of rectangularity, R*, which gives the area under the survival curve in relation to the area of a rectangle the height of which equals the population at the starting age (birth or other) and the length equals *life endurancy*, defined as the age at which 0.01 of the initial population is still alive, and denoted γ (gamma). The purpose of truncating the

survival curve and the rectangle at gamma is to avoid volatility that one or a few extreme long-livers might cause. It also makes, we think the index more realistic in size.

In life table terms, when l (0) = 1.00, the index for the entire survival curve is:

$$R(0) = \frac{T(0) - T(\gamma)}{\gamma} \tag{2}$$

If all people die at the same (whichever) age, this index will equal 100 percent, and rectangularization will be completed.

The general case where rectangularity is measured beginning with age x, is:

$$R(x) = \frac{T(x) - T'(\gamma)}{l(x) \cdot (\gamma - x)} \tag{3}$$

When both the lower and upper age limit are purposively selected, we have:

$$R(a, b) = \frac{T(a) - T(b)}{l(a) \cdot (b - a)} \tag{4}$$

Wilmoth and Horiuchi (1999) list ten possible measures for rectangularity, one of which, called "moving rectangle" is same as our R (0), except that while the right boundary of our rectangle is set at the age at which 0.01 of the original number is still alive, these authors extend the rectangle to the point 0.001. In this extension the area under the survival curve is negligible—by definition less than one percent—and thus adds considerable dead weight to the indicator pressing it down. This does not help in comparisons between populations or overtime. On the other hand, if the boundary is set further left, it cuts significantly into years lived and suppresses relevant information. We therefore propose to maintain the right boundary always at life endurancy, the point where 0.01 of the initial number is still alive.

These measures seem to give a good account of rectangularity as it has developed historically. Its course in France over a period of nearly 200 years is shown in Figure 7.

The most rectangular forms, with relatively flat tops, are found in limited age periods. Thus, the index for working age (15–65) was rather high already in the early 19th century, followed by the childhood (0–15) index: 77 and 70 respectively. Towards the end of the century, the latter began to rise reflecting the decline in child mortality, and by 1900 it surpassed the former.

The remaining four indexes in Figure 7 follow the survival up to the specific life endurancies which makes their form less rectangular and the index lower. In the past, the index for the entire survival curve, R(0), was considerably lower than R (15) which describes the adult life. Only around 1950 the former overtook the latter and grew to over 80 percent.

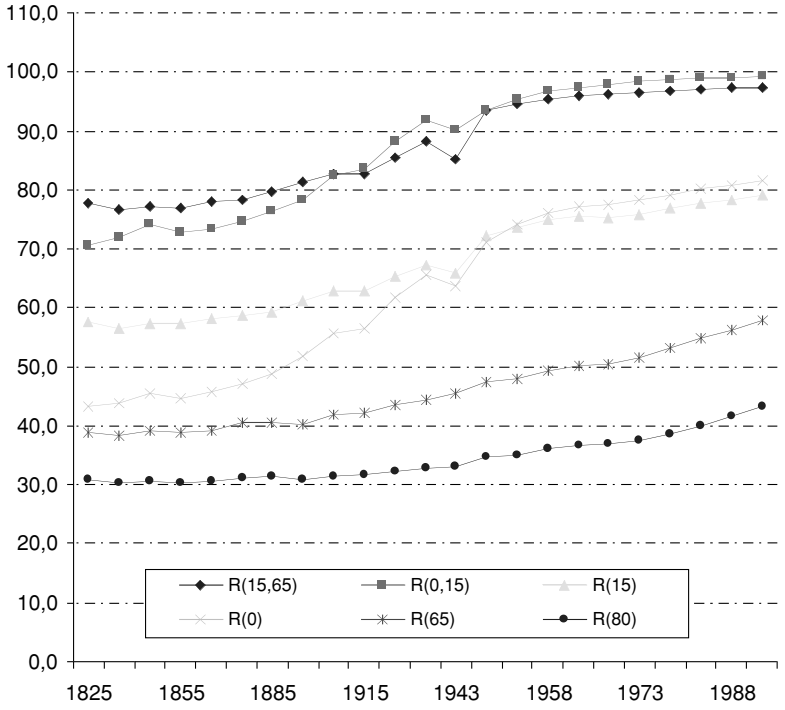

Figure 7. Indexes of rectangularity. France, female.

The survival curves of old age are naturally the least rectangular of all and did not change significantly before mid-20th century. R (80) which represents the oldest age has increased in the last half-century more than ever before, but still quite modestly: from about 33 to 43. This is not enough to give it an even remotely rectangular form but signifies nevertheless a certain development toward a more common age at death.

To return to the most important of these indexes, R (0), which represents the entire survival curve, we notice that it keeps increasing with hardly any tendency to decelerate, taking small but measurable steps towards full rectangularity. In the last decade alone, even as life endurancy grew by as much as one-and-a-half years (from 98.4 to 99.9), R (0) increased from 80.2 to 81.5. This means that the expanding rectangle was being increasingly filled with life.

The diverging courses of rectangularization of the entire survival curve and that of old age are illustrated on a broader international front in Figure 8. All countries shown conform to a common historical pattern in which from about 1850 to 1950 a rapid increase lifted R (0) from less than 50 to nearly 80 percent, while R (80) remained essentially stationary. Then, when the former had reached a high level and slowed down, the latter began a sustained growth. The claw-like picture is quite similar for both sexes, with the difference that the

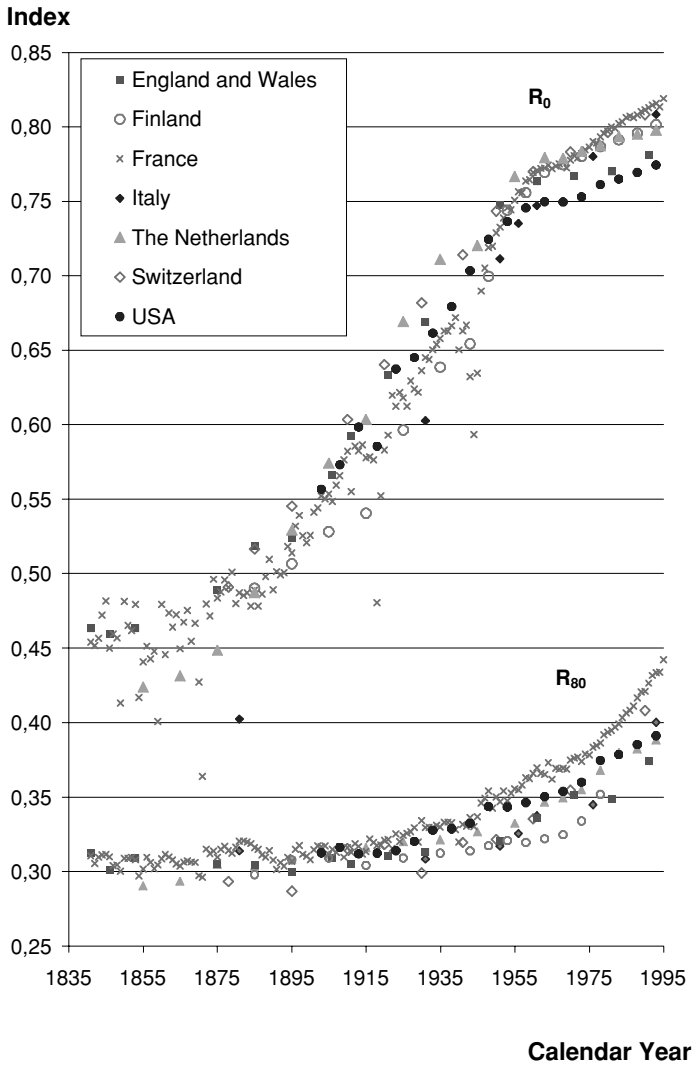

Figure 8. Secular trends in rectangularity. Several countries, females.

survival of females is at all times slightly more rectangular and enters each stage slightly earlier.

This advance in female rectangularization is connected with higher life expectancy. Figure 9 shows that the two are highly correlated. The correlation is not quite linear but forms a regular arch which suggests that further increases in life expectancy are likely to produce diminishing increases in rectangularity. In other words, rectangularity is entering a certain

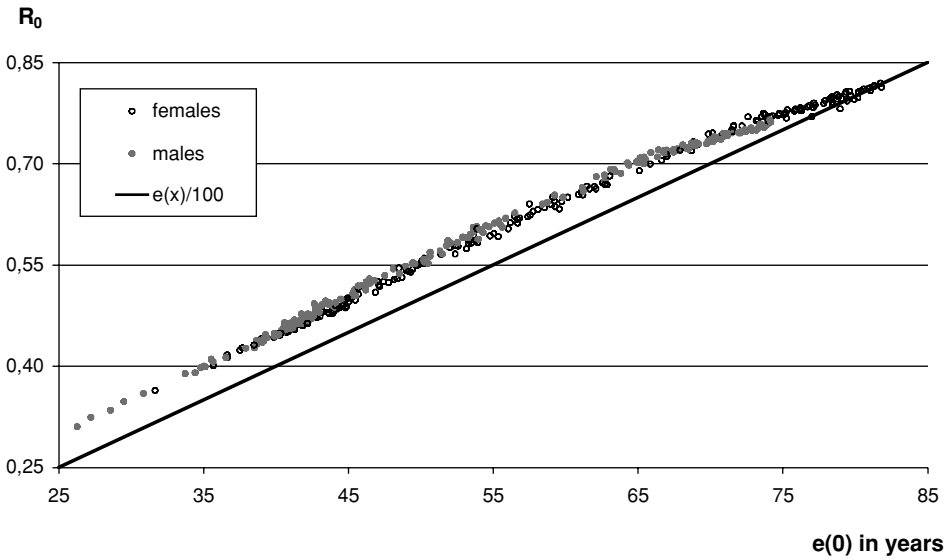

Figure 9. Life expectancy at birth and rectangularity. England & Wales, Finland, France, the Netherlands and Switzerland.

maturity and possibly approaching a saturation point. The path, however, is about identical for both sexes.

4. Myth or Reality?

The reality of the double phenomenon of compression of mortality and rectangularization of the survival curve has been questioned by some writers. Myers and Manton raise the question in the stark terms of "myth or reality" and, upon examining U.S. data, imply—without expressly saying so—that the answer is: myth (Myers and Manton 1984a). Their study was, however, flawed by the use of a fixed lower age limit. In a later study, the same authors admitted that the use of percentiles instead of an age limit shows that the standard deviation of lifetimes remained almost constant (Myers and Manton 1984b). Some authors give a qualified answer as to the reality of compression, and Paccaud (2000) draws from an observation of death percentiles in Switzerland the timid conclusion that their slight convergence "might be an early sign of compression of mortality".

It would seem sufficient to have a glance at the age distribution of deaths in any low-mortality country now and before the transition in order to convince the observer of a massive compression of mortality, and likewise to take a glance at the survival curve now and in the past, to convince him of the reality of rectangularization. If any doubt would remain, the analysis by Robine (2001) or by Wilmoth and Horiuchi (1999) should prove the point and the present paper should contribute to the same effect.

5. Conclusion

In the study of the length of life the late life mode should in our view receive more attention than it has been given. Representing the typical lifetime under a given mortality regime, it imparts valuable information. Observation of the development of the mode during the great mortality transition shows around 1970 a fundamental change in trend—an acceleration which signified that mortality entered an entirely new stage. Observing instead the life expectancy at birth in the same period, this new stage would pass completely unnoticed.

A notable fact about the late life mode is that in all situations which we have observed—in different countries and under widely different mortality regimes—the length-of-life distribution on the right side of it closely resembles the slope of a normal curve, not only by visual inspection but also when measured by dispersion indicators.

Indicators which deserve attention in addition to the age of the late life mode, are the height of the mode d (M) and the standard deviation above it SD (M+). Still another is the proportion of all lives which end under a curve produced when the slope on the right side of the mode is replicated on the left. This comprises what in the given circumstances might be called lives of full length.

Closer to the frontier of survival, the length of life and its dispersion can be measured by the mean and standard deviation in the highest quartile.

Regarding the double phenomenon of compression of mortality and the rectangularization of the survival curve, it may be asked which one is the cause and which one is the effect. As we see it, the prime mover behind both is the dynamics of mortality, expressed as changes in the age-specific probability of dying. These changes move the inevitable death of persons forward or backward creating compression or decompression as well as a change in rectangularity. Though the two effects are closely interrelated, we propose precise and unambiguous measurement of each: compression by a family of C-indicators and rectangularity by a family of R-indexes. The former are more neutral in character, being free from both the age scale and the percentile scale, while the R-indexes require an arbitrary decision concerning the x-axis of the rectangle.

Application of the proposed measures to a very large variety of populations and situations indicate with hardly any room for doubt that the secular transition from high to low mortality has always been accompanied by a reduction of individual variability, by compression of mortality and by rectangularization, all on a massive scale. However, on all three fronts, the development has slowed down to near standstill at a stage where even approximate uniformity in the length of life is still so far off that it seems unrealistic to expect it ever to be attained (Kannisto 2000).

Even in this situation it is of interest to keep monitoring the development of the indicators, particularly of those which still display considerable movement. Our data show this to be the case of C90 and R (0).

A factor influencing the concentration of mortality by age, is population heterogeneity (Vaupel *et al.* 1979), which is partly genetic but probably to a greater extent environmental (Christensen and Vaupel 1996; Valkonen *et al*. 1993). If the data were divided into sub-populations according to occupation, education, marital status, availability of medical care, and life-style factors such as diet, smoking, and so on, we would probably observe greater uniformity within each of them. However, no sub-population could conceivably die out in a truly short age span.

To sum up, we consider it relevant to the study of mortality to monitor these processes which describe important aspects of the length of life and reflect internal mortality differentials in a population. Of the recommended indicators, C50 seems to express best the development until now as well as the existing differences by country and sex but, as the situation matures, C90 may become illustrative.

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References

Christensen, K., and Vaupel, J. W. (1996) "Determinants of longevity: Genetic, environmental and medical factors", *Journal of Internal Medicine*, 240:333–341.

Fries, J. F. (1980) "Aging, natural death and the compression of morbidity", *New England Journal of Medicine*, 303:130–135.

Kannisto, V. (1994) *Development of Oldest-old Mortality, 1950–1990: Evidence from 28 Developed Countries*. Odense: Odense University Press.

Kannisto, V. (2000) "Measuring the compression of mortality", *Demographic Research,* 3/6. [Available http://www.demographic-research.org/volumes/Vol3/6/].

Kannisto, V. (2001) "Mode and dispersion of the length of life", *Population,* 13/1:159–171.

Lexis, W. (1877) *Zur Theorie der Massenerscheinungen in der menschlichen Gesellschaft*. [Quoted by Porter, T. M. (1986) *The Rise of Statistical Thinking 1820–1900*.]

Myers, G. C., and Manton, K. G. (1984a) "Compression of mortality: Myth or reality?", *The Gerontologist,* 24/4:346–353.

Myers, G. C., and Manton, K. G. (1984b) "Recent changes in the US age distribution: Further observations", *The Gerontologist*, 24:572–575.

Paccaud, F. (2000) *Rectangularization of the Survival Curve: An Assessment in Switzerland*. Paper presented at IUSSP seminar on human longevity, Montpellier.

Robine, J.-M. (2001) "Redefining the stages of the epidemiologic transition by a study of the dispersion of life spans: The case of France", *Population,* 13/1:173–193.

United Nations (1999) “Department of economic and social affairs, population division”, *Health and Mortality Issues of Global Concern*. New York: UN.

Valkonen, T., Martelin, T., Rimpelä, A., Notkola, V., and Savela, S. (1993) “Socio-economic mortality differentials in Finland 1981–90”, *Statistics Finland, Population*, 1.

Vaupel, J. W., Manton, K. G., and Stallard, E. (1979) “The impact of heterogeneity in individual frailty on the dynamics of mortality”, *Demography,* 16/3:439–454.

Wilmoth, J. R., and Horiuchi, S. (1999) “Rectangularization revisited: Variability of age at death within human populations”, *Demography,* 36/4:475–495.

CHAPTER 6. RECENT TRENDS IN LIFE EXPECTANCY AND RECTANGULARISATION OF THE SURVIVAL CURVE AT ADVANCED AGES IN THE NETHERLANDS

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Introduction

The Netherlands and other low mortality countries have experienced a long period of mortality decline. Life expectancy had already risen since the eighteenth century in some European countries, including England, France, and Scandinavia; in the Netherlands mortality reductions are likely to have started in the nineteenth century (Mackenbach 1992; Mackenbach 1993; Wrigley and Schofield 1983). From 1840/51 to 1995/99 life expectancy at birth increased from 36.1 to 75.0 years in Dutch men and from 38.5 to 80.5 years in Dutch women (Mackenbach 1992; Statistics Netherlands annually-a, annually-b).

This dramatic increase in life expectancy has been accompanied by substantial changes in the age-at-death and cause-of-death patterns. These shifts are described in the 'epidemiologic transition theory' (Mackenbach 1993; Omran 1971) which is an extension of the mortality component of the 'demographic transition'. Originally, three phases were distinguished: 'the age of pestilence and famine', 'the age of receding pandemics' and 'the age of degenerative and man-made diseases'. During the epidemiologic transition changes in the cause-of-death pattern from mainly infectious diseases to chronic diseases were accompanied by a shift in the age pattern of mortality from younger towards older ages. In the third stage mortality was concentrated at older ages and was mainly caused by chronic diseases. Olshansky and Ault (1986) added a fourth stage, labelled 'the age of delayed degenerative diseases'. This phase is characterised by the delay of mortality from degenerative diseases to older ages, implying rapidly falling death rates and rising life expectancy at older ages, and a significant rise in the mean age of death from these diseases. The most important difference between the last two phases is that in the latter the shift of mortality towards older ages is not accompanied by a shift in the cause-of-death pattern.

Whether the delay in mortality towards increasingly older ages will continue to generate substantial increases in life expectancy in the near future is still a matter for debate. Two opinions are prevalent: one stating that life expectancy at birth will not increase beyond

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85 years of age (Fries 1980; Keyfitz 1978; Olshansky and Carnes 1997; Olshansky and Carnes 1994; Olshansky, Carnes, and Desesquelles 2001); the second arguing that a life expectancy at birth of 100 years or more is within reach somewhere in the near future (Manton, Stallard, and Tolley 1991; Oeppen and Vaupel 2002; Vaupel and Lundstrom 1994). The increasingly rectangular shape of the survival curve, seen as a manifestation of the life expectancy approaching the average life span (Fries 1980), and the enormous reductions in mortality rates which would be needed to achieve a life expectancy at birth of 85 years (Olshansky, Carnes, and Cassel 1990), are used as arguments to support the first view. Opponents of this view point to observed decreases of mortality rates at advanced ages by 1–2 per cent per year, very low mortality rates in subpopulations with healthy life styles, and an increase of record life expectancy by 2.5 years per decade for 160 years, to underpin their vision of substantial future increases in life expectancy (Manton *et al.* 1991; Oeppen and Vaupel 2002; Vaupel and Lundstrom 1994).

Diverging views on the likely size of future increases in life expectancy play an important role in a closely related debate on whether a longer life will be associated with worsening or improving health of the elderly population. The opposing views can be summarised as the 'expansion-of-morbidity hypothesis' (Gruenberg 1977; Kramer 1980; Olshansky *et al.* 1991; Verbrugge 1984) and the 'compression-of-morbidity hypothesis' (Fries 1980, 1983, 1989), respectively. According to Fries—the main proponent of the compression-of-morbidity hypothesis—the survival curve has obtained an ever more rectangular form ('rectangularisation'), as life expectancy reaches the fixed human life span. In such a situation, postponement of chronic diseases by adopting healthier life styles results in a shorter span between the increasing age of onset of morbidity and the fixed age at death. This is known as the compression of morbidity. Opponents of Fries argue that the average age at death can still be delayed substantially. If this life extension results from advances in medical treatment that reduce the lethal sequelae of chronic diseases, persons will live longer *with* chronic diseases and disability (Gruenberg 1977; Kramer 1980). This is known as expansion of morbidity. But besides mortality reductions among the chronically ill, improvements in the chances of surviving up to advanced ages might imply that the proportion of the population that faces the risks of chronic diseases and associated disability will increase, due to the strong age-dependence of these risks (Olshansky *et al.* 1991; Verbrugge 1984). Thus as a consequence of mortality declining at advanced ages the health status of the oldest-old population might deteriorate—morbidity might expand. A third view, the 'dynamic-equilibrium hypothesis' (Manton 1982) stands in between and predicts further increases in life expectancy caused by a reduction of the rate of progression of certain degenerative diseases in an earlier (less severe) stage of the disease process in the elderly population by medical interventions and lifestyle changes. As a result, survival will increase, which will produce an increase in years with morbidity. However, years with severe morbidity and disability will be relatively constant.

Apart from the significance of developments in old-age mortality for scientific debates about limited life span and compression of morbidity, the important fact is that mortality changes strongly affect the size of the oldest-old population (Ahlburg and Vaupel 1990). In turn, the size of the elderly and oldest-old population is an important determinant of the demand for medical care and other long-term care services and the many other age-related assets and needs.

Empirical studies on mortality have described substantial mortality reductions in the oldest-old. In the Netherlands too, life expectancy at age 60 and age 85 has increased (Statistics Netherlands 1994); but life expectancy at advanced ages (age 85+) stopped increasing during the 1980s in the Netherlands (Nusselder and Mackenbach 2000). This lack of increase in life expectancy of the elderly was accompanied by a tendency towards rectangularisation ever since the beginning of the 1980s (Nusselder and Mackenbach 1996, 1997). To date it is uncertain whether these developments at older ages are only temporary or more permanent.

The objective of this paper is to assess whether the lack of increase in life expectancy and the tendency towards rectangularisation have continued, stopped, or reversed in the second half of the 1990s in the Netherlands. By looking at both a central mortality indicator (life expectancy) and a dispersion indicator (compression of mortality), we will obtain insight into the recent developments of old-age mortality in the Netherlands. We will use data on all-cause mortality for the Dutch population during the period 1950–1999, and add seven years to previous analyses of rectangularisation of the survival curve and five years to previous analyses of life expectancy at advanced ages.

Data and Methods

DATA

Data on the number of deaths and the population by sex, age, and calendar year for 1970–1999 were obtained from Statistics Netherlands (*Statistics Netherlands* annually-a, annually-b, multiple years; Tabeau, Van Poppel, and Willekens 1994). Population data were classified by single year of age, and data on the number of deaths by single year of age and year of birth. These data had originally been derived from the municipal population registers. Population registers are considered to be reliable and consistent (Condran, Himes, and Preston 1991), as age recording is based on the birth certificate, and the registers provide data on both the population at risk by single year of age and the number of deaths. As a result, mortality risks can be obtained from one single source, avoiding numerator–enumerator bias.

METHODS

Before moving to more aggregated central and dispersion measures of mortality (and survival) we first examined changes in age- and sex-specific mortality rates. We calculated standardised mortality rates by ten-year age groups, using the population of 1990 by single year of age as the standard. In this way we could avoid the possibility that a changing population distribution within the ten-year age intervals might affect our results.

Second, we examined changes in life expectancy at ages 60 and 85 in the period 1970/74 to 1995/99. Life expectancy, being the most commonly used central measure in mortality research, is the average age at death in the stationary (that is, the life-table) population. Life expectancy can be calculated at different ages and can be interpreted as the average number of years a person of a given age (and sex) can expect to live, given that current

mortality rates will remain unchanged. Life expectancies at ages 60 and 85 are derived from complete life tables, which we constructed for each five-year period (e.g. 1970/74) with age 105 as the final age, using a period-cohort observational plan. This observational plan includes one calendar year, one cohort, and two age groups. As a result, age refers to half ages, for example 60.5. We assumed that deaths were uniformly distributed over the (one-year) age interval (Namboodiri 1991; Namboodiri and Suchindran 1987).

Third, we looked at rectangularisation of the survival curve. rectangularisation is defined as a trend towards a more rectangular shape of the survival curve due to increased survival and concentration (compression) of deaths around the mean age at death (Fries 1980; Myers and Manton 1984a; Nusselder and Mackenbach 1996). Concentration of deaths and, consequently, rectangularisation, can take place in an absolute or in a relative sense. When mortality is concentrated into a shorter age range, absolute variability of the age at death (expressed in years) declines, indicating an absolute compression of mortality. On the other hand, when mortality is compressed into a smaller proportion of total life expectancy, relative variability (i.e. relative to the mean) declines, indicating a relative compression of mortality. A reduction in the variability in the age at death (in the absolute or the relative sense), in combination with an increase in life expectancy, indicates rectangularisation (in the absolute or the relative sense). If life expectancy is increasing, absolute rectangularisation automatically means relative rectangularisation, but the reverse is not true. In particular, when the age distribution only shifts to the right, without becoming more compressed, rectangularisation occurs only in a relative sense. For fuller descriptions of the concept and measurement of rectangularisation we refer to Nusselder and Mackenbach (1996) and Wilmoth and Horiuchi (1999).

To assess Rectangularisation, we used Keyfitz' H (H) and its numerator (NH) (Demetrius 1978; Keyfitz 1977; Keyfitz and Golini 1975; Smith 1992) in combination with life expectancy. NH is a measure of absolute variability, just like the standard deviation; whereas H, like the coefficient of variation, is a measure of relative variability. If the survival curve is completely rectangular, H is zero. In that case everybody dies at exactly the same age and the variability of the age at death is zero. If the force of mortality is equal at all ages, H is one. If the survival curve declines linearly with age (the number of deaths is equal at all ages), H is 0.5. H is also a measure of the elasticity of life expectancy for proportional changes in mortality rates. Finally, H can be viewed as the average years of future life that is lost by the observed deaths, relative to life expectancy.

The calculation of NH and H requires some additional steps, in which the number of deaths and the mid-interval life expectancy at age $x + 0.5n$ obtained from the complete life table are used as input. We used a discrete approximation of H, based on the linear method, to calculate H from a complete life table with an initial cohort of one at the starting age x ($l_x = 1$) :

$$H_x = \frac{\sum_{a=x}^{\omega} {}_nd_a \; e_{a+0.5n}}{e_x}$$

where x is the starting age; ${}_nd_a$ is the number of persons alive at age x who will die in the age interval a, $a + n$; ω is the final age (105 in our study); $e_{a+0.5n}$ is the mid-interval life

expectancy at age $a + 0.5n$ (i.e. local life expectancy), and n is the length of the age interval (one year in our study, except for age 105, which includes ages 105 and over). H multiplied by the life expectancy at the starting age gives NH. The measures of variability can be calculated easily for survival curves starting at any age. We used age 60 as the starting age.

A decline in H indicates a relative compression of mortality, and, in combination with an increasing life-expectancy, rectangularisation in a relative sense. Similarly, a decline in NH indicates an absolute compression of mortality and rectangularisation in an absolute sense. In addition, a decline in H and NH show that equivalent proportional mortality decline produce smaller gains in life expectancy (i.e. diminishing returns) in a relative and an absolute sense, respectively (Keyfitz 1978).

Results

STANDARDISED MORTALITY RATES

Figure 1 shows the standardised mortality rates by ten-year age groups for the ages 60 and over. For ease of interpretation, we expressed the rate in each five-year period as the ratio of the standardised mortality rate in 1970/74 (i.e. 1970/74 = 100). A ratio larger than 100 indicates an increase in mortality as compared to 1970/74; whereas a ratio smaller than 100 indicates a decline.

For both sexes the standardised mortality ratios decreased between 1970/74 and 1995/99, indicating a mortality decline in all age groups, although at various speeds for the different age groups and sexes. In general, mortality decline was substantially larger in women than in men. Despite the overall mortality decline—for men the decline in the age group 80–89 was only small—the age group 90 years and over did not show a continuous decline during the entire period. In fact, mortality in this age group has increased since 1980/84. This increase was also found in women, but less pronounced than in men. The mortality increase in the age group 90 years and over continued in the second half of the 1990s.

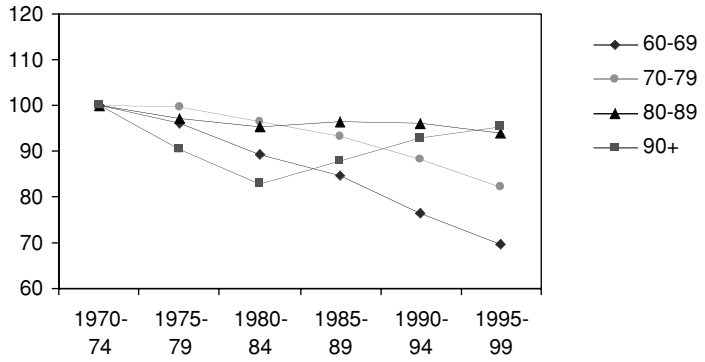

Figure 1a. Standardised mortality rates by ten-year age groups (1970/74 = 100), men, the Netherlands.

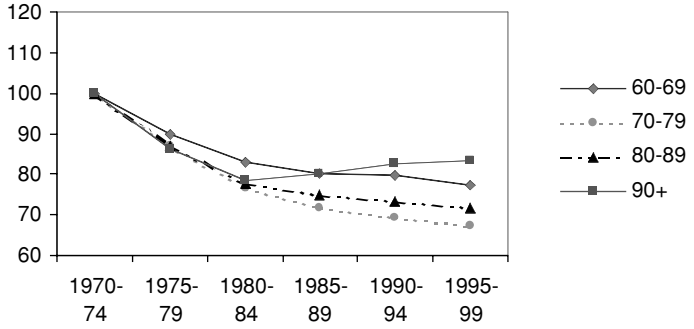

Figure 1b. Standardised mortality rates by ten-year age groups (1970/74 = 100), women, the Netherlands.

LIFE EXPECTANCIES AT AGES 60 AND 85

Over the past 25 years, life expectancy at ages 60 and 85 has increased in the Netherlands. Table 1 shows that life expectancy at age 60 increased from 16.6 years in 1970/74 to 18.3 years in 1995/99 in men, and from 20.5 to 22.9 years in women. Life expectancy at age 85 showed a slight increase from 4.3 to 4.5 years in men and a larger increase from 4.8 to 5.6 years in women in the same period. This overall improvement does not imply that life expectancy increased during the whole period 1970/74 to 1995/99. As could be anticipated from the description of the standardised mortality rates, a reversal took place from an increasing life expectancy at age 85 prior to 1980/84 to a decreasing life expectancy in men, and a virtually constant life expectancy in women ever since 1980/84. In the second half of the 1990s the lack of increase in life expectancy at age 85 continued.

COMPRESSION OF MORTALITY AND RECTANGULARISATION

Visual inspection of the distribution of life-table deaths by age, presented in Figure 2, gives some indication of the changes in the variability of the age at death. Since the area under

Table 1. Life expectancy at ages 60 and 85 by sex, the Netherlands.[1]

	Men		Women	
	Age 60 years	**Age 85 years**	**Age 60 years**	**Age 85 years**
1970/74	16.60	4.32	20.45	4.79
1975/79	16.78	4.61	21.47	5.28
1980/84	17.16	4.74	22.29	5.65
1985/89	17.42	4.62	22.59	5.67
1990/94	17.84	4.51	22.72	5.62
1995/99	18.34	4.50	22.90	5.63

[1] Life expectancy is derived from the life table based on a period-cohort observational plan, and therefore the age refers to half ages, like 60.5 and 85.5.

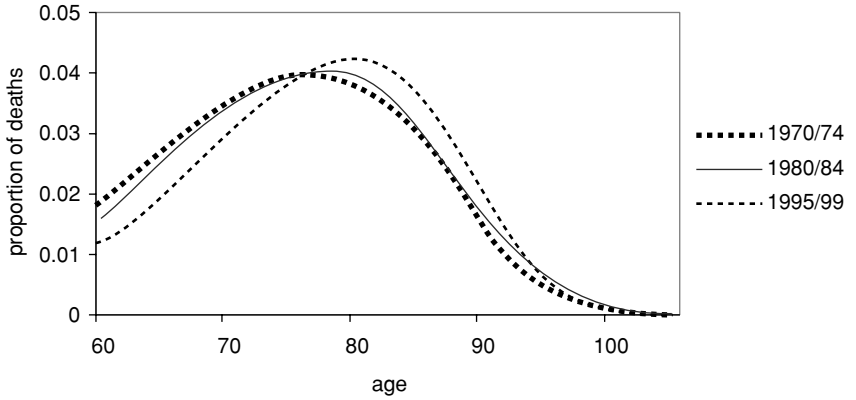

Figure 2a. Age distribution of life-table deaths at age 60, men, the Netherlands.

the curve is per definition 1, a lower peak indicates more dispersion—i.e. less compression of mortality—and a higher peak more compression. Figure 2 shows that in 1995/99 as compared to 1980/84 the peak of the age-at-death distribution was higher, indicating a compression of mortality.

To quantify compression of mortality and rectangularisation, measures of the variability in the age at death are helpful. Therefore we calculated Keyfitz' H and its numerator on the basis of the complete life tables. Table 2 shows that relative compression of mortality took place during the whole period (women) and since 1975/79 (men). From 1980/84 onwards absolute compression of mortality occurred as well in both sexes. That is, since 1980/84 the decline in the relative variability in the age at death was no longer caused by an increase in life expectancy, but reflects a reduction in absolute variability of the age at death. This tendency, in combination with an increasing life expectancy at age 60, implies

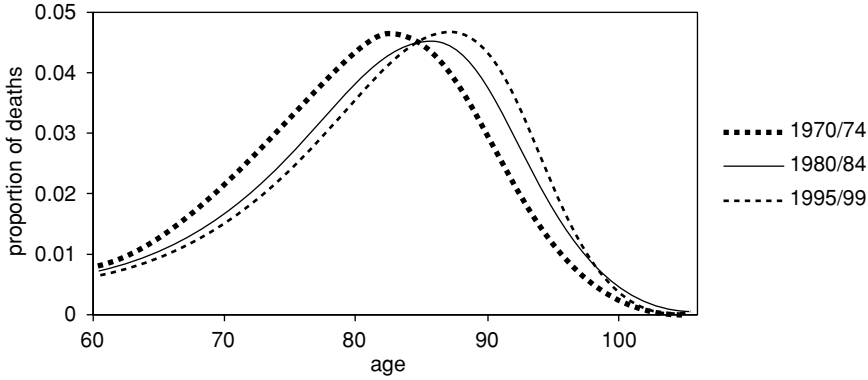

Figure 2b. Age distribution of life-table deaths at age 60, women, the Netherlands.

Table 2. Keyfitz' H (H) and Numerator of Keyfitz' H (NH) at age 60, by sex, the Netherlands.

	Men		Women	
	H	**NH**	**H**	**NH**
1970/74	0.478	7.93	0.364	7.44
1975/79	0.480	8.06	0.357	7.67
1980/84	0.471	8.08	0.349	7.77
1985/89	0.456	7.94	0.341	7.70
1990/94	0.437	7.79	0.335	7.62
1995/99	0.420	7.70	0.330	7.57

absolute rectangularisation of the survival curve. In men this rectangularisation was more pronounced than in women. Focussing on developments in recent years, a continuation of the rectangularisation in the second half of the 1990s can be seen.

Discussion

This study examined the recent developments in old-age mortality in the Netherlands, by looking at both a central indicator (life expectancy) and a dispersion indicator (compression of mortality) in the period 1970/74–1995/99. We found that life expectancy at age 60 increased during the whole period, but that life expectancy at age 85 has stopped increasing since 1980/84. In fact, in men, life expectancy at age 85 declined in the 1980s and 1990s, whereas in women it remained virtually constant. This lack of increase in life expectancy of the oldest-old can be traced back to increasing standardised mortality rates in men aged 85 and over and in women aged 90 and over. Our analyses of compression of mortality, based on Keyfitz' H and its numerator, indicated that compression of mortality took place in a relative sense during the whole period in women and, since 1975/79, in men. From 1980/84 onwards, in both sexes compression of mortality took place in an absolute sense as well. That is, since 1980/84 deaths became concentrated in a more narrow age range. In combination with the increasing life expectancy at age 60, this means that rectangularisation took place both in a relative sense and in an absolute sense. We found that changes in compression and rectangularisation were more pronounced in men than in women. During the second half of the 1990s, the lack of increase in life expectancy at advanced ages and the processes of compression of mortality and rectangularisation continued.

METHODOLOGICAL ISSUES

Two methodological issues deserve special attention. First, we used period life tables to assess changes in life expectancy and compression of mortality (and rectangularisation). These period life tables combine the mortality of different birth cohorts into one synthetic cohort. We could not use cohort life tables, because analyses of recent changes in life expectancy and compression of mortality would be impossible without making assumptions

about the development of mortality of birth cohorts who have not completed their mortality in 1995/99. Second, we did not formally test whether the described changes in life expectancy and compression of mortality (and rectangularisation) were statistically significant. Nevertheless we consider it very unlikely that chance fluctuations have driven our results. Our analyses were based on data of the entire population, and not on a sample of subjects. In addition, we merged five calendar years (1970/74, 1975/79 and so on) to avoid small numbers. As the observed trends in life expectancy, compression of mortality, and rectangularisation persisted for more than one decade, we believe that some systematic change in old-age mortality occurs in the Netherlands. Considering that the generally observed pattern of old-age mortality in current low mortality countries is one of a continuing increase in life expectancy of the oldest-old (Kannisto *et al.* 1994; Vaupel and Lundstrom 1994), a constant life expectancy at advanced ages would already mean a deviation from the general pattern—the more so is the observed decrease in life expectancy at advanced ages in men. Despite the fact that the reductions in Hand NH appear to be small, we consider them to be relevant (especially for men), taking into account trends in the Netherlands above age 60 since 1950 (Nusselder and Mackenbach 1996), and considering that the survival curve will never become perfectly rectangular (i.e. Hand NH will never equal zero). Even in the extreme case where the genetically endowed limit is approached, there will be genetic variability in the age at death (Myers and Manton 1984a, 1984b). Given that NH was 8.1 in men and 7.8 years in women in 1980/84 and expecting that the minimum level of NH would still be a few years, we consider the decline in NHby 0.4 years in men over a 20-year period to be of importance. The decline in Hover the same period was 0.5 in men. The order of magnitude of the latter was similar to the increase in H observed in the period 1950/54 to 1975/79 (Nusselder and Mackenbach 1996).

Although when dealing with old age mortality, unreliability of age reporting at advanced ages is generally a drawback for accurate age-specfic mortality rates (Myers and Manton 1984a; Paccaud *et al.* 1998; Rothenberg, Lentzner and Parker 1991), it is very unlikely that this problem has biased our results. Mortality and population data are based upon the municipal population registers that have been kept in the Netherlands since 1850 (Tabeau *et al.* 1994). This guaranteed a high validity of age recording, because at birth a personal card based on the birth certificate was made and all changes in vital status, including death, were recorded on this card. Another important advantage of using dates based on the population register is that data on the population at risk by single year of age and sex can also be obtained from this source. That is, the numerator and denominator of mortality rates are based on one single source. Therefore mortality rates (and probabilities) could be used as the basis of our analysis, rather than only information on the number of deaths by age, used in the so called 'numerator analysis'. The latter type of analysis is often chosen to avoid a combination of different data sources, but a disadvantage is that changes in the population structure can affect the results. In addition, when the analysis is confined to a specific age range (e.g., 60 and over), a changing proportion of deaths included in the analysis might affect the outcomes of a numerator analysis.

Rectangularisation can be measured using several measures of variability in the age at death (Wilmoth and Horiuchi 1999). We do not expect that using Keyfitz' H and its numerator has affected our results. Wilmoth and Horiuchi (1999) reported a very high correlation between H and most of the other possible indicators of rectangularisation. In addition, we

re-analysed our data using the standard deviation as an indicator of absolute variability and the coefficient of variation as an indicator of relative variability. The outcomes were very similar to those presented for NH and H, respectively (data not shown). We used measures of variability based on Keyfitz' H for several reasons. First, H and NH not only measure the variability in the age at death, but also quantify the effect of small proportional mortality reductions at all ages on life expectancy. Due to this property, which expresses the fact that the effect of mortality changes on life expectancy depends on the rectangularity of the survival curve, even without making inferences about whether or not the maximum life span is being reached, there exists a relationship between rectangularisation and further increases in life expectancy. Second, measures based on Keyfitz' H can be decomposed by age and cause of death (Nusselder and Mackenbach 1997). Decomposition is an important explanatory tool to examine changes in the rectangularity of the survival curve. Finally, H and NH are more balanced measures of changes occurring over the entire survival curve than for instance the SD and the interquartile range (IQR) used by Wilmoth and Horiuchi (1999). In SD-based measures the outliers (i.e. the youngest and oldest ages) have an important weight because, in the calculations, deviations are squared and life expectancy at the starting age is used as the reference point. Measures based on Keyfitz' H, on the other hand, use the local life expectancy, which links up better with the concept of rectangularisation, since, in general, rectangularisation occurs when the age- at-death distribution shows an increased concentration around the life expectancy, as the latter moves to older age (or its maximum). The interquartile range (IQR), being the difference between ages where the survival curve crosses 0.25 and 0.75, does not take into account mortality in the upper quartile. In particular, changes in old-age mortality play an important role in the rectangularisation debate and proved to be very indicative of the observed rectangularisation in the Netherlands.

COMPARISON WITH OTHER COUNTRIES

Comparison of our findings for the Netherlands with other countries shows that the recent lack of increase in life expectancy as found in the Netherlands is not found in most other countries. Only in Norway did mortality at advanced ages increase slightly between 1986/90 and 1991/94 (Mamelund and Borgan 1996). Most other countries, also those with low mortality levels, showed a continuing decrease in old-age mortality (Kannisto 1994; Kannisto *et al.* 1994). A comparison of our results on rectangularisation with studies on this topic for other countries is difficult, as the measures of rectangularisation differ between the studies; and most studies examine rectangularisation of the survival curve starting at birth. Wilmoth and Horiuchi (1999) described a recent stability in the variability of ages at death (all ages included) in the United States and Sweden, and a slight decompression in Japan. These conclusions refer to rectangularisation of the survival curve starting at birth and are based on the IQR, which does not take into account the highest age groups. Nevertheless, based on these findings we do not expect that rectangularisation of the survival curve above age 60 is taking place for these countries, as continuing mortality reductions in the oldest-old are documented (Manton and Vaupel 1995; Rothenberg *et al.* 1991; Vaupel and Lundstrom 1994). A recent study concluded that a compression of mortality took place in Switzerland (Paccaud *et al.* 1998). This conclusion was based on the finding that the annual rate of increase in the age of death diminishes with increasing age. However, it is worth mentioning that the reduction in the variability of the age at death in Switzerland was

not accompanied by a lack of increase in life expectancy at advanced ages as we found for the Netherlands, and that a reduction in the annual rate of increase of the age at death with increasing age has been documented on a wide geographic scale (Kannisto 1994). Further research, reanalysing the Swiss data using the same measures of rectangularisation as used in our study, is needed to investigate whether similar developments in the variability in the age at death took place in both countries.

EXPLANATIONS FOR THE OBSERVED TRENDS

Explanations for the recent developments in old-age mortality in the Netherlands are still being sought. Here we will evaluate possible explanations for the increase in oldest-old mortality. First, one could point to influenza epidemics in 1989/90, 1993, 1995/96, 1996/97 and 1998 (Prins 1990, 1991, 1993, 1996, 1998) as an explanation for the increase in mortality. However, it is unlikely that influenza epidemics have caused the observed patterns, because (1) in 1975 and 1978, influenza produced substantial excess mortality (Prins 1990) without seriously interrupting the mortality decline among the oldest-old, and (2) our results are not very sensitive to annual perturbations due to influenza epidemics, for we used quinquennial data.

Second, we considered whether the alleged liberalisation of euthanasia policy could have brought forward the average age at death. Considering the low frequency of physician assistance in death at advanced ages (in only 1.8 per cent [1.3–2.5 per cent] of all deaths above age 80), and the estimated small decrease in the length of life due to euthanasia (less than one week in 76 per cent of these cases) (Van der Wal and Van der Maas 1996), we do not consider euthanasia a significant factor. This is not to say that differences in medical care, especially in the withdrawing and withholding of interventions, played no part in the increase in mortality found in the Netherlands. The frequency of these end-of-life decisions was about 30 per cent in 1995—(in 20% of all deaths the nontreatment decision was the most important end-of-life decision)—and the estimated decrease in the length of life following from these decisions is larger as compared to euthanasia. In addition, the frequency of withdrawing and withholding interventions increased between 1990 and 1995 by about 2 per cent (Groenewoud *et al.* 2000; Van der Wal and Van der Maas 1996). Nonetheless, as the estimated effect of the decision to withhold treatment on patient life expectancy was still small (less than one month in approximately 90% of the cases), the effect on life expectancy will be less than 0.01 year (Janssen *et al.* 2003).

Third, changing living arrangements of the elderly could have had an effect on oldest-old mortality. Generally, an increasing 'individualisation' and 'independence' characterise the developments in the Netherlands. More specifically, three developments have been taking place. First, the percentage of the population aged 75 and over living in an institution declined from 22 per cent in 1983 to 17 per cent in 1994 (Social and Cultural Planning Office 1997). Second, more extramural care facilities became available to assist those who are living outside institutions (Social and Cultural Planning Office 1997). These developments reflect a shifting focus of Dutch policy from institutionalisation and intramural care towards facilities enabling the elderly to stay longer at home (Knipscheer 1996). Third, in the non-institutionalised population, the percentage of persons aged 80 living with (grand)children has decreased from about 16 per cent to 9 per cent in the period 1981 through 1993 (Social

and Cultural Planning Office 1997). Until more research provides information on the likely effects of these changes on old-age mortality, it is unclear what the net effect is of these developments.

Fourth, past smoking behaviour might have contributed to the increase in mortality in men. A reconstruction of smoking prevalence by male birth cohort has indicated that smoking prevalence increased from birth cohorts 1897 to 1917 (Gunning-Schepers 1988). This implies that the percentage of (ex)smokers aged 85 and over has increased in the period 1980/84–1995/99. Considering the cause-of-death groups for which mortality rates among the oldest-old increased, such as chronic obstructive lung disease (COPD), mental disorders (senile dementia), cancer (prostate and lung for men, and other cancers), diabetes mellitus, ill-defined conditions (senility), and diseases of the nervous system (Nusselder and Mackenbach 1996, 1997), smoking might have contributed to the increase in mortality—as in particular in the cases of lung cancer and COPD the excess risks of death remain present for a long period of time after smoking cessation (U.S. Department of Health and Human Services 1990). However, smoking cannot explain an increase in female mortality at advanced ages, as the percentage of (ex)smokers aged 85 and over was too small to have had a significant effect on old age mortality. We found that the increase in oldest-old mortality was present in both sexes, although more pronounced in men. Therefore, although smoking behaviour may have contributed to the recent mortality developments, it cannot be the only factor. This is confirmed by a recent study by Janssen *et al.* (2003), which showed that after excluding mortality from smoking related cancers and COPD, the stagnation of the mortality decline for people aged 80 and over in the Netherlands still prevailed.

Finally, less selection due to decreased mortality at younger ages may have contributed to the mortality increase. Two mechanisms might be important. First, decreased mortality from circulatory diseases might have created a pool of persons *with* circulatory diseases, who survived from circulatory diseases at younger ages, but additionally run a higher risk of developing severe stages of these diseases and dying from them at higher ages (Bonneux *et al.* 1994; Bonneux *et al.* 1997). For congestive heart failure, an increase in mortality at higher ages was found recently (Bonneux *et al.* 1997). Secondly, reduced mortality from circulatory diseases might have increased the prevalence of diseases that share the same risk factors or are themselves a risk factor for circulatory diseases, such as some cancers or diabetes mellitus. Although it is likely that increased frailty has contributed to the mortality increase in the oldest-old, it remains puzzling why these mechanisms, which might be expected to operate in other countries as well, have not (yet) caused an increase in old-age mortality there.

IMPLICATIONS

Our results show that we cannot take for granted that mortality reductions in the oldest-old population will continue forever. There might be factors that temporarily or more permanently prevent further increases in life expectancy. Whether or not this is a sign that a biological limit to life expectancy is being reached as predicted by Fries (1980) cannot be decided from mortality data alone. Even with a fixed life-span there will be variability in the age at death, which makes it impossible to determine whether the remaining variability

in the age of death is due to environmental influences or to heterogeneity in the endowment for longevity. On the other hand, considering that in other countries with equal or higher life expectancies, such as Iceland and Japan, the decrease in mortality persisted, it is not likely that the stagnation of mortality decline in the Netherlands is an indication that the limit to life expectancy is being approached. Although our results do not indicate whether a biological limit to life expectancy is being reached, they show that similar mortality reductions have increasingly less impact on life expectancy: increasingly larger mortality reductions are needed to obtain the same increase in life expectancy. Whether this implies that the lack of increase will continue or whether other countries will follow is not clear. It might be that the Netherlands (and Norway) are trendsetters. On the other hand, it is also possible that the experience of the Netherlands will remain an exception, whereby factors unique for the Netherlands can be found to explain the recent trends. A third possibility is that the recent lack of increase in life expectancy at advanced ages in the Netherlands reflects only a temporary interruption in the mortality decline.

Conclusion

Trends in old age mortality in the period 1980/84–1995/99 in the Netherlands showing a lack of increase in life expectancy at advanced ages, compression of mortality, and a tendency towards rectangularisation indicate that a continuing increase in life expectancy of the elderly cannot be taken for granted.

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References

Ahlburg, D. A., and Vaupel, J. W. (1990) "Alternative projections of the U.S. population", *Demography*, 27(4):639–652.

Bonneux, L., Barendregt, J. J., Meeter, K., Bonsel, G. J., and van der Maas, P. J. (1994) "Estimating clinical morbidity due to ischemic heart disease and congestive heart failure: The future rise of heart failure", *American Journal of Public Health*, 84(1):20–28.

Bonneux, L., Looman, C. W., Barendregt, J. J., and van der Maas, P. J. (1997) "Regression analysis of recent changes in cardiovascular morbidity and mortality in The Netherlands", *British Medical Journal*, 314(7083):789–792.

Condran, G. A., Himes, C. L., and Preston, S. H. (1991) "Old-age mortality patterns in low mortality countries: An evaluation of population and death data at advanced ages, 1950 to the present", *Population Bulletin of the United Nations*, (30):23–60.

Demetrius, L. (1978) "Adaptive value, entropy and survivorship curves", *Nature*, 275(5677):213–214.

Fries, J. F. (1980) “Aging, natural death, and the compression of morbidity”, *New England Journal of Medicine*, 303(3):130–135.

Demetrius, L. (1983) “The compression of morbidity”, *Milbank Memorial Fund Quarterly/Health and Society*, 61(3):397–419.

Demetrius, L. (1989) “The compression of morbidity: Near or far?”, *Milbank Quarterly*, 67(2):208–232.

Groenewoud, J. H., van der Heide, A., Kester, J. G., de Graaff, C. L., van der Wal, G., and van der Maas, P. J. (2000) “A nationwide study of decisions to forego life-prolonging treatment in Dutch medical practice”, *Archives of Internal Medicine*, 160(3):357–363.

Gruenberg, E. M. (1977) “The failures of success”, *Milbank Memorial Fund Quarterly/Health and Society*, 55(1):3–24.

Gunning-Schepers, L. J. (1988) *The Health Benefits of Prevention. A Simulation Approach*. Rotterdam: Erasmus University.

Janssen, F., Nusselder, W. J., Looman, C. W. N., Mackenbach, J. P., and Kunst, A. E. (2003) “Stagnation in mortality decline among elders in The Netherlands”, *The Gerontologist*, 43:722–734.

Kannisto, V. (1994) *Development of Oldest-old Mortality, 1950–1990: Evidence from 28 Developed Countries*. Odense: Odense University Press.

Kannisto, V., Lauristen, J., Thatcher, A. R., and Vaupel, J. W. (1994) “Reductions in mortality at advanced ages: Several decades of evidence from 27 countries”, *Population and Development Review*, 20(4):793–809.

Keyfitz, N. (1977) “What difference would it make if cancer were eradicated? An examination of the Taeuber paradox”, *Demography*, 14(4):411–418.

Keyfitz, N. (1978) “Improving life expectancy: An uphill road ahead”, *American Journal of Public Health*, 68(10):654–656.

Keyfitz, N., and Golini, A. (1975) “Mortality comparisons: The male-female ratio”, *Genus*, 31:1–34.

Knipscheer, C. P. (1996) “[A silent revolution. Towards a balanced tuning of informal and formal care] Een stilzwijgende revolutie. Naar een evenwichtige afstemming van informele en formele zorg”, *Tijdschr Gerontol Geriatr*, 27(4):138–140.

Kramer, M. (1980) “The rising pandemic of mental disorders and associated chronic diseases and disabilities”, *Acta Psychiatrica Scandinavia*, 62(Suppl. 285):382–397.

Mackenbach, J. P. (1992) *De veren van Icarus. Over achtergronden van twee eeuwen epidemiologische transitie in Nederland*. Utrecht, the Netherlands: Wetenschappelijke Uitgeverij Bunge.

Mackenbach, J. P. (1993) “The epidemiologische transitie in Nederland [The epidemiological transition in The Netherlands]”, *Nederlands Tijdschrift voor Geneeskunde*, 137(3):132–138.

Mamelund, S., and Borgan, J. (1996) *Kohort- og periodedodelighet i Norge 1846–1994* [*Cohort and Period Mortality in Norway 1846–1994*]. Oslo, Norway: Oslo-Kongsvinger.

Manton, K. G. (1982) “Changing concepts of morbidity and mortality in the elderly population”, *Milbank Memorial Fund Quartely Health and Society*, 60(2):183–244.

Manton, K. G., Stallard, E., and Tolley, H. D. (1991) “Limits to human life expectancy: Evidence, prospects and implications”, *Population and Development Review*, 17(4):603–637.

Manton, K. G., and Vaupel, J. W. (1995) "Survival after the age of 80 in the United States, Sweden, France, England, and Japan", *New England Journal of Medicine*, 333(18):1232–1235.

Myers, G. C., and Manton, K. G. (1984a) "Compression of mortality: myth or reality?", *The Gerontologist*, 4(4):346–353.

Myers, G. C., and Manton, K. G. (984b) "Recent changes in the U.S. age at death distribution: Further observations", *The Gerontologist*, 24(6):572–575.

Namboodiri, K. (1991) *Demographic Analysis. A Stochastical Approach*. San Diego: Academic Press.

Namboodiri, K., and Suchindran, C. M. (1987) *Life Tables and their Applications*. Orlando, FL: Academic Press.

Nusselder, W. J. (1998) *Compression of Morbidity: A Life Table Approach*. Rotterdam: Erasmus Universiteit.

Nusselder, W. J., and Mackenbach, J. P. (1996) "Rectangularisation of the survival curve in The Netherlands, 1950–1992", *The Gerontologist*, 36(6):773–782.

Nusselder, W. J., and Mackenbach, J. P. (1997) "Rectangularisation of the survival curve in The Netherlands: An analysis of underlying causes of death", *The Journals of Gerontololy: Social Sciences*, 52(3):S145–154.

Nusselder, W. J., and Mackenbach, J. P. (2000) "Lack of improvement of life expectancy at advanced ages in The Netherlands", *International Journal of Epidemiology*, 29(1):140–148.

Oeppen, J., and Vaupel, J. W. (2002). "Demography. Broken limits to life expectancy", *Science*, 296(5570):1029–1031.

Olshansky, J., and Carnes, B. A. (1997) "Ever since Gompertz", *Demography*, 34:1–15.

Olshansky, S. J., and Ault, A. B. (1986) "The fourth stage of the epidemiologic transition: The age of delayed degenerative diseases", *Milbank Quarterly*, 64(3):355–391.

Olshansky, S. J., and Carnes, B. A. (1994) "Demographic perspectives on human senescence", *Population and Development Review*, 20(1):57–80.

Olshansky, S. J., Carnes, B. A., and Cassel, C. (1990) "In search of Methuselah: Estimating the upper limits to human longevity", *Science*, 250(4981):634–640.

Olshansky, S. J., Carnes, B. A., and Desesquelles, A. (2001) "Demography. Prospects for human longevity", *Science*, 291(5508):1491–1492.

Olshansky, S. J., Rudberg, M. A., Carnes, B. A., Cassel, C. K., and Brody, J. A. (1991) "Trading off longer life for worsening health", *Journal of Aging and Health*, 3(2):194–216.

Omran, A. R. (1971) "The epidemiologic transition. A theory of the epidemiology of population change", *Milbank Memorial Fund Quarterly*, 49(4):509–538.

Paccaud, F., Pinto, C. S., Marazzi, A., and Mili, J. (1998) "Age at death and rectangularisation of the survival curve: trends in Switserland, 1969–1994", *Journal of Epidemiology and Health*, 52:412–415.

Prins, C. J. M. (1990) "Hoge sterfte rond jaarwisseling door griep [Many influenza deaths at the turn of the year]", *Maandstatistiek voor de Bevolking* [*Monthly Bulletin of Population Statistics*], 38(5):8–9.

Prins, C. J. M. (1991) "Grote fluctuaties in maandelijkse aantallen overledenen [Big fluctuations in 1990 monthly death figures]", *Maandstatistiek voor de Bevolking* [*Monthly Bulletin of Population Statistics*], 39(5):8–9.

Prins, C. J. M. (1993) "Sterftepiek in maart en april van dit jaar [Many deaths in March and April of this year]", *Maandstatistiek voor de Bevolking* [*Monthly Bulletin of Population Statistics*], 41(9):6–8.

Prins, C. J. M. (1996) "Hoge sterfe in winter 1995/96 [Many deaths in winter of 1995/96]", *Maandstatistiek voor de Bevolking* [*Monthly Bulletin of Population Statistics*], 44:7–10.

Prins, C. J. M. (1998) "Veel sterfgevallen in maart en april 1998 [Many deaths in March and April 1998]", *Maandstatistiek voor de Bevolking* [*Monthly Bulletin of Population Statistics*], 44:7–8.

Rothenberg, R., Lentzner, H. R., and Parker, R. A. (1991) "Population aging patterns: The expansion of mortality", *Journal of Gerontology*, 46(2):S66–70.

Smith, D. P. (1992) *Formal demography*. New York, NY: Plenum Press.

Social and Cultural Planning Office. (1997) *Vraagverkenning wonen en zorg voor ouderen.* Rijswijk, the Netherlands: Social and Cultural Planning Office (SCP).

Statistics Netherlands. (1994) *Vijfennegentig jaren statistiek in tijdsreeksen: 1899–1994*. 's-Gravenhage, the Netherlands: SDU/uitgeverij.

Statistics Netherlands. annually-a. "Bevolking naar leeftijd en burgerlijke staat op 1 januari 19. [Population by age and marital status per January 1, 19]", *Statistics Netherlands*.

Statistics Netherlands. annually-b. "Overledenen naar burgerlijke staat, geslacht en leeftijd en geboortejaar in het jaar 19. [Number of deaths by marital status, sex, age and year of birth in the year, 19]", *Statistics Netherlands*.

Statistics Netherlands. (1970–1999) *Overlevingstafels naar leeftijd en geslacht* [*Life tables by age and sex*]. 's-Gravenhage, the Netherlands: State Publishers/Statistics Netherlands.

Tabeau, E., van Poppel, F., and Willekens, F. (1994) *Mortality in the Netherlands: The Data Base*. The Hague, the Netherlands: Netherlands Interdisciplinary Demographic Institute.

U.S. Department of Health and Human Services. (1990) *The Health Benefits of Smoking Cessation: A Report of the Surgeon General*. Rockville, MD: Centre for Chronic Disease Prevention and Health Promotion.

Van der Wal, G., and Van der Maas, P. J. (1996) *Euthanasie en andere beslissingen rond het levenseinde. De praktijk en de meldingsprocedure*. Den Haag, the Netherlands: SDU Uitgevers.

Vaupel, J. W., and Lundstrom, H. (1994) "The future of mortality at older ages in developed countries". In: Lutz, W. (ed.), *The Future Population of the World. What Can We Assume Today?*, London, UK: Earthscan Publications, pp. 295–315.

Verbrugge, L. M. (1984) "Longer life but worsening health? Trends in health and mortality of middle-aged and older persons", *Milbank Memorial Fund Quartely/Health and Society*, 62(3):475–519.

Wilmoth, J. R., and Horiuchi, S. (1999) "Rectangularisation revisited: variability of age at death within human populations", *Demography*, 36(4):475–495.

Wrigley, E. A., and Schofield, R. S. (1983) "English population history from family reconstitution: Summary results 1600–1799", *Population Studies*, 37:157–184.

CHAPTER 7. THE VALIDATION OF EXCEPTIONAL MALE LONGEVITY IN SARDINIA

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Introduction

An analysis of the Italian life tables at provincial level put the population of Sardinia and especially the Nuoro province beyond the usual range. The life expectancies at 60 and 85 are higher and the difference between men and women is less pronounced compared to what is usually observed elsewhere. Exceptionally, in the Nuoro province, the life expectancy at 85 was higher for males compared to females between 1971 and 1991.

Considering these observations, the mortality pattern of the Sardinian population, and more particularly the one observed for the Nuoro province, should be definitively regarded as unique and therefore the question of age validation has been raised as a really critical point. In fact extreme longevity in Sardinia may be the result of age exaggeration especially for males and this point has never been investigated. During the last decades several authors[1] presented detailed figures on the variation of mortality in Italy at provincial levels, showing clearly the uniqueness of male mortality in the Nuoro province. However none of these authors made remarks about these exceptional figures, probably assuming that these data were biased and unreliable and considered this as normal for a mountainous and remote

[1] Mattioli (1980), Caselli *et al.* (1981), Bellini *et al.* (1992), ISTAT (1997), Caselli *et al.* (1999), Caselli *et al.* (2003a)

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area. The aim of this contribution is to demonstrate that these data are reliable and therefore to validate the exceptional male longevity in Sardinia.

Exceptional Male Longevity in Sardinia

Exceptional longevity may be traced for age and sex distribution in census data. Data from the 1981 Italian census analysed by Cantalini and Lori (1990), data from the 1991 census and the most recent data from the 2001 census show large differences between the population age structure in Sardinia and Italy as a whole. Moreover, among the Sardinian provinces that of Nuoro may be considered as presenting the most extreme situation with the highest proportion of oldest-old and the lowest sex ratio (Table 1).

Table 1. Comparison of the prevalence and the sex ratio for the population aged 85+ and 100+ for Italy, Sardinia and the Nuoro Province in 1981, 1991 and 2001.

Year	1981	1991	2001
Proportion of males aged 85 and over in the total male population			
Italy	0.48%	0.78%	1.34%
Sardinia	0.65%	0.88%	1.35%
Nuoro	1.04%	1.29%	1.60%
Proportion of females aged 85 and over in the total female population			
Italy	1.07%	1.78%	2.96%
Sardinia	0.97%	1.44%	2.27%
Nuoro	1.17%	1.77%	2.61%
Proportion of male centenarians in the total male population			
Italy	0.0012%	0.0030%	0.0039%
Sardinia	0.0034%	0.0060%	0.0066%
Nuoro	0.0037%	0.0118%	0.0123%
Proportion of female centenarians in the total female population			
Italy	0.0034%	0.0088%	0.0178%
Sardinia	0.0052%	0.0097%	0.0161%
Nuoro	0.0050%	0.0167%	0.0245%
Sex ratio for the population aged 85 and over			
Italy	2.343	2.409	2.345
Sardinia	1.522	1.673	1.760
Nuoro	1.151	1.401	1.691
Sex ratio for centenarians			
Italy	2.976	3.084	4.845
Sardinia	1.556	1.653	2.528
Nuoro	1.400	1.438	2.063

Source: ISTAT (Istituto Nazionale di Statistica).

Table 2. Comparison of life expectancies at birth, 60 and 85 for Italy, Sardinia and Nuoro Province from 1971 to 2000.

	1971	1981	1988–1993	1998–2000
Life expectancy at birth for males				
Italy	68.97	71.09	73.84	76.02
Sardinia	70.33	72.07	73.60	75.76
Nuoro	71.46	72.22	74.31	75.32
Life expectancy at birth for females				
Italy	74.99	77.85	80.30	82.14
Sardinia	75.24	78.38	80.42	82.34
Nuoro	75.98	78.69	80.68	82.42
Life expectancy at 60 for males				
Italy	16.66	17.19	18.73	20.06
Sardinia	18.36	18.54	19.11	20.33
Nuoro	19.87	19.07	19.97	20.37
Life expectancy at 60 for females				
Italy	20.16	21.60	23.21	24.59
Sardinia	20.47	21.86	23.43	24.77
Nuoro	21.23	22.11	23.56	24.88
Life expectancy at 85 for males				
Italy	4.12	4.24	4.80	5.19
Sardinia	4.91	4.75	5.49	5.50
Nuoro	5.85	5.36	6.25	5.58
Life expectancy at 85 for females				
Italy	4.82	5.10	5.67	6.36
Sardinia	5.15	5.00	5.94	6.25
Nuoro	5.46	5.22	5.97	6.44

Source: ISTAT.

Another way to demonstrate the exceptional longevity in Sardinia is to compare life tables. Life expectancies at birth, at 60 and 85 may be compared from 1971 to 2000 between Italy, Sardinia, and the province of Nuoro (Table 2). And again all figures demonstrate the exceptional longevity of Sardinian males especially in the Nuoro province with life expectancies at 85 years that are higher in 1971, 1981 and 1991.

Both age and sex structures extracted from census and life tables emphasize the exceptional longevity of men in Sardinia and call for an in-depth age validation. At this stage it is worth remembering that when a centenarian is identified an age validation must be systematically performed since age exaggeration is frequently observed, mainly among the oldest-old (Jeune and Vaupel, 1999). The observed exceptional male longevity may be simply the result of age exaggeration—as is often observed in illiterate populations mostly living in island or remote mountainous areas and more particularly among men compared to women.

Table 3. Prevalence rate and population sex ratio of the centenarians from the AKEA study.

Province	Resident population (1991 census)	Centenarians Found (in brackets, the centenarians interviewed during the AKEA study) Women	Men	Total	Prevalence (to 100,000)	Population sex ratio (women/men)
Sassari	444 863	41 (34)	17 (11)	58 (45)	12.95	2.4
Nuoro	271 065	35 (24)	31 (21)	66 (45)	24.35	1.1
Oristano	156 498	16 (8)	8 (6)	24 (14)	15.34	2.0
Cagliari	762 279	57 (30)	17 (7)	74 (37)	9.71	3.4
Sardinia	1 637 705	149 (96)	73 (45)	222 (141)	13.56	2.0

Source: Deiana *et al.* 1999.

The Age Validation of the Oldest-Olds

Concretely the starting point of the Sardinian age validation programme was a presentation held in Montpellier on October 1999 concerning the preliminary results of the AKEA[2] study. During this presentation before an audience composed mainly of geneticists and demographers, the Sardinian researchers presented the table set out above (Table 3), where they proposed a count for the centenarians studied within the context of the AKEA project and calculated the associated prevalence and sex ratio by province. This study was carried out in 1997 on 141 centenarians who agreed to participate to a survey, to answer a questionnaire, to undergo a clinical examination and have a blood sample taken. These 141 centenarians were selected from a list of 222 possible centenarians born before January 1st 1898, living in one of the 377 Sardinian municipalities. Table 3 details the 141 and 222 centenarians subdivided by gender and province of birth.

Beyond the purely genetic interest of the results presented, the authors disclosed a really high prevalence of centenarians and low population sex ratio compared to the values previously observed in other European countries. However, no attention has been devoted to possible bias due to the fact that centenarians were grouped by province of birth and divided by the total resident population of each province at the 1991 census, one century later. More concretely, the existence of unbalanced migration flows between provinces for centenarians along their long life and the existence of differential increase in population of each province would directly introduce a bias in the estimation of the prevalence. This point will be considered later in this contribution.

Despite this potential bias, when compared with similar figures in other European countries, these data seem to indicate a higher prevalence of centenarians in Sardinia, particularly men.

[2] AKEA is an acronym derived from the Sardinian expression *a kent' annos*, a very commonly used traditional greeting which broadly translates as "Life and health up to the age of 100".

As a consequence, the sex ratio among centenarians is lower than the one usually observed.[3] At the Montpellier meeting, the reaction of the demographers was fairly unanimous, calling into question the quality of the demographic data and hinting at some exaggeration of age, principally for the elderly men, as the cause of these wholly unusual findings. This attitude was further reinforced by the fact that the province of Nuoro, a poorly urbanized area covering a large part of the mountainous heart of Sardinia, which was the province displaying the majority of these extreme values. The prevalence rate in this province was close to one centenarian in every 4,000 inhabitants and an almost equal number of centenarians of the two sexes. The isolated and presumably archaic nature of the villages in this province favour the hypothesis of the poor reliability of the data and a marked overestimation of the number of male centenarians due to an exaggeration of age.

If the validity of the age of the Sardinian centenarians was to be called into question, and more particularly those of the men, it would be evident that any result of the AKEA study would lose its validity. Furthermore, all scientific efforts to explain the highest longevity of men in Sardinia would be without interest.

Data Quality and Age Validation

The primary objective of this validation process is the validation of the ages of the AKEA centenarians at individual level. This implies the verification of whether all AKEA study participants were truly centenarians and were born before January 1st 1898 according to the selection criteria. This age validation was carried out during the year 2000.

The main data source which is available for the validation of the Sardinian centenarians is the *civil registers* containing all births[4], marriages[5] and deaths[6] records. These registers are held in each municipality, hand-written in Italian, and date back to the year 1866. They are generally in very satisfactory state of preservation and readability. The registers are

[3] Passarino *et al.* (2002) as well as Robine *et al.* (2006) have observed similar levels for the sex ratio among centenarians in Calabria and Sicily; while a sex ratio of over eight is observed in the Frioul region, North-East of Italy.

[4] Each *birth* certificate includes the name and forename(s) of the newly born, those of his/her parent and the age of the father if he was the declaring person. As in France, marginal annotations, relating to the legitimisation with the patronymic change, upon the marriage(s) and upon the death of the newly born, facilitate research. For the newly born generations from the end of the nineteenth century, we can estimate that almost all of the marriages were registered as a marginal inscription on the birth certificate, while only 30 to 40% included a marginal annotation regarding their death. For deaths subsequent to 1950, the marginal inscription is a standard procedure. Thus, for all of the deceased centenarians whose birth certificates we have looked for, the marginal annotation was always present. These annotations are, of course, very precious for facilitating research relating to the marriages and deaths of the subjects concerned.

[5] For the *marriage* certificates, we find the name and forename(s) of the spouses, those of their parents with details of their death or place of residence. We also have the age of the spouses and, more recently, their dates of birth.

[6] For the *death* certificates, we find the name and forenames(s) of the deceased with those of their parents, the age of the deceased and, more recently, the date of birth. The civil status of the deceased is detailed, along with the name and forename of the possible spouse, whether surviving or not.

most commonly annual and differ according to the three certificate types, and each annual register includes a table facilitating name-based research. Less common are the decennial tables, which evidently facilitate name-based research. The *parochial registers* kept in the parish or, during earlier times, in the bishopric archives may be also useful as they dated back, in the majority of the parishes, in the seventeenth century. This permits a more in-depth genealogical approach to the family research. The information gathered from this source is, nonetheless, frequently terse. In the numerous cases where an obvious risk of errors owing to a high isonymy is present, the forenames of the father and the patronymic of the mother are associated to the name and forename(s) of the subject concerned. The parochial registers were rarely used within our validation procedure, except for a few particular cases. The *population register* or *anagrafe* is a permanent register which, at any one time, gives composition and characteristics of the population usually living in a municipality.[7] Specifically, this register is made up of a set of sheets ordered in an alphabetical file, one sheet corresponding to each individual living in the municipality. For all of the municipalities visited, this file is kept updated both in the form of hand-written and computerised files. On the basis of these computerised files, the local authorities are able to produce, almost instantly, the list of the living nonagenarians or centenarians in the municipality with their dates of birth, civil status and their residence address. Upon each birth or immigration event, a form is created relating to the person concerned while, upon each death or emigration event, the corresponding form is removed. These removed forms are kept in a different dossier whose arrangement and temporal interval varies from one municipality to another. Among these removed forms in the numerous municipalities visited, we found forms relating to the parents of centenarians with precious information on the place and date of their death.

During the validation procedure we visited the municipalities where most of the 222 centenarians have been found in the AKEA survey. And during the course of these visits we also identified and validated all of the centenarians who had died in each of these municipalities from 1980 to the present day, in addition to those still alive in the year 2000. As a result, more than 600 centenarians were validated and demographic information on more than 3,000 people, the father and mother, the brothers and sisters, or the children of the centenarians was collected, both in the *anagrafe* and in the civil status registers.

The following points were therefore verified for each identified centenarian to be validated:

1. The complete compatibility between the information taken from the death and birth certificates if the centenarian was already dead or between the *anagrafe* and the birth certificate if they were alive (name and forename(s) given to the newly-born,[8] name and forename(s) of the parents, age of father at birth if he is the reporting person)

[7] The *anagrafe* provides the following information: name and forename(s), place and date of birth, name and forename(s) of the parents, place and date of marriage and possible widow/widowhood, place, date and cause of death, date of emigration and destination municipality, date of immigration and municipality of origin. As the information gathered from the individual forms of the *anagrafe* is not first-hand information, we have to take into account additional information only with caution.

[8] In several cases, the forenames given at birth and those found in the *anagrafe* or in the death certificate are not systematically the same. Their order may have changed and some may have been omitted. Notwithstanding, there were no cases where these differences called the entire age-validation into question for the people concerned.

2. Compatibility with the data found in the parents' marriage certificate, including the plausibility of the parent's age at marriage of the parents.
3. Verification of the birth and death certificates of all the brothers and sisters of the centenarians in order to check the plausibility of the birth intervals but also to ensure that no errors arose from the repetition of a forename. This occurs frequently when the first to carry the name dies soon after the birth. Thus, if two brothers or sisters have the same forename(s), and the first has died at a young age and is in some way replaced by the next one, it is advisable to verify that the latest birth date has been correctly attributed in order to establish the age of the surviving party.
4. If the person under age-checked had been married, we also validated whether all of the information found in the marriage certificate was consistent when compared to the information gathered from the birth and death certificates and the *anagrafe*. More specifically, the age indicated in the marriage certificate had to be coherent with the age appearing on the birth certificates of the children.
5. Finally, in case of high isonymy within the municipality concerned, we verified that there was no possibility of making an erroneous comparison between the birth and death certificates of two different subjects. There is often less risk of error linked to high isonymy with the presence of the father's forename and the name of the mother for the people concerned.

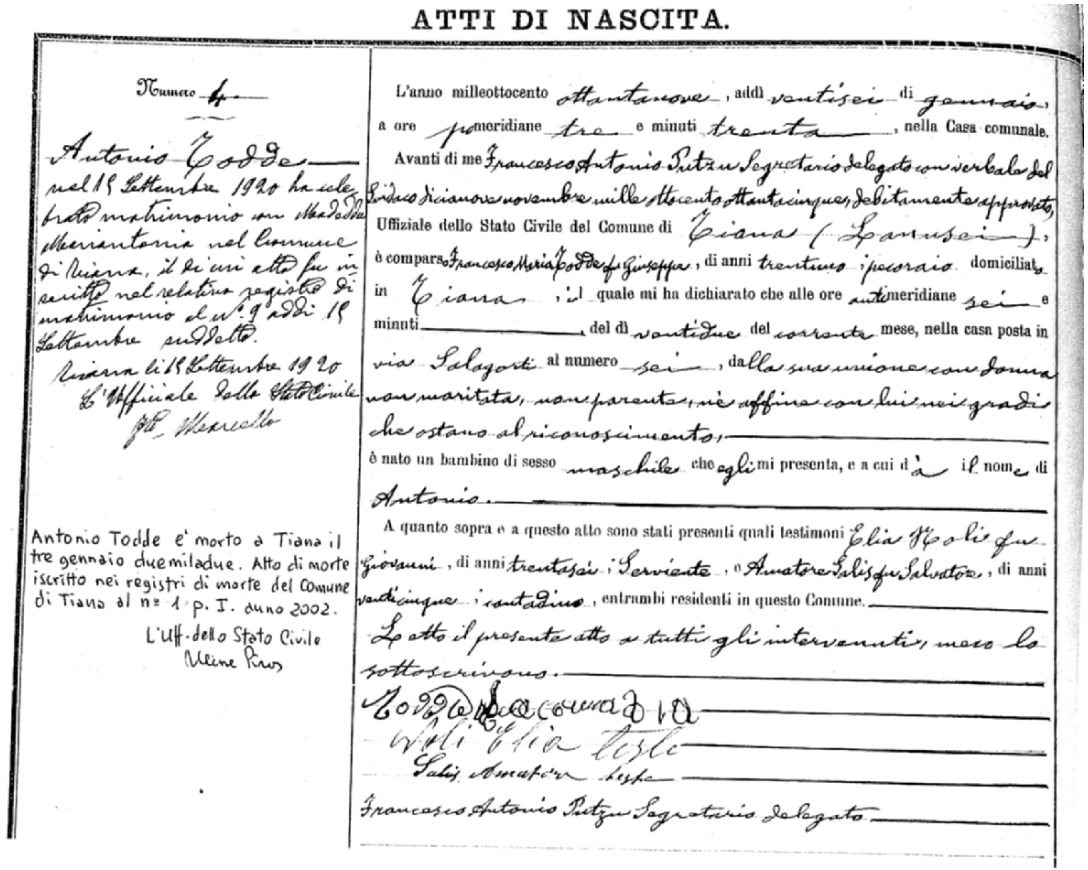
All these elements were thoroughly examined for all selected centenarians but only the cases of Antonio Todde and Damiana Sette will be presented hereafter. Notably, these elements allowed us to attest that Antonio Todde, born on 22 January 1889 had truly celebrated his 112th birthday and died on 3 January 2002 at the age of 112 years and 346 days.

The Validation of the Age of Antonio Todde

Antonio Todde was declared the oldest documented man on earth in July 2001. Antonio was born in Tiana (Nuoro province, Sardinia) on 22 January 1889 and his birth record stated that he was the son of Francesco Maria Todde and *della sua unione con donna non maritata* without giving the name of his mother (Figure 1). The missing name for the mother was a negative element for the validation of the exceptional age of Antonio. Fortunately, the baptism record in the parish register (Figure 2) gives the missing information and confirmed that Antonio was effectively born on 22 January 1889 and was son of Francesco and Francesca Angela Deiana. In fact his parents were married according to church laws but not yet according to the civil registration. Their civil marriage was celebrated only on 30 December 1908 when Antonio was 18 and, in the marriage record, all Antonio's brothers and sisters are correctly listed with their age. Antonio died in Tiana on 3 January 2002, a few days before reaching 113 years and his death record (Figure 3) has been correctly linked with his birth record where a marginal note has been added (Figure 1, left). The family reconstruction of Antonio Todde is presented in Table 4.

The Invalidation of the Age of Damiana Sette

At the beginning of our investigations Damiana Sette was considered to be a supercentenarian. Figure 4 shows a *facsimile* of the death certificate of Maria Angelica Damiana



ATTI DI NASCITA.

Numero 4

Antonio Todde nel 19 Settembre 1920 ha celebrato matrimonio con Maddalena Merientoria nel Comune di Tiana, il Re civile atto fu iscritto nel relativo registro di matrimonio al n. 9 addì 19 Settembre suddetto.

Tiana li 19 Settembre 1920

L'Ufficiale dello Stato Civile

G. Mereu

Antonio Todde e' morto a Tiana il tre gennaio duemiladue. Atto di morte iscritto nei registri di morte del Comune di Tiana al n° 1 p. I. anno 2002.

L'Uff. dello Stato Civile

Ilene Piras

L'anno milleottocento ottantanove, addì ventisei di gennaio, a ore pomeridiane tre e minuti trenta, nella Casa comunale.

Avanti di me Francesco Antonio Putzu Segretario delegato con verbale del Sindaco di cinque novembre mille ottocento ottantacinque, debitamente approvato, Ufficiale dello Stato Civile del Comune di Tiana (Lanusei), è comparso Francesco Maria Todde fu Giuseppe, di anni trentuno pecoraio domiciliato in Tiana, il quale mi ha dichiarato che alle ore antemeridiane sei e minuti _____, del dì ventidue del corrente mese, nella casa posta in via Salaporti al numero sei, dalla sua unione con donna non maritata, non parente, nè affine con lui nei gradi che ostano al riconoscimento, _____ è nato un bambino di sesso maschile che egli mi presenta, e a cui dà il nome di Antonio. _____

A quanto sopra e a questo atto sono stati presenti quali testimoni Elia Nioli fu Giovanni, di anni trentasei, Serviente, e Amatore Salis fu Salvatore, di anni cinquantacinque, contadino, entrambi residenti in questo Comune. _____

Lo atto il presente atto a tutti gli intervenuti, meno lo sottoscrivono. _____

Todde Antonio _____

Nioli Elia testis _____

Salis Amatore testis _____

Francesco Antonio Putzu Segretario delegato _____

Figure 1. Birth record of Antonio Todde, born in Tiana (Sardinia) on 22 January 1889 (Civil registers, Municipality of Tiana).

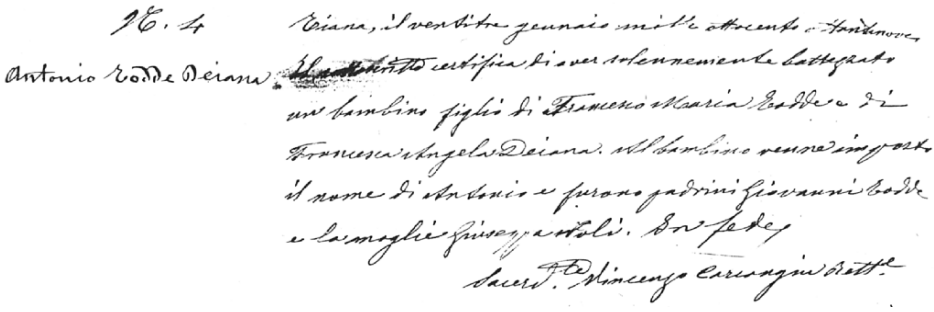
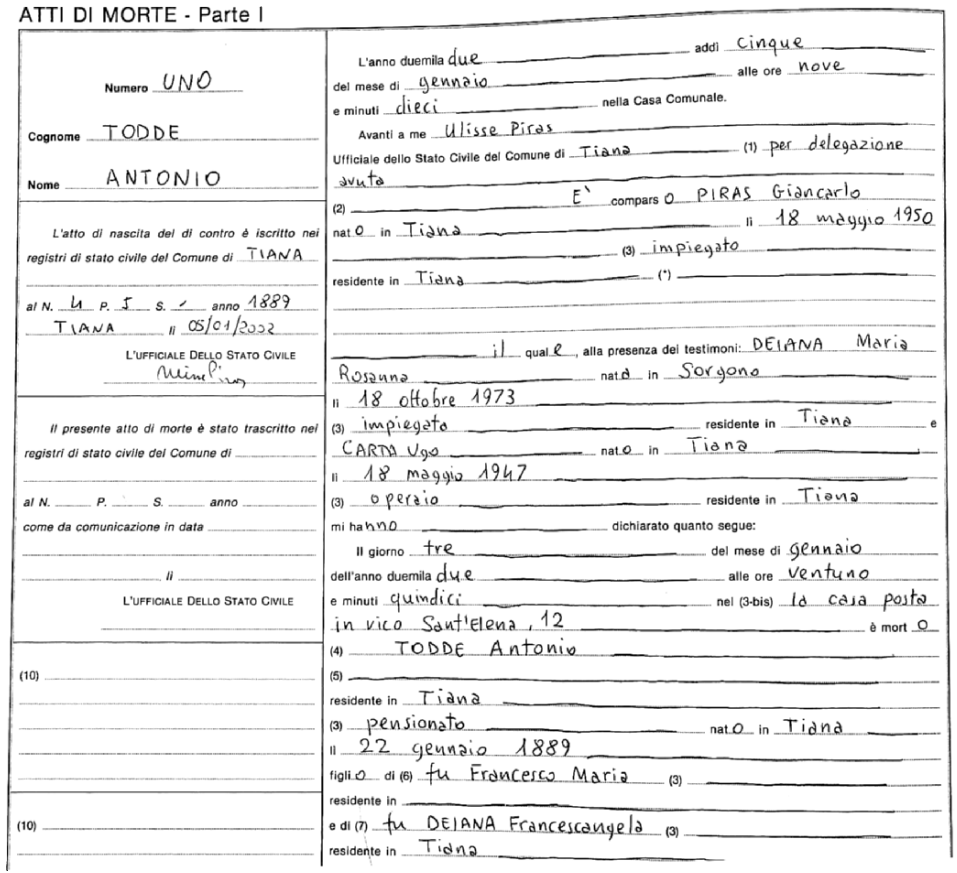


Figure 2. Baptism record of Antonio Todde, (Parish registers of Tiana conserved in Ovodda).

Sette, who died in Villagrande at the age of 110 on 25 February 1985. According to this document, she was born in Villagrande on 8 August 1874 and was the daughter of Pietro Sette and Monserrata Pirroni. Maria Angelica Damiana Sette was effectively born in Villagrande on 8 August 1874 and was the daughter of Pietro Sette and Monserrata Pirroni as shown on her birth record (Figure 5). The death record is wholly compatible with this birth record. We observe in the birth record the marginal note of the death dated 25 February 1985 and therefore a unique link has been established by the civil registration officer between both events and records. Consequently the age validation of Damiana Sette was achieved at level C of certainty.[9] Moreover Damiana Sette never married and appeared only a few times in the *anagrafe* but all information collected was consistent with the presumption that she was effectively a supercentenarian.

At this stage of the validation process, everything would seem to confirm the fact that Damiana Sette really did die at the venerable age of 110, and this information is transcribed elsewhere on her gravestone in the Cemetery of Villagrande. However, the meticulous reconstruction of the family composition of Damiana Sette, based on the civil status registers and the *anagrafe* (Table 5) allows us to conclude that the person who died in 1985 was not Maria Angelica Damiana Sette, born 8 August 1874, but her younger sister called Maria Monserrata Damiana Sette who was born on 5 May 1877. The birth record of the younger sister is shown in Figure 6; while the real death record of Maria Angelica Damiana Sette, in this document named Angelica, on 10 June 1876 at the age of 22 months, is shown in Figure 7. This type of error occurs frequently in historical demography when producing family reconstruction's and the linkage of different data related to births and deaths. This is due to the fact that when a child dies at a young age, it is customary to consider that the child with the same sex born immediately after this death in some way will replace the deceased. Therefore the next child will be given the same forename or at the very least certain identical forenames. This was the case for Maria Angelica Damiana Sette, who died at the young age of 22 months and was replaced by her younger sister called Maria Monserrata Damiana Sette. Damiana Sette never married and it was only when the

[9] The level C of validation is reached when birth and death records have been found and are consistent (Skytte *et al*. 1995).



ATTI DI MORTE - Parte I

Numero UNO

Cognome TODDE

Nome ANTONIO

L'atto di nascita del di contro è iscritto nei registri di stato civile del Comune di TIANA

al N. 4 P. 1 S. - anno 1889

TIANA li 05/01/2002

L'UFFICIALE DELLO STATO CIVILE

Il presente atto di morte è stato trascritto nei registri di stato civile del Comune di

al N. P. S. anno

come da comunicazione in data

li

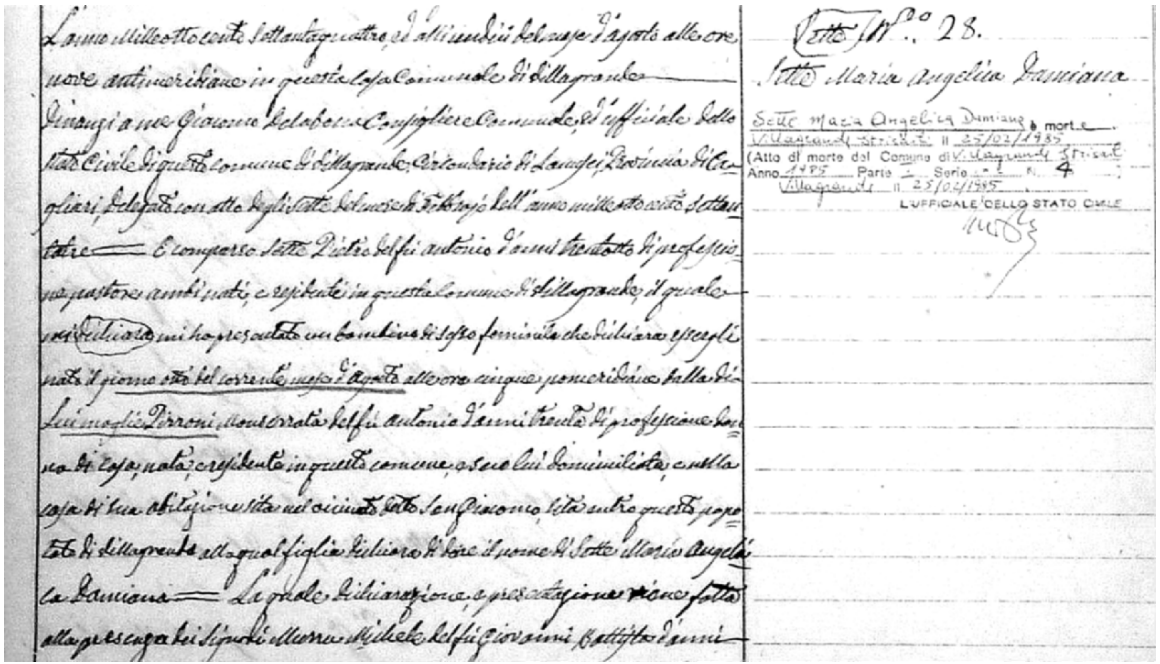
L'UFFICIALE DELLO STATO CIVILE

(10)

(10)

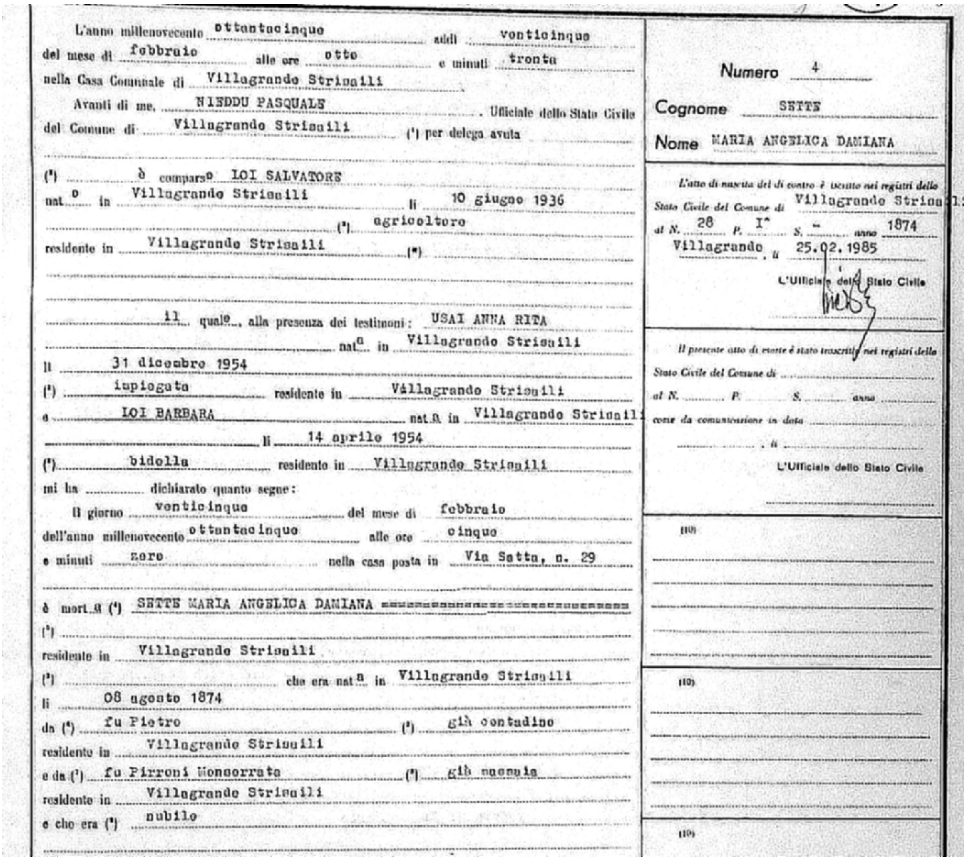
L'anno duemila due addì cinque
del mese di gennaio alle ore nove
e minuti dieci nella Casa Comunale.
Avanti a me Ulisse Piras
Ufficiale dello Stato Civile del Comune di Tiana (1) per delegazione avuta
(2) E' compars o PIRAS Giancarlo
nat o in Tiana li 18 maggio 1950
(3) impiegato
residente in Tiana (*)
il qual e, alla presenza dei testimoni: DEIANA Maria Rosanna nat a in Sorgono
il 18 ottobre 1973
(3) impiegato residente in Tiana e
CARTA Ugo nat o in Tiana
il 18 maggio 1947
(3) operaio residente in Tiana
mi hanno dichiarato quanto segue:
Il giorno tre del mese di gennaio
dell'anno duemila due alle ore ventuno
e minuti quindici nel (3-bis) la casa posta in vico Sant'Elena, 12 è mort o
(4) TODDE Antonio
(5)
residente in Tiana
(3) pensionato nat o in Tiana
il 22 gennaio 1889
figli o di (6) fu Francesco Maria (3)
residente in
e di (7) fu DEIANA Francescangela (3)
residente in Tiana

Figure 3. Death record of Antonio Todde, died in Tiana (Sardinia) on 3 January 2002 (Civil register, Municipality of Tiana).



Sette N.° 28.
Sette Maria Angelica Damiana
Sette Maria Angelica Damiana morte
Villagrande Strisaili il 25/02/1985
(Atto di morte dal Comune di Villagrande Strisaili
Anno 1985 Parte I Serie a.° 1 N. 4
Villagrande il 25/04/1985
L'UFFICIALE DELLO STATO CIVILE

L'anno millenovecento settantaquattro, il diciannovesimo del mese di Febbrajo dell'anno millenovecento settantatre — E comparso Sette Pietro Delfi antonio d'anni trentatre di professione pastore ambi nati, e residenti in questo Comune di Villagrande, il quale mi ha presentato un bambino di sesso femminile che dichiara aver egli nato il giorno otto del corrente mese d'Agosto alle ore cinque pomeridiane dalla di Lui moglie Perroni Mariagrazia delfi antonia d'anni trenta di professione casalinga di Lui moglie, nata, e residente in questo Comune, a cui dichiarano di dare il nome di Sette Maria Angelica Damiana — La predetta dichiarazione, e presentazione viene fatta alla presenza dei signori Murreddu Michele delfi Giovanni Battista d'anni



L'anno millenovecento ottantacinque addì venticinque
del mese di febbraio alle ore otto e minuti trenta
nella Casa Comunale di Villagrande Strisaili
Avanti di me, NIEDDU PASQUALE, Ufficiale dello Stato Civile
del Comune di Villagrande Strisaili (*) per delega avuta
(*) è comparso LOI SALVATORE
nato in Villagrande Strisaili li 10 giugno 1936
(*) agricoltore
residente in Villagrande Strisaili (*)
il quale, alla presenza dei testimoni: USAI ANNA RITA
nata in Villagrande Strisaili
li 31 dicembre 1954
(*) impiegata residente in Villagrande Strisaili
e LOI BARBARA nata in Villagrande Strisaili
li 14 aprile 1954
(*) bidella residente in Villagrande Strisaili
mi ha dichiarato quanto segue:
Il giorno ventidue del mese di febbraio
dell'anno millenovecento ottantacinque alle ore cinque
e minuti zero nella casa posta in Via Setta, n. 29
è morta (*) SETTE MARIA ANGELICA DAMIANA
(*) residente in Villagrande Strisaili
(*) che era nata in Villagrande Strisaili
li 08 agosto 1874
da (*) fu Pietro (*) già contadino
residente in Villagrande Strisaili
e da (*) fu Pirroni Mongorrata (*) già casalinga
residente in Villagrande Strisaili
e che era (*) nubile

Numero 4
Cognome SETTE
Nome MARIA ANGELICA DAMIANA

L'atto di nascita del di cui sopra è iscritto nei registri dello Stato Civile del Comune di Villagrande Strisa
al N. 28 P. I° S. anno 1874
Villagrando, li 25.02.1985
L'Ufficiale dello Stato Civile

Il presente atto di morte è stato trascritto nei registri dello Stato Civile del Comune di
al N. P. S. anno
come da comunicazione in data
, li
L'Ufficiale dello Stato Civile

(10)

(10)

(10)

Figure 5. Birth record of Maria Angelica Damiana Sette, born in Villagrande (Sardinia) on 8 August 1874 (Municipality of Villagrande) with the marginal note about her death on 25 February 1985.

family forms were established around 1930 that it was noted that the birth date of her older sister who died at a young age was erroneously attributed to Damiana Sette. This administrative error remained until her death and, consequently, the marginal annotation relating to her death appeared on the death certificate of her older sister and all given names were also those of her older sister even if she was usually called Damiana.

From the Individual Validation of Sardinian Centenarians to the Validation of a Population of Exceptional Male Longevity in Sardinia

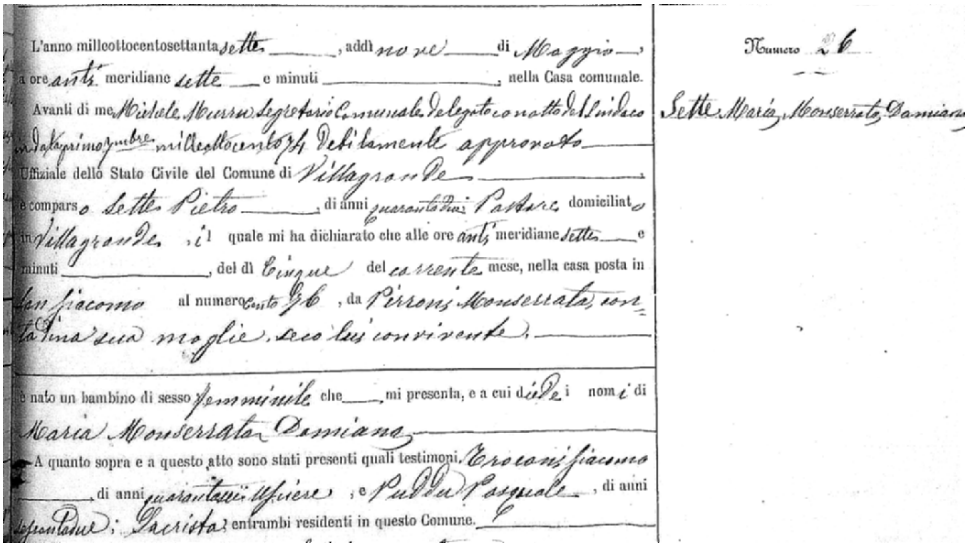
Apart from the case of Damiana Sette all centenarians involved in the AKEA survey have been validated. But this individual validation does not mean in any way that the prevalence and the population sex ratio shown in Table 3 are also valid. In order to ensure that this validation is likely to lead to the identification of a population whose longevity is exceptional, we need to verify the exhaustiveness of the identification process of all

Table 4. Family reconstruction for Antonio Todde (1889–2002)

Parents
Todde Francesco Maria (°1.1.1857 + 6.12.1945)
Deiana Francesca Angela (°3.2.1863 + 17.11.1961)
Married in Tiana on 30 December 1908.
Brothers and sisters
Todde Antonio Domenico (°30.9.1883 + 3.8.1887)
Todde Angela Rosa (°30.1.1886 + 19.8.1984)
Todde Antonio (°22.1.1889 + 3.1.2002)
Todde Giuseppe (°4.8.1891 + 17.8.1921)
Todde Maria Agostina (°7.12.1893 + 7.12.1893)
Todde Giovanni (°4.3.1895 + 8.1.1966)
Todde Salvatore (°31.1.1898 + 24.2.1944)
Todde Agostino (°26.5.1901 + 13.8.1973)
Todde Maria Agostina (°6.2.1904 Alive)
Todde Francesco Angelo (°11.11.1906 + 22.3.1967)
Todde Antioco (°11.11.1906 + 20.8.1979)
Spouse
Married on 15 September 1920 with Maddeddu Maria Antonia (°6.12.1899 + 29.5.1987)
Children
Todde Laura (°23.7.1921 +30.4.2004)
Todde Angela (°13.2.1924 Alive)
Todde Giuseppe (°27.3.1926 Alive)
Todde Isabella (°18.11.1928 + 9.9.1930)
Todde Antonino (°5.4.1933 Alive)

Table 5. Family reconstruction of Damiana Sette.

Parents
Sette Pietro (°1835 + 2.10.1905)
Pirroni Monserrata (°1844 + 21.11.1913)
Married in Villagrande on 29 November 1866
Brothers and sisters
Sette, Maria Barbara Lucia (°7.5.1867 + 14.8.1945)
Sette, Maria Agostina (°4.2.1870 + 5.4.1898)
Sette, Maria Luigia Vittoria (°7.4.1872 + 16.7.1922)
Sette, Maria Angelica Damiana (°8.8.1874 + 10.6.1876)
Sette, Maria Monserrata Damiana (°5.5.1877 + 25.2.1985)
Sette, Domenico Antonio Daniele (°2.5.1880 + 8.12.1968)
Sette, Serafino Giovanni Francesco (°18.2.1883 + 19.8.1946)
Sette, Tomaso Salvatore Angelo (°12.3.1886 + 17.8.1981)



Numero 26

Sette Maria, Monserrata, Damiana

L'anno milleottocentosettanta sette, addì nove di Maggio, a ore sante meridiane sette e minuti _____, nella Casa comunale. Avanti di me Nicolò Mauro Segretario Comunale Delegato con atto del Sindaco in data primo mese mille ottocento 77 debitamente approvato Ufficiale dello Stato Civile del Comune di Villagrande _____ è comparso Sette Pietro di anni quarantatre Pastore domiciliato in Villagrande, il quale mi ha dichiarato che alle ore sante meridiane sette e minuti _____, del dì cinque del corrente mese, nella casa posta in San Giacomo al numero cento 96, da Pirroni Monserrata sua Donna sua moglie, seco lui convivente, è nato un bambino di sesso femminile che mi presenta, e a cui dà i nomi di Maria Monserrata Damiana _____ A quanto sopra e a questo atto sono stati presenti quali testimoni, Erocani Giacomo di anni quarantatre ufficiale, e Pudda Pasquale di anni _____ impiegato; Sacristia entrambi residenti in questo Comune. _____

Figure 6. Birth record of Maria Monserrata Damiana Sette born in Villagrande on 5 May 1877, daughter of Pietro Sette and Monserrata Pirroni, without marginal note of the death.

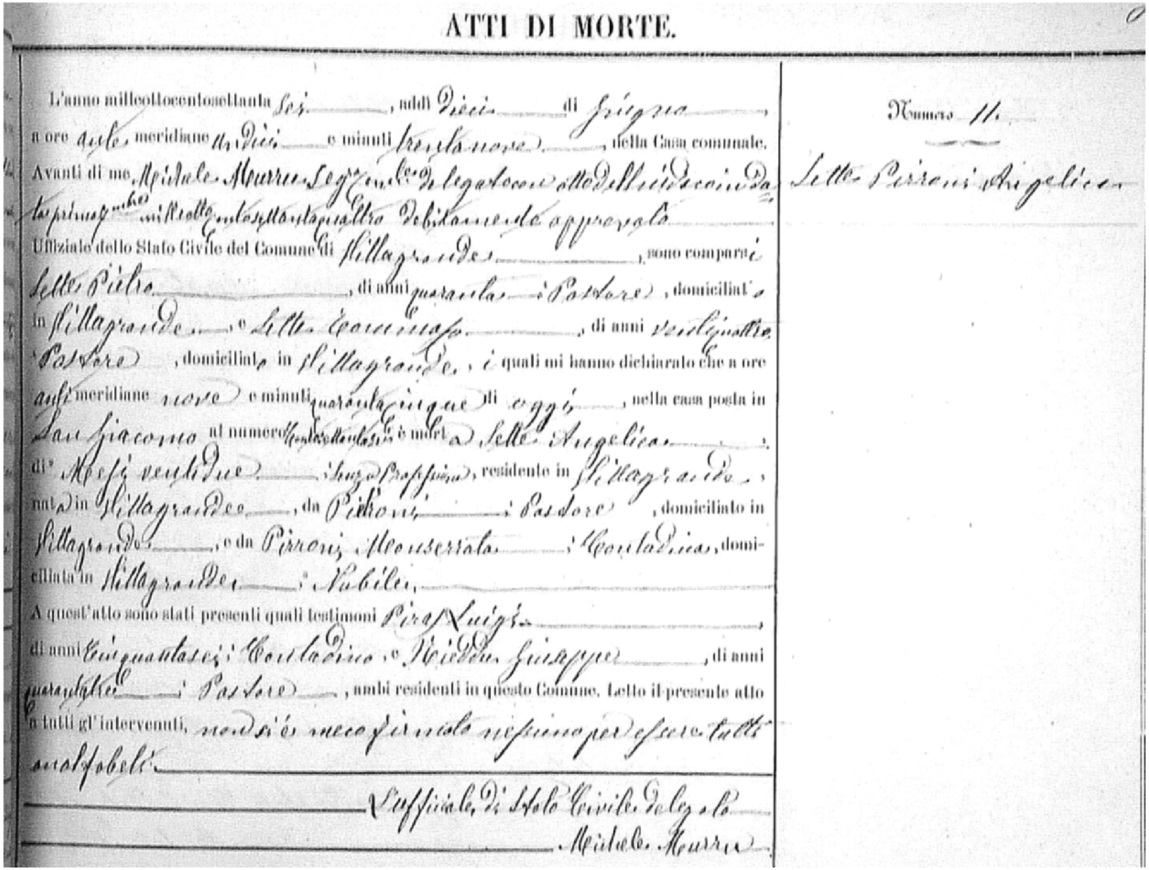
Sardinian centenarians. Indeed, the validation of the age of a centenarian is completely different from the validation of a population of exceptional longevity. The data sources used for this second type of validation are statistical and must cover the whole Sardinian population. To this aim, we have used the following data sources gathered by ISTAT, the Italian Institute of Statistics:

- the censuses of 1981, 1991 and 2001;
- the population estimations offered annually on the basis of the updating of the data of the most recent census with the help of the population movement detected by the *anagrafe*[10];
- the tables based on the death statistical forms that give the age of death which allowed for the creation of life tables.

By referring to the census data and the ISTAT annual estimations based on the *anagrafe*, we found that on 1st January 1998 Sardinia had fewer centenarians compared to the figure mentioned in the AKEA survey (147 as opposed to 222)[11] and the population sex ratio

[10] These annual estimations have been recently revised for the period 1992–2001 by ISTAT in the light of the 2001 census (www.demo.istat.it).

[11] The differences observed between the AKEA and ISTAT data could be explained by the fact that the AKEA centenarians were approached during a period of several months covering until the end of 1997 and not strictly to 1st January 1998. Some of them had already died at that date. Morever the ISTAT data constitutes a population estimation based on the updating of the 1991 census and largely revised considering the 2001 census.


ATTI DI MORTE.

Numero 11.

Sette Pirroni Angelica

L'anno milleottocentosettanta sei, addì Dieci di Giugno, a ore ante meridiane undici e minuti trentanove, nella Casa comunale. Avanti di me, Michele Murru Segretario delegato con atto del Sindaco in data ... Uffiziale dello Stato Civile del Comune di Villagrande, sono comparsi Sette Pietro, di anni quaranta, Pastore, domiciliato in Villagrande, e Sette Giuseppe, di anni ventiquattro, Pastore, domiciliato in Villagrande, i quali mi hanno dichiarato che a ore ante meridiane nove e minuti quarantacinque di oggi, nella casa posta in San Giacomo al numero ... è morta Sette Angelica, di mesi ventidue, senza professione, residente in Villagrande, nata in Villagrande, da Pietro, Pastore, domiciliato in Villagrande, e da Pirroni Monserrata, Contadina, domiciliata in Villagrande, Nubile.

A quest'atto sono stati presenti quali testimoni Pira Luigi, di anni cinquantasei, Contadino, e ... Giuseppe, di anni quarantatre, Pastore, ambi residenti in questo Comune. Letto il presente atto a tutti gl'intervenuti, non si è meco firmato nessuno per essere tutti analfabeti.

L'Uffiziale di Stato Civile delegato
Michele Murru

Figure 7. Death record of Angelica Sette daughter of Pietro and Monserrata Pirroni, aged 22 months and deceased on 10 June 1876 in Villagrande.

is somewhat smaller (1.83 as opposed to 2.04). When considering these Sardinian figures and comparing them with similar ones for Belgium and Denmark we may conclude that the sex ratio is clearly lower for Sardinia centenarians while the prevalence is higher only for men (Table 6).

Discussion

To demonstrate the exceptional character of the longevity of men in Sardinia the reliability of the statistical indexes concerning the measurement of this longevity have to be first assessed.

By calculating the proportion of centenarians within a given population, and by trying to deduce from this an unbiased measurement of longevity, one flouts the ageing process specific to the population concerned and at the same time we ignore the bias introduced by migratory flows. As an example, a population that has experienced a substantial drop in fertility from the beginning of the century would automatically have a higher proportion of centenarians in comparison to a population which has sustained high fertility levels until recent decades, with all other aspects being the same. The same logic can be applied to migratory movements. Thus, a population that has experienced high migratory movements in the aftermath of the Second World War (as in the case in Sardinia, where this post-WWII emigration movement would have had very little effect on the current centenarians) and very low immigration flows would have a higher proportion of centenarians. In contrast another hypothetical population characterised by very little emigration movements and large immigration movements would have a low proportion of centenarians. Therefore it is essential that the impact of ageing and migratory flows is taken into account when the longevity of two populations is compared.

The population sex ratio value among the centenarians is also highly sensitive to the influence of emigration movements, the significance of which, for the generations concerned, would vary depending on the gender. As a specific example, the high level of female emigration from the generations born prior to 1900 could largely justify the low actual population sex ratio value without accounting for an exceptional longevity for the men in comparison to the women. The same would be observed if men among the generations born after 1900 were the most affected by emigration compared to women.

Life expectancies at various ages are not better indicators for longevity if they are calculated on a period base. The proposed values only describe the level of survival from a synthetic perspective at a given point in time but not the overall longevity of a population.

Recently Gatti and Salaris (2004) reviewed several indexes in order to evaluate the longevity of the Sardinian population by comparing different age groups. They found that the most appropriate index is the ratio between the number of centenarians in a given population and the population aged 60–64 enumerated in the same population forty years ago. This index tries to estimate the survival between 60 and 100 and may be really useful for comparing the longevity, except that migration flows may not be considered as negligible after

Table 6. Comparison of the proportion of centenarians in Sardinia, Belgium and Denmark in 1981, 1991 and 1998 (including the AKEA centenarians for this last year).

	Male centenarians	Male population (× 1000)	Prevalence (to 100,000)	Female centenarians	Female population (× 1000)	Prevalence (to 100,000)	Female/ male ratio
1981 Census							
Sardinia	27	788	3.4	42	807	5.2	1.56
Belgium	54	4810	1.1	189	5038	3.8	3.50
Denmark	41	2400	1.7	117	2500	4.7	2.85
1991 Census							
Sardinia	48	814	5.9	81	834	9.7	1.69
Belgium	108	4876	2.2	440	5103	8.6	4.07
Denmark	76	2500	3.0	266	2600	10.2	3.50
1998 *Anagrafe and Population Registers*							
Sardinia	52	805	6.5	95	828	11.5	1.83
Belgium	114	4983	2.3	731	5210	14.0	6.41
Denmark	89	2600	3.4	369	2700	13.7	4.15

Table 7. Comparison of the Extreme Longevity Index (ELI) (proportion of centenarians from the generations born between 1880 and 1899)

Populations concerned	Male centenarians (born in 1880–1899)	Male births (× 100,000) (1880–1899)	ELI for males (to 100,000 births)	Female centenarians (born in 1880–1899)	Female births (× 100,000) (1880–1899)	ELI for females (to 100,000 births)	Female/ male ratio For ELI
Sardinia	408	2.8	146	800	2.6	308	2.11
Nuoro	149	0.57	263	163	0.53	299	1.14
Belgium	1120	18.9	59	4380	17.2	255	4.32
Denmark	858	6.9	124	2900	6.6	441	3.56

60 years of age.[12] Ideally, the most suitable index allowing the comparison of exceptional longevity between two populations is the *proportion of new-borns who, within a group of given generations, reach the age of 100*. For sure this index is more difficult to estimate. Moreover it is worth abandoning the idea of using the number of centenarians living within a given population at a given date. In fact, their numbers may be low and less reliable; and, furthermore, they all belong to different generations. In order to best define the populations that are likely to become centenarians, we will consider all new-borns during a given period and we will determine, how many of these lived 100 years or more. To calculate this *Extreme Longevity Index (ELI)*, the number of people born in a place at a given period who have celebrated their one hundredth birthday, irrespective of where they are in the world one century later, is divided by the total number of births in this same place during the initially selected period. Such an index can be estimated for Sardinia and, comparatively, for Belgium and Denmark by choosing the generations born between 1880 and 1899 and, one century later, enumerating the number of neo-centenarians for the years 1980 to 1999. Table 7 shows a comparison of ELI according for the three countries considered.

These figures clearly reveal the exceptional longevity of males in Sardinia and show that the absolute values of ELI are in no way comparable with the prevalence values calculated previously. This is not surprising since ELI is a probability, and its calculation only involves the numbers of newly-borns that are likely to be counted as centenarians in the denominator. At this stage of the analysis, if we consider that Sardinia is essentially a country of emigration, that this phenomenon mainly affects the men, and that the number of centenarians proposed here is the number of centenarians living in Sardinia and not elsewhere in the world, ELI is only likely to be underestimated (which is also true for the Belgian and Danish data, although to a lesser extent as the emigration movements are more limited). The exceptional longevity of men in Sardinia is consequently a very solid finding and subsequent research has identified a specific area within Sardinia where this phenomenon is maximised. In the so-called *Blue Zone*, an aggregation of municipalities mainly located in the mountainous part of the province of Nuoro and Sassari, one fourth of the population of Sardinia, includes half of the centenarians living on the island during the last two decades and the male ELI is twice higher than in the rest of Sardinia (Poulain *et al.*, 2004).

[12] This hypothesis may be valid for international migrations but not for internal migrations, as elderly people may often experience migration towards the city where their children are living.

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References

Bellini, P., Dalla, Zuanna, G., and Marsili, M. (1992) "Trends in geographical differential mortality in Italy (1970–1990): Tradition and change", *Genus*, 48(1–2):155–182.

Cantalini, B., and Lori, A. (1990) "Geography of ageing in the Italian population". In: Loriaux *et al*. (eds.), *Populations Agées et Révolution Grise*. Actes de la Chaire Quetelet '86, Louvain-la-Neuve. Ciaco, pp. 151–175.

Caselli, G., and Egidi, V. (1981) "La géographie de la mortalité italienne: Différences territoriales et milieu", *Genus*, 37(1–2):101–153.

Caselli, G., and Reale, A. (1999) "Does cohort analysis contribute to the study of the geography of mortality?", *Genus*, 55(1–2):27–59.

Caselli, G., Cerbara, L., Heins, F., and Lipsi, R. M. (2003a) "What impact do contextual variables have on the changing geography of mortality in Italy?", *European Journal of Population*, 19(4):339–373.

Deiana, L., Ferrucci, L., Pes, G. M., Carru, C., Delitala, G., Ganau, A., Mariotti, S., Nieddu, A., Pettinato, S., Putzu, P., Franceschi, C., and Baggio, G. (1999) "AKEntAnnos. The sardinia study of extreme longevity", *Aging Clinical and Experimental Research*, 11(3):142–149.

Gatti, A. M., and Salaris, L. (2004) "'Grandi vecchi' in Sardegna tra Ottocento e Duemila. La longevità attraverso i Censimenti della popolazione", *Quaderni del Dipartimento di Ricerche Economiche e Sociali*, (19):48.

ISTAT (1997) *La Mortalita in Italia nel Periodo 1970–1992: Evoluzione e Geografia*, a cura di Luisa Frova, Sabrina Pratti, Giovanna Boccuzzo, Riccardo Capocaccia, Susanna Conti, Maria Masocco, Virgilia Toccaceli, Roma, Arduino Verdecchia, p. 435.

Jeune, B., and Vaupel, J. (1995) *Exceptional Longevity: From Prehistory to the Present*. Odense: Odense University Press, p. 169. (Odense Monographs on Population Aging, no. 2).

Jeune, B., and Vaupel, J. (1999) *Validation of Exceptional Longevity*. Odense: Odense University Press, p. 249. (Odense Monographs on Population Aging, no. 6)

Mattioli, E. (1980) "Una prima analisi della struttura della mortalita nelle province italiane al 1960–62 ed al 1970–72", *Genus*, 36(1–2):23–58.

Passarino, G., Calignano, C., Vallone, A., Franceschi, C., Jeune, B., Robine, J.-M., Yashin, A., Cavalli, S. Luigi, L., and de Benedicts, G. (2002) "Male/female ratio in centenarians: A possible role played by population genetic structure", *Experimental Gerontology*, 37:1283–1289.

Poulain, M., Pes, G., Grasland, C., Carru, C., Ferrucci, L., Baggio, G., Franceschi, C., and Deliana, L. (2004) "Identification of a geographic area characterized by extreme longevity in the Sardinia Island: The AKEA study", *Experimental Gerontology*, (39):1423–1429.

Robine, J.-M., Caselli, G., Rasulo, D., and Cournil, A. (2006) "Differentials in the femininity ratio among centenaarians: Variations between northern and southern Italy from 1870", *Population Studies*, 60(1):99–113.

Skytte, A., and Jeune, B. (1995) "Danish centenarians after 1800". In: Jeune, B., Vaupel, J. (eds.), *Exceptional Longevity: From Prehistory to the Present*. Odense: Odense University Press, pp. 55–66 (Odense Monographs on Population Aging, no. 2).

CHAPTER 8. MORTALITY AT EXTREME AGES AND DATA QUALITY: THE CANADIAN EXPERIENCE

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As the number of observations is ineluctably small at the extreme ages, the exact level and patterns of mortality at the upper end of the life table are difficult to measure. The problem is often enhanced by errors in age declarations in official documents due to underestimation or exaggeration, attraction for some ages ending with particular digits (age heaping), transcription errors, etc. Contrary to what one might expect, these errors are not specific to countries with poor registration systems. Studies by Coale and Kisker (1986, 1990), Condran *et al*. (1991), and Kannisto (1988, 1994), among others, have shown evidence of errors in age at death declarations in vital statistics and age reporting in censuses in developed countries also, sufficient to produce biases in mortality measurement at very old ages in particular (Preston *et al*. 1999).

These doubts reached a point where it was thought that only a dozen European countries and Japan had data of sufficient quality to study old age mortality. When Manton and Vaupel (1995) concluded from an analysis of ages at death registered for Whites between 1962 and 1990 that old age mortality in the United States was lower than in Europe and Japan, Preston, and Elo (1996) expressed skepticism about these results because of data problems. The data were later shown to stand up rather well under intensive scrutiny (Hill *et al*. 2000), but a doubt still lingers on from the sum of the available evidence, because validation of age at death for the native born might not extend to immigrants, and because observation of centenarian mortality remains problematic.

It thus appears that the Canadian experience would be most useful to corroborate the existence of a North American old-age mortality advantage. But Canadian statistics were severely questioned in terms of age at death and at census for the oldest segments of the population, to the point where they were classified as being of inferior quality in a systematic review of the information available in different countries (Kannisto 1994; Kannisto *et al*. 1994). An investigation of the Canadian situation in terms of mortality measurements at the oldest ages has thus been undertaken, of which the first stages form the basis of the present paper. Specifically, it reviews the most recent information on the mortality of the very old in Canada and addresses the problem of quality of age declarations at death; it then

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presents the results of a linkage study validating reported ages at death and the ensuing mortality measures which they permitted.

Mortality at Very Old Ages in Canada

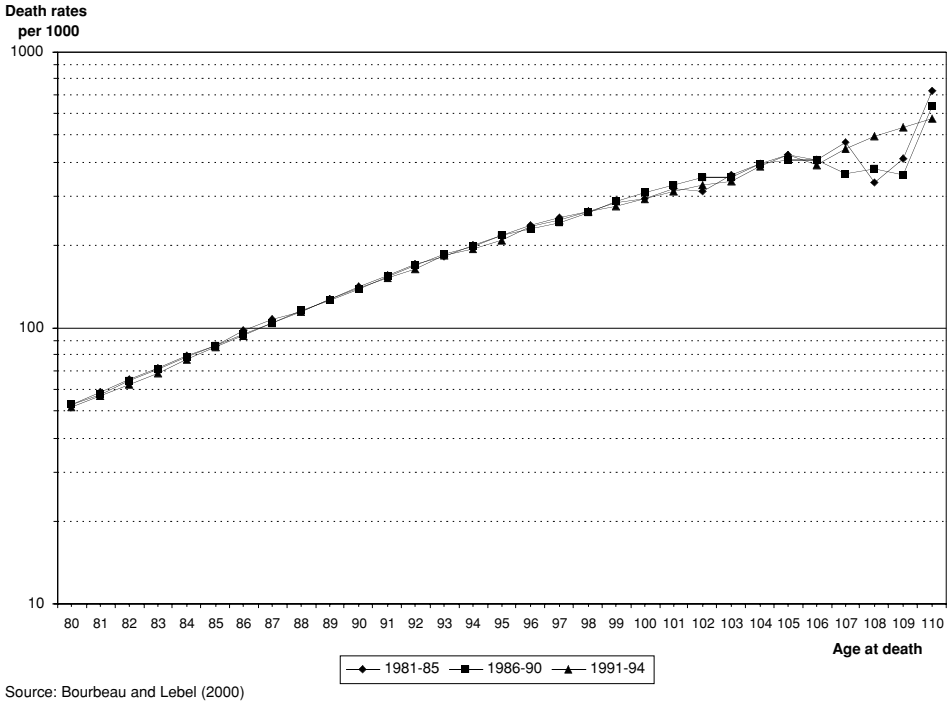
Contrary to what one would expect for a most developed country, the level and age trajectory of mortality at old ages in Canada are not readily and exactly obtained from the official statistics. Cohort life tables estimated by Bourbeau *et al*. (1997) as well as life tables produced by Statistics Canada (2002) give an estimation of mortality over age 90 obtained by graduation and extrapolation methods, but of course they rely on hypotheses which are precisely what one would want to verify. These statistical procedures are used because of persistent doubts about the reliability of data on deaths and on population counts from age 90 in Canadian official data.

In an earlier study (Bourbeau and Lebel 2000), it was confirmed these doubts were legitimate for the 1951–1995 period, using indicators suggested by Coale and Kisker (1990), and Kannisto (1988). Compared to countries known to have high quality data, the maximum ages at death in Canada were too high, as was also the proportion of centenarians in the population (106 per million compared to an expected 60 to 70); furthermore, the ratio of deaths at 105 and over to deaths among 100 and over, at about 8%, exceeded the proportions generally found in countries known to have good data, where they are below 5%. Although results were somewhat better from the 1980s, it remained clear that census data had problems and that age at death counts were suspect from age 100.

To overcome the problem of bad declarations of age in Canadian censuses, death rates among the oldest-old in Canada were estimated, using the extinct generation method, which relies only on death registration. Defined by Paul Vincent (1951), the method consists in calculating the number of survivors of each generation at any given age by cumulating the deaths of the generation "downwards" from the highest age at death. They are presented in Figures 1 and 2 for ages 80 to 110 for both males and females, starting in 1981. It must be remembered that although they are free from errors in population counts at old ages, these new estimations of mortality still depend on the quality of age at death declarations in vital statistics, which from our evaluation, are quite reliable for ages 80 to 99 but suspect for centenarians.

Consequently, here is the state of the art concerning Canadian mortality of the oldest-old:

- There has been a decline in mortality over time (from 1951 to 2000), as has been observed in many developed countries (Kannisto 1994; Manton and Vaupel 1995).
- Mortality for ages 80 to 99 is lower than that of most of the low-mortality countries (Denmark, Netherlands, Norway, and Sweden). As measures are quite reliable, quality of data should not be evoked to explain this particular profile.
- There is evidence of a slowing down in the age-associated increase in mortality. This deceleration process has also been identified in other countries (Horiuchi and Wilmoth 1998).



Source: Bourbeau and Lebel (2000)

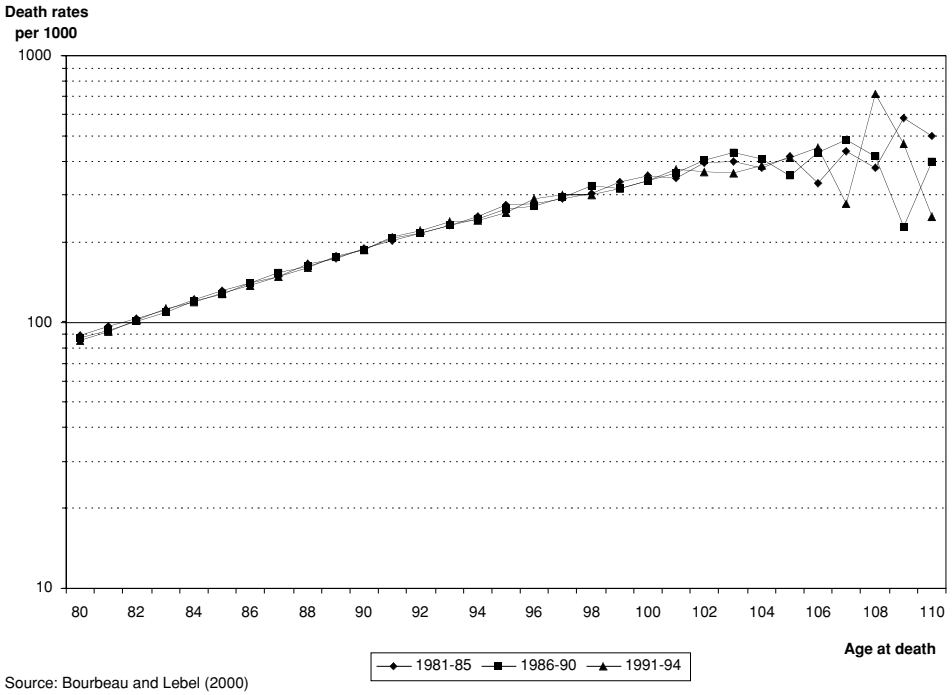
Figure 1. Life table death rates by age for females (80+), Canada, 1981–85 to 1991–1994.

- Mortality does not show evidence of a decline in the death rate itself at the very old ages, as has been suggested by some researchers (Thatcher *et al*. 1998). But measures are still uncertain, because when compared to other countries with very good data, some indicators point to the existence of problems with the Canadian data for centenarians.

It thus appears appropriate to look more closely at the data for centenarians in Canada. This in-depth study is difficult to undertake for many reasons, as will be seen below, but is essential in order to assess more precisely the quality of age declaration at death in Canada and to get a better knowledge of the mortality profile at very old ages.

About the Quality of Age-At-Death Information in Canada

Canada is a federation created in 1867 by an initial group of four provinces to which six others were since added, the latter as late as 1949. Under the constitution in which are



Source: Bourbeau and Lebel (2000)

Figure 2. Life table death rates by age for males (80+), Canada, 1981–1985 to 1991–1994.

defined the responsibilities of each order of government, all aspects of civil registration fall to the individual provinces, who handle the initial collecting and processing of data. Although gathered by the central government since the 1920s and the object of standardization efforts as to content, the information is thus reliant on ten different administrations, each with their own history and traditions, and with their own set of rules and methods, varying over time of course.

This has an impact on the quality of age-at-death information in Canada at both ends of the spectrum. In the early days of government registration of births, marriages, and deaths, not all events were reported and recorded. Many people and local institutions were often suspicious of why the government wanted such information and refused to comply; in Ontario, Canada's most populous province, for example, it has been estimated that birth registration was only two-thirds complete for the 1875–1895 time period and no more than 85% complete for any of the next 25 years (Emery 1993). Added to the pioneer character of many areas of the country at the turn of the twentieth century, this entails that a significant number of people born in Canada and dying at very high ages today could be without documentary evidence of their date of birth.

As for contemporary death registration, practices vary greatly across the recent decades and the different provinces. Modern records tend to give quite complete information; but even when a new requirement was made for additional information to be recorded, it often took many years for the new forms to reach all offices and agencies and to be implemented systematically across the country. Provincial data collection agencies were slow to adopt (costly) controls at the time of data entry: as recently as 15 years ago, for example, the death of a 10-year-old in Quebec could be registered as a 110-year-old by typing his birth date in the 1800s instead of the 1900s, without any further ado.

Unreliable extreme age-at-death information is thus a clear possibility in the Canadian context. As awareness has finally reached the administrations, some efforts have been made to implement quality control methods and to cross-check information relating to extreme age declarations for example, but a lot remains to be done. And the problem of the relatively late implementation of systematic birth registration in Canada will of course never go away. Church registration of births can be counted on to compensate to a certain degree, but here again quality and coverage vary greatly, according to religious denomination, territory, and period.

The province of Quebec represents here the very fortunate exception. The very first missionaries from France implemented comprehensive registration of baptisms, marriages, and burials in the Catholic tradition of their home country. Better still, the authorities prescribed in 1679 that this registration would be done in two copies, the second one being turned over to the government as civil registration of these events, a system which was maintained without interruption for centuries. Their society being homogeneously Catholic, French-Canadians of Quebec have thus benefited from long-standing quality civil registration. These records were never used as such by the authorities to produce statistics of ages at death for example, with the exception of records for the city of Quebec used as a historical sample in the 1871 census of Canada (Canadian Ministry of Agriculture 1878). But through the linking of the baptism and burial certificates of individuals, they have allowed fascinating advances in data quality evaluation and in exact measurements for mortality in particular.

Foremost in this line is the work done by members of the *Programme de recherche en démographie historique* (PRDH) at the Université de Montréal (Légaré 1988). Within the PRDH, the first 700 000 baptisms, marriages and burials registered in Quebec, covering the whole of the seventeenth and eighteenth centuries, were computerized and used to establish family files up to 1765, genealogical mapping up to 1799, and exact age-at-death information of adults born before 1705. This information immediately illustrated, if necessary, the need for caution in using extreme age at death declarations: out of 76 reported ages at death of 100 and over for persons born in the colony whose exact age could then be calculated, none corresponded to a genuine centenarian! (Charbonneau and Desjardins 1990). However, it was established that out of the some 20 000 persons born in the St-Lawrence valley before 1700, 140–65 men and 75 women—reached the age of 90. It was then proven that a woman born in 1648 celebrated her 99th birthday, a rare and valuable insight when trying to establish the parameters of the extreme age reached by human beings in the past and its evolution to today (Desjardins 1999).

Reverting to age declaration quality, the information on 1346 people who were actually aged 80 or over when they died—the top 15% of the distribution of deaths of adults born before 1705 for which both an age declaration and a calculated age were available—was used to estimate the degree of inexactitude in age-at-death declarations. Only a little over a third of the ages in the burial registration were accurate; 9% were underestimated and the rest, 55%, were overestimated, with some errors reaching 20 years. On average, some four years separated the declaration from the true value, corresponding, because of offsetting errors, to an overestimation of some 2.5 years in the average age at death of octogenarians and nonagenarians estimated from age declarations.

Of course, these historical results, where people were mostly illiterate and did not relate to age as people today are expected to, are not transposable to contemporary data in developed countries. But although their use is much more difficult for more recent times, parish registers still offer a privileged source of information to estimate the quality of age-at-death declarations in the late twentieth century in Quebec. Hubert Charbonneau led the way with a verification of an investigation on centenarianism published along with the results of the 1871 census of Canada, which reduced a list of nine deaths of centenarians authenticated by the Chief Statistician of the country to one, most notably invalidating the long standing myth that a man born in 1701 had reached the age of 113 (Charbonneau 1991). More recently, parish registers were used to verify deaths of super-centenarians—110 years and over—in Quebec (Bourbeau and Desjardins 2000). Of ten such ages officially registered for French-Canadians of Quebec since 1975, only four proved to be authentic. Not surprisingly, they were the most recent declarations, the first real super-centenarian having died in 1983. The data since 1980 contained only one false super-centenarian, pointing to better controls by the Quebec statistical office when collecting and processing age information.

Following this first experience with parish registers to verify the accuracy of official statistics, it was decided to extend the study to deaths registered in the 100–109 age group in Quebec as a first step leading towards a comprehensive investigation of extreme age at death in Canada.

Verification of the Quality of Reported Extreme Ages at Death in Quebec

Age at death is obtained from the difference between date of death and date of birth as written on the person's death certificate. The principle behind using parish registers to validate that age is to find the baptism of the person and then to perform a linking of two documents recorded a century apart, basically on the basis of the person's name. This is a standard procedure in historical demography, and relatively simple to achieve when all baptisms have been indexed, as in Quebec up to 1800. Parish registers of Quebec up to the 1930s are readily available on microfilms for each parish, but unfortunately, although events were indexed at least annually at the parish level, no comprehensive index of baptisms exists for the nineteenth century. Because death certificates do not record the person's exact place of birth—only the country or province is required—finding a specific baptism would be impossible if the name of the parents and of the spouse were not there to help pinpoint where in Quebec

the person might have been born. Indeed, as information on marriages in Quebec has been systematically indexed in the 1930s and recently made available in one comprehensive repertory by a genealogical firm, it is possible to identify among the hundreds of Quebec parishes the one or ones where the baptism of a specific person should be found. Nominative census returns up to 1901 are also available as a secondary source of information.

Nominative information in administrative documents is kept out of the public domain for one hundred years, but can be obtained for research purposes through specific permission, given by a commission set up by the government to monitor access to official documents, within a strict protocol governing use and publication of the data. For technical reasons due to differences in computerization protocols through time, it was only possible at this first stage to obtain data from 1985, which was ample to establish the feasibility of the project and obtain basic information on data quality.

DEATHS OF CENTENARIANS IN QUEBEC FOR THE 1985–1999 PERIOD

Of the 754,632 deaths registered in Quebec for the 1985–1999 period, 3031 (0.4%) are of people aged 100 and over; they were made available for the needs of this research in a file containing for each case: first and family names of the deceased, sex, date of birth, date of death, age at death, place of birth (province in Canada or country), first and last name of the father and of the mother and family name of the spouse for those who were once married. Males form 21% of the total and died 0.2 year younger than females on the average (Table 1); super-centenarians represent 0.46% of deaths of centenarians. Kannisto (1994) suggested an indication of possible problems in age declarations could be inferred from a ratio of deaths at age 105 and over within deaths of centenarians greater than 5%; here the ratio is at 7% for males and 8.4% for females (Sweden, recognized as having quality age reporting, has a ratio of 2.4% for males and 3.7% for females). Preliminary examination of the data thus pointed to some problems for Quebec, in the same order as those for the whole of Canada.

Given the nature of the validation to be performed, it is necessary to distinguish outright within the data set the deaths of persons who were born outside Quebec. They represent about one out of five cases and, as can be seen in Table 2, the group shows some slight differences as to average age at death and proportion of deaths at 105+ when compared with the Quebec born; it is also interesting to note they comprise nine of the fourteen super-centenarians in the file.

Of course, this comes as no surprise. 80% of those born outside Quebec are from another country, and one would expect that for different countries of origin and periods of immigration problems could be present in birth information. If up to the 1970s immigrants predominately originated from European countries—the United Kingdom, southern Italy, France, Greece, and Poland for example—the more recent arrivals are much more diversified, including the West Indies and countries of Asia previously absent, and they already begin to show up in the extremely aged group (Table A.1 in Appendix). This raises the question of heterogeneity in the cases recorded in national statistics, a problem certainly

Table 1. Recorded deaths of centenarians by sex and year of age, Quebec 1985–1999.

Age	Males	Females	Total
100	253	838	1091
101	168	586	754
102	97	367	464
103	53	227	280
104	30	167	197
105	17	100	117
106	14	42	56
107	7	29	36
108	2	10	12
109	1	9	10
110	3	4	7
111	0	5	5
112	0	0	0
113	1	1	2
Total	646	2385	3031
Avg. age	101.9	102.1	102.1
D(105+)/D(100+)	7.0%	8.4%	8.1%

to be addressed in the whole question of quality of age declarations at extreme ages for a given country.

Notwithstanding, the 105+ proportion remains high even for the 2280 cases born in Quebec, indicating that the quality of ages recorded could still present a problem.

Table 2. Average age at death and proportion of deaths at 105+ according to place of birth and sex, Quebec, 1985–1999.

Place of birth	Sex	N	Avg. age at death	D(105+)/D(100+)
Born in Quebec	M	480	101.88	6.7%
	F	1800	102.08	7.8%
	T	2280	102.03	7.5%
Born outside Quebec	M	139	102.19	10.5%
	F	487	102.32	9.4%
	T	626	102.27	10.2%

Note: In 125 cases it was not possible to ascertain if the person was born in Quebec or not. Their average age at death and proportion of 105+ is in between the two above groups in every category.

VALIDATION OF THE AGE AT DEATH OF A SAMPLE OF CENTENARIANS BORN IN QUEBEC

The population of Quebec of the 19th century included a proportion of English speakers, generally Protestants. The exact nature and availability of the information for validation meant in practical terms the operation should be carried out strictly on French-Canadians, who represent the immense majority of Catholics in Quebec, setting aside people with English or foreign names. This should not alter the results of the validation as no reason has been suggested why Protestants might particularly be imprecise in their age at death declarations. The number of deaths involved was thus reduced to 2039 cases. A sample was then established containing all deaths at ages 107 and over, half of the deaths at age 106, a quarter of the deaths at age 105, 10% of deaths at ages 102 to 104, and 5% of deaths at 100 and 101, for a total of 209 cases, 41 males and 168 females, distributed over the entire 1985–1999 time period (Table A.2 in Appendix). Each case was investigated individually, in the following manner. First the record of the marriage of the parents was looked up, both to find eventual inconsistencies between the proposed date of birth and the date of marriage of the parents and to establish a location for the baptism to be found. Parish registers of the place of marriage or of residence of the spouses were then used to research the centenarian's baptism. Nominative census returns were used to fill gaps, corroborate information, or solve problems when necessary. The person's own marriage, when containing an age or a place of residence proved sometimes useful. Using the wealth of information available, quite satisfactory results were obtained; the important issue was to make sure the unsolved cases were not selected as to having a greater risk of being incorrect than the others, and great pains were taken in this respect. The results are presented with this in mind.

First the easy ones: 158 cases out of the 209 (76%) were confirmed as being precise ages by finding the baptism of the person either at the exact date appearing in the death certificate, or within a couple of days. One case was included although an inversion had been made between the month and the day on the death certificate, yielding a difference of seven months but no age difference.

Equally easy, but of a very different nature, were four cases of error. As could be expected, they pertain to very high ages: one super-centenarian and three 107-year-olds. Three of them were in fact ten years younger but an alleged 107-year-old was actually 108 years old! These errors represent 2% of the total number of cases that were examined, but 5% of those 105 or over.

In 18 cases, the record of baptism could not be found, usually because the family had moved around in an unpredictable manner, but the information was corroborated either through an age at marriage of the person or through secondary evidence (age of mother making a later birth improbable, for example).

The next 25 cases, 12% of the sample, could not be classified in the above categories. They were analysed in detail to establish as high a probability as possible that they had not been selected in virtue of an inexact age at death declaration. To this end, many elements were

used: date of marriage of the parents and age of mother at the alleged date of birth; date of the person's marriage and age of spouse; the existence of kin; the age of the person's own children, sometimes found in newspaper necrologies or articles; probable place of birth, the city of Montreal being difficult to work with because of the numbers involved. Of course, this kind of evidence would not withstand the test for longevity records, but in the context of this research, they suffice to render highly improbable a significant bias against age quality in Quebec death registration data.

Finally, four cases were left without any possibility for verification whatsoever, clearly a negligible proportion in a statistical context.

To sum up, after careful examination of the results of the operation, we feel it can safely be said that age-at-death information for centenarians since 1985 in Quebec is exact for people born in Quebec, with a caveat to be expressed at the highest ages, for which a systematic verification should probably always be performed.

This positive assessment would seem to be contradicted by the relatively high proportion of deaths at 105 and over among the centenarian deaths. However, this proportion is lower than in Canada as a whole, and is comparable to the proportion among Whites in the United States, for which a recent record linkage study has concluded age at death on death certificates is of high enough quality to produce a reliable measure of mortality at very old ages (Hill *et al*. 2000). This higher proportion of deaths at ages 105+ may then be an indication of a lower mortality among centenarians in North America. Furthermore, the ratio of deaths of women to those of men, at 3.7 for people born in Quebec, is similar to the ratio for France, Japan, and England and Wales, another sign of the reliability of the Quebec data. This ratio is lower in the Nordic countries (at about 2), but this could be specific to the region.

These results are but a first step in a broader effort to establish the overall quality of extreme age-at-death information in Canada. But already they have the interesting payback of allowing a validated measure of centenarian mortality for a group of North Americans, which can be compared to measures that have been done in other countries.

The Centenarian Mortality of Quebec 1885–1889 Cohorts

The extinct generation method was used to estimate the centenarian mortality of those cohorts under observation up to age 110 with validated Quebec age at death for the 1985–1999 period, that is people born in Quebec from 1885 to 1889. The q_x values of the life tables are shown in Figure 3.

For males, the small numbers of survivors at age 100 lead to quite volatile measures of mortality, with perhaps an upward trend in the death rates from age 100 to 106. The female curve shows an increase of the death probabilities from age 100 to age 105, with signs of deceleration in the rate of increase, as the best fitting curve for females is a quadratic rather than an exponential model. Beyond age 105, the numbers are too small to yield a definitive

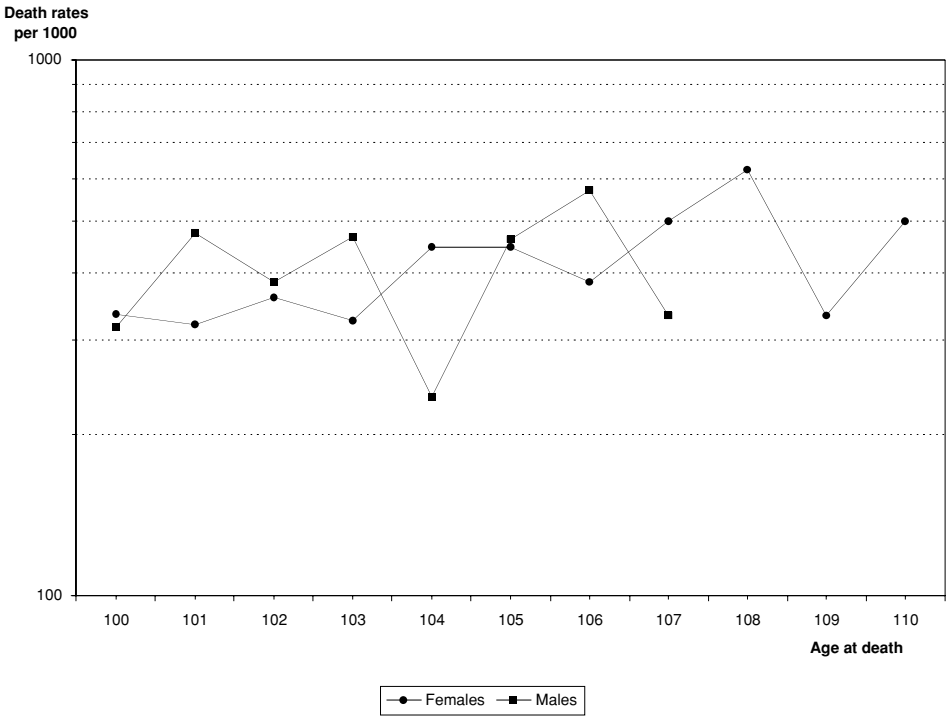


Figure 3. Age-specific life table death rates among centenarians by sex, Quebec (Native Born), 1885–1889 Cohorts.

pattern and thus to give any support to the hypothesis of a decrease in death rates at very old ages.

To identify a possible North-American specificity, these measures were compared to mortality data from the Human (Mortality Database) (Wilmoth 1997). To optimize comparison, only measures obtained using the extinct generation method were chosen, presented either as cohort tables (Sweden) or period tables (France, Japan, United States Whites); as deaths from the 1885–1889 cohorts span the 1985–1999 period, using period tables from the early 1990s seemed appropriate and sufficient for the comparison. We added the tables we ourselves calculated for Canada using again the same method. The others are taken as they are and may include incorrect ages at death, as is the case for Canada.

Death rates from age 100 are shown in Figures 4 and 5. The female series of q_x show a rather common pattern, at least up to age 106, the curves being almost parallel. The United States, Canada, and Quebec have the lowest rates, followed by Japan, France, and Sweden. Deaths rates are still increasing with age; there are some signs of a leveling off in France and Japan, but not in Sweden, Canada, and the United States. Male rates rest on fewer cases

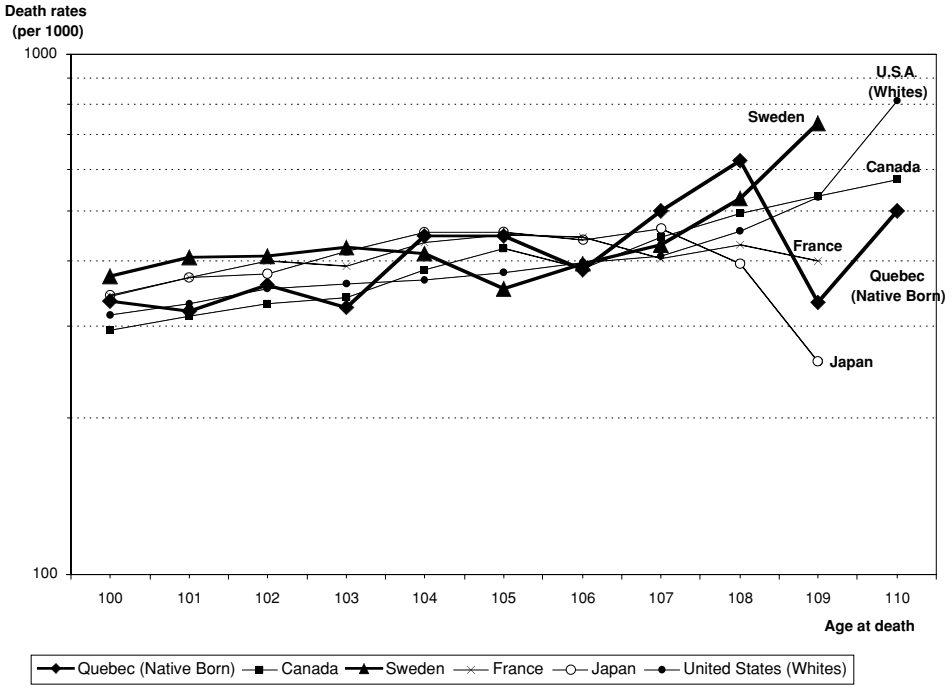


Figure 4. Age-specific life table death rates among Centenarians for Quebec (1885–1889 Cohorts) and a selection of countries, females.

of course; Quebec rates are quite close to Sweden's, with the Canadian and American rates clearly lower than in other countries up to age 105.

Expressed either through life expectancy at age 100 or probability of survival from age 100 to age 105, mortality in Quebec is lower than in Sweden, France, and Japan, with levels quite similar to those for the United States (Table 3). These results give more support to the existence of a North American mortality pattern, characterized by a lower mortality among the oldest-old (Bourbeau and Lebel 2000).

Conclusion

Our understanding of mortality patterns at the upper limits of life is limited by observation problems present with the great majority of the data available for the very old from official statistics. Mathematical methods exist to circumvent the problem by using the rates at ages preceding the upper limits to estimate the rates of the last few ages, but the choice of one pattern or another would still benefit from foolproof observations. In this matter, universal

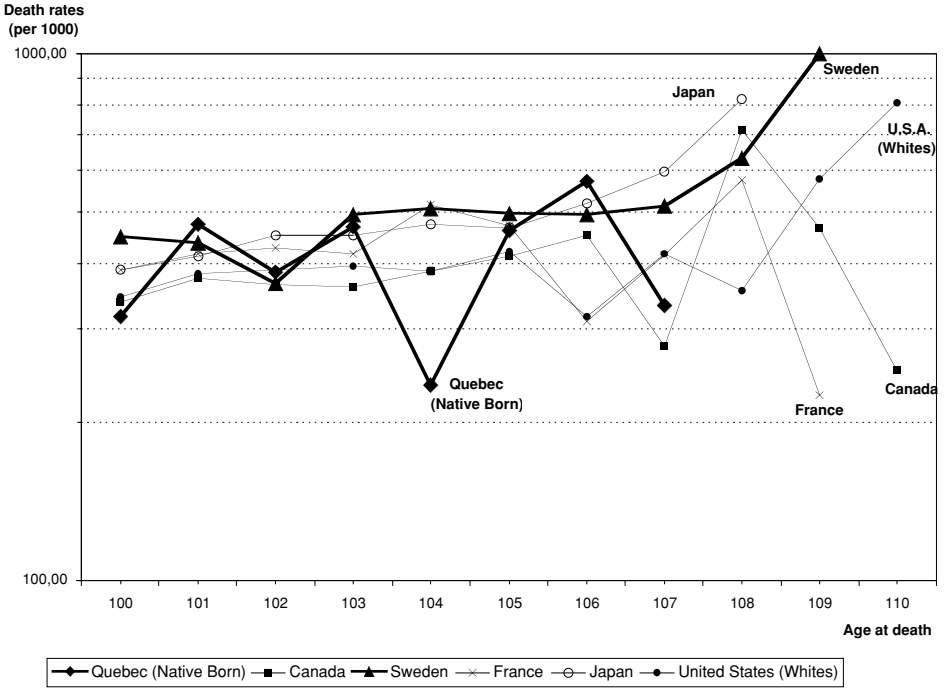


Figure 5. Age-specific life table death rates among Centenarians for Quebec (1885–1889 Cohorts) and a selection of countries, males.

knowledge cannot rest on the use of data from Sweden alone! This is why a systematic examination has been undertaken of very-old-age information in Canadian statistics, with reported centenarian deaths of the last 15 years in the Province of Quebec being investigated at the first stage.

Table 3. Life expectancy at age 100 and probability of survival from age 100 to 105, for Quebec and a selection of countries.

		Males		Females	
Countries	**Cohorts or Period**	e_{100}	$_5p_{100}$	e_{100}	$_5p_{100}$
Quebec (Native Born)	Cohorts 1885–1889	2.05	0.0897	2.34	0.1078
Canada	Period 1991–1994	2.24	0.1030	2.53	0.1312
Sweden	Cohorts 1886–1890	1.69	0.0443	1.98	0.0742
France	Period 1991–1995	1.88	0.0571	2.12	0.0849
Japan	Period 1991–1995	1.84	0.0572	2.11	0.0811
United States (Whites)	Period 1991–1992	2.14	0.0922	2.38	0.1195

Sources: Canada: Bourbeau and Lebel 2000; other countries: Human Mortality Database.

Ages at death reported for a given area often concern a heterogeneous population in terms of ethnic and/or place of birth composition, with a resulting heterogeneity in the quality of declarations along these lines. In the Canadian context, it appears advisable to delimit sub-populations where data quality might be better and use them only when specific needs preclude incorrect information of any proportion; following our analysis, French Canadians born and having died in Quebec form such a group. Using information relating to them only, for the 1985–1999 period, convincing evidence pointing towards a specific North American mortality pattern at the later stages of life was obtained.

Many hypotheses have been presented to explain the relatively low mortality level at older ages for Canada and the United States: data quality (exaggeration of age at death) (Coale and Kisker 1986, 1990; Elo and Preston 1994; Kannisto *et al*. 1994); adverse selection (Vaupel, Manton, and Stallard 1979); socio-economic inequalities; existence of a universal medical care for the elderly (Manton and Vaupel 1995; Himes 1994; Bennett and Olshansky 1996); selection induced by immigration (Trovato 1985, 1993, 1998; Chen *et al*. 1996a, 1996b).

Some hypotheses have been discarded or challenged by new findings; for example, data proved to be better than expected, as least for people born in Canada, as the present paper demonstrates, and for the United States (Hill *et al*. 2000). The healthy immigrant effect is still an interesting hypothesis but not a sufficient one, as the Canadian born also show a relatively lower mortality. More effective medical care has been proposed as another explanation for the better survival among the oldest-old in North America. The existence of a universal heath care program in Canada may explain some of the difference between Canadian and American mortality patterns, in particular at young ages. However it cannot be offered as an explanation for the differences with other developed countries without some thorough analysis of health care programs in those countries.

A more promising explanation might be found in the different health and living conditions experienced at the younger ages. Populations in many European countries and in Japan before the 1950s experienced the hardships of wars which could have left lasting effects leading to relatively higher mortality at older ages in those countries; conversely, North Americans benefited from a combination of several factors (better living conditions throughout the twentieth century, health care programs, selection induced by immigration, etc.), which could all contribute to a relatively lower mortality at higher ages (Bourbeau 2002).

Notwithstanding, observations beyond the age of 107 remain few and it is possible they could contain a somewhat higher proportion of mistakes; extreme cases should then probably be systematically validated when possible. Along these lines, the pooling of validated data at the international level seems a most interesting initiative; the work under way on super-centenarians coordinated by Jean-Marie Robine within the IDL project (International Database on Longevity) with the support of the Max-Planck Institute for Demographic Research is a perfect example of such an effort. In Canada, the present investigation will be extended to the other major provinces, in order to identify within the data for Canada which areas, groups, periods, and age intervals can be used with confidence for mortality studies of the extremely aged.

Appendix

Table A.1. Deaths of Centenarians by age and place of birth, both sexes, Quebec, 1985–1999.

Province or country of birth	100	101	102	103	104	105	106	107	108	109	110	111	112	113	Total	%
Algeria					1										1	0.03
Austria	3		1			1									5	0.16
Barbados	1				1										2	0.07
Belgium	5	2	1		2		1				1				12	0.40
Brazil	1														1	0.03
Bulgaria	1														1	0.03
China	2	2	1									1			6	0.20
Czechoslovakia	1		1												2	0.07
Czech Republic			1												1	0.03
Danemark	1														1	0.03
France	3	5	2	1	4	2	1			1					19	0.63
Germany	5		3	1		2									11	0.36
Greece	2	6			2										10	0.33
Guyana					1				1						2	0.07
Haiti	1	1		1	1										4	0.13
Hong Kong				1											1	0.03
Hungary	6	2		3											11	0.36
India		1		1											2	0.07
Iraq			2												2	0.07
Ireland	3	6	1	1			1	1							13	0.43
Italy	24	8	6	5	1	3	2								49	1.62
Jamaica	1	1													2	0.07
Japan		1				1									2	0.07
Laos	1														1	0.03
Lebanon	1			1											2	0.07
Lettonia			1												1	0.03
Netherlands			1												1	0.03
Poland	17	6	8	4										1	36	1.19
Portugal				1											1	0.03

(*Cont.*)

Table A.1. Continued

Province or country of birth	100	101	102	103	104	105	106	107	108	109	110	111	112	113	Total	%
Guinea-Bissau	1														1	0.03
Romania	4	6	3	2			1								16	0.53
Russia	9	5	2	3	3	1				1					24	0.79
Viet-Nam		1													1	0.03
Spain						1									1	0.03
Svalbard	1														1	0.03
Switzerland	1	2			1	2									6	0.20
Syria		1													1	0.03
Trinidad and Tobago	1					1									2	0.07
Tunisia			1												1	0.03
Turkey	3	1	3	1		2			1		1				12	0.40
Ukrainia	1	1													2	0.07
U.R.S.S.	7	5	3	3	2		1				1			1	23	0.76
Egypt	1		1												2	0.07
United Kingdom	48	31	20	17	11	4	1	1	2	1					136	4.49
United States	26	18	6	6	6	1	2	2		1					68	2.24
Wallis and Futuna	1														1	0.03
Canada (province unknown)	11	9	6	1	7	2	2								38	1.25
Newfoundland	2	1	1	1				1							6	0.20
Prince Edward Island	1			1		1									3	0.10
Nova Scotia	3	2	3			1					1	1			11	0.36
New Brunswick	2	6				1									9	0.30
Quebec	738	494	305	185	124	80	34	24	6	4	1	2			1997	65.89
Ontario	18	16	12	3	2		3	1				1			56	1.85
Manitoba		2													2	0.07
Other country	1														1	0.03
Unknown	132	112	69	37	28	11	7	7	1	2	2				408	13.46
Total	1091	754	464	280	197	117	56	37	11	10	7	5	0	2	3031	100.00
Quebec among Unknown (1)	94	79	44	24	21	9	4	5	1	1	1				283	
Quebec (Total)	832	573	349	209	145	89	38	29	7	5	2	2	0	0	2280	75.22

Table A.2. Distribution of deaths by age and sex in the sample, Quebec, 1985–1999.

	Female		Male			
Age at death	Number	%	Number	%	Total	Sampling fraction
100	27	67.5	13	32.5	40	0.053
101	24	88.9	3	11.1	27	0.052
102	26	86.7	4	13.3	30	0.098
103	17	89.5	2	10.5	19	0.103
104	11	78.6	3	21.4	14	0.110
105	19	90.5	2	9.5	21	0.269
106	13	76.5	4	23.5	17	0.500
107	19	73.1	7	26.9	26	1.000
108	5	71.4	2	28.6	7	1.000
109	4	100.0		0.0	4	1.000
110	1	50.0	1	50.0	2	1.000
111	2	100.0		0.0	2	1.000
Total	168	80.4	41	19.6	209	0.103

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References

Bennett, N. G., and Olshansky, S. J. (1996) "Forecasting US age structure and future of social security: the impact of adjustments to official mortality schedules", *Population and Development Review*, 22 (4):703–727.

Bourbeau, R. (2002) "L'effet de la "sélection d'immigrants en bonne santé" sur la mortalité canadienne aux grands âges", *Cahiers québécois de démographie*, 31(2):249–274.

Bourbeau, R., and Desjardins, B. (2000) "An overview of Canadian data on super-centenarians: Official data and validation procedures". *Presentation for the Super Centenarian Workshop*, Max Planck Institute for Demographic Research, Rostock, pp. 15–16.

Bourbeau, R., and Lebel, A. (2000) "Mortality statistics for the oldest-old: An evaluation of Canadian data", *Demographic Research*, 2(2):35.

Bourbeau, R., Légaré, J., and Émond, V. (1997) *New Birth Cohort Life Tables for Canada and Quebec, 1801–1991.* Ottawa (Demographic Document, Current Demographic Analysis, no. 3, Statistics Canada, catalogue no. 91F0015MPE).

Canada (Ministry of Agriculture). (1878) *Censuses of Canada, 1608 to 1876: Statistics of Canada.* Vol V., Ottawa: Maclean, Roger & Co., pp. 282–345.

Charbonneau, H., and Desjardins, B. (1990) "Vivre cent ans dans la vallée du Saint-Laurent avant 1800", *Annales de démographie historique*, pp.217–226.

Charbonneau, H. (1991) "Les centenaires officiels du XIXe siècle", *Mémoires de la Société Généalogique Canadienne-Française*, 42:219–226.

Chen, J., Ng, E., and Wilkins, R. (1996*a*) "The health of Canada's immigrants in 1994–95", *Health Reports*, 7(4):33–45.

Chen, J., Wilkins, R., and Ng, E. (1996*b*) "Health expectancy by immigrant status, 1986 and 1991", *Health Reports*, 8(3):29–37.

Coale, A.J., and Kisker, E. E. (1986) "Mortality crossovers: Reality or bad data?", *Population Studies*, 40:389–401.

Coale, A. J., and Kisker, E. E. (1990) "Defects in data on old-age mortality in the United States: New procedures for calculating mortality schedules and life tables at the highest ages", *Asian and Pacific Population Forum*, 4(1):1–31.

Condran, G. A., Himes, C. L., and Preston, S. H. (1991) "Old age mortality patterns in low mortality countries: an evaluation of population and death data at advanced ages, 1950 to present", *Population Bulletin of the United Nations*, 30:23–60.

Desjardins, B. (1999) "Validation of extreme longevity cases in the past: The French-Canadian experience". In: Jeune, B., Vaupel, J. W. (eds.), *Validation of Exceptional Longevity*. (*Odense Monographs of Population Aging*). Vol 6. Odense: Odense University Press, pp. 65–78.

Elo, I. T., and Preston, S. H. (1994) "Estimating African-American mortality from inaccurate data", *Demography*, 31(3):427–458.

Emery, G. (1993) *Facts of Life: The Social Construction of Vital Statistics*. Montreal: Mc-Gill-Queen's University Press.

Hill, M. E., Preston, S. H., and Rosenwaike, I. (2000) "Age reporting among White Americans aged 85+: Results of a record linkage study", *Demography*, 37(2):175–186.

Himes, C. L. (1994) "Age patterns of mortality and cause-of-death structures in Sweden, Japan, and the United States", *Demography*, 31(4):633–650.

Horiuchi, S., and Wilmoth, J. R. (1998) "Deceleration in the age pattern of mortality at older ages", *Demography*, 35(4):391–412.

Human Mortality Database. University of California, Berkeley (USA) and Max Planck Institute for Demographic Research (Germany). Available at www.mortality.org or www.humanmortality.de .

Kannisto, V. (1988) "On the survival of centenarians and the span of life", *Population Studies*, 42:389–406.

Kannisto, V. (1994) *Development of Oldest-Old Mortality, 1950–1990: Evidence from 28 Developed Countries*. Vol 1. Odense: Odense University Press (*Odense Monographs of Population Aging*).

Kannisto, V., Lauritsen, J., Thatcher, R., and Vaupel, J. W. (1994) "Reductions in mortality at advanced ages: Several decades of evidence from 27 countries", *Population and Development Review*, 20(4):793–810.

Légaré, J. (1988) "A population register for Canada under the French Regime: Context, scope, content and applications", *Canadian Studies in Population*, 15:1–16.

Manton, K. G., and Vaupel, J. W. (1995) "Survival after the age of 80 in the United States, Sweden, France, England and Japan", *The New England Journal of Medicine*, 333(18):1232–1235.

Preston, S. H., and Elo, I. T. (1996) "Letter to the editor on the theme— survival after age 80", *The New England Journal of Medicine*, 334(8):537–538.

Preston, S. H., Elo, I., and Stewart, Q. (1999) "Effects of age misreporting on mortality estimates at older ages", *Population Studies*, 53:165–177.

Statistics Canada. (2002) *Life Tables, Canada, Provinces and Territories, 1995—1997*. Ottawa: Health Statistics Division (Cat. No. 84–537).

Statistics Canada. (1997) "Deaths by age, sex and year of birth, Canada, 1951–1995"*, Vital Statistics*, Special Data; *Population by Age and Sex, Canada, 1971–1991 Censuses*, Special Data.

Thatcher, A. R. (1992) "Trends in number and mortality at high ages in England and Wales", *Population Studies*, 46:411–426.

Thatcher, A. R., Kannisto, V., and Vaupel, J. W. (1998) "*The Force of Mortality at Ages 80 to 120*". Vol 5. Odense: Odense University Press (*Odense Monographs of Population Aging*).

Trovato, F. (1998) "Nativity, marital status and mortality in Canada", *Canadian Review of Sociology and Anthropology*, 35(1):65–91.

Trovato, F. (1993) "Mortality differences by nativity during 1985–1987", *Canadian Studies in Population*, 20(2):207–223.

Trovato, F. (1985) "Mortality differences among Canada's indigenous and foreign-born populations, 1951–1971", *Canadian Studies in Population*, 12(1):49–80.

Vaupel, J. W., Manton, K. G., and Stallard, E. (1979) "The impact of heterogeneity in individual frailty on the dynamics of mortality", *Demography*, 16(3):439–454.

Vincent, P. (1951) " La mortalité des vieillards ", *Population*, 6(2):181–204.

Wilmoth, J. R., and Lundström, H. (1996) "Extreme longevity in five countries: Presentation of trends with special attention to issues of data quality", *European Journal of Population/Revue Européenne de Démographie*, 12(1):63–93.

Section 3
Causes of Death and Biological Frailty

SECTION 3. CAUSES OF DEATH AND BIOLOGICAL FRAILTY

Data quality is also a main concern for the reporting of the causes of death of the oldest-old. Despite the fact that an increasing large part of the deaths occurred after the age of 85 years, studies of the causes of death of the oldest-old are still rare. In Chapter 9, France Meslé evaluates the accuracy of reported causes of death for old people using findings of previous studies which compared death certificates with medical records or autopsy results, focusing specifically on "senility and other ill-defined conditions." Then she analyses the contribution of mutiple causes using data from the United States and France. She also examines the underlying causes of death in France since 1925 and tries to identify the main patterns and trends in oldest-old mortality during the twentieth century. More people will die at higher ages. Therefore it is important to improve our understanding of the pathological process that leads to death among the oldest-old. For that we need to improve the quality and the comparability of their death statistics through a set of common rules, suitable to the main features of oldest-old causes of death pattern.

In the next chapter (Chapter 10), Shiro Horiuchi compares the cause-of-death distribution between the oldest-old (85+) and the younger-old (65–84) in the United States of America. The author shows that the diseases and injuries of old ages do not constitute a homogeneous group. Causes of death that are more prevalent among the oldest-old (heart failure, pneumonia, influenza, etc.) seem to be strongly associated with senescent processes that could increase general vulnerability to multiple pathologies. Causes of death that are more prevalent among the younger-old include malignant neoplasm, acute myocardial infarction (particularly for males), haemorrhagic stroke, chronic liver disease and cirrhosis, diabetes mellitus, and multiple sclerosis. These diseases tend to develop selectively and prematurely in some high-risk individuals at middle ages and younger old ages. This chapter helps us better understanding the relations between senescent processes and disease development.

Chapter 11 by Kaare Christensen and Anne Maria Herskind explores the question of the heritability of longevity. They provide formal definitions and describe design options to obtain heritability estimates, such as traditional family studies, adoption studies or twin studies, noting the limitations of this concept of heritability in being time- and population-specific and sensitive to changes in the overall and the environmental variances as well as to violations of underlying assumptions. Despite these limitations, heritability estimates can usefully outline the potential for identifying specific genetic or environmental factors of importance affecting longevity in a population. The authors summarize estimates of the heritability of various measures of human life duration such as lifespan, early and late death, and age-specific susceptibility to death, i.e. frailty. The current evidence, based primarily on Nordic contemporary populations, suggests that approximately a quarter of the variation in adult lifespan can be attributed to genetic factors. Frailty, as the age-specific

susceptibility to death, seems to have a higher heritability. These results suggest that the individual inherits a susceptibility to death rather than a fixed lifespan.

In Chapter 12, Douglas Ewbank focuses on the APOE genes. Firstly, he provides a brief summary of the literature on the APOE genes as a risk factor for chronic disease and mortality. Secondly, he outlines a demographic model of the effects of unobserved heterogeneity on relative risks of death. The model is applied to data on changes in APOE gene frequencies by age and prospective studies of mortality by genotype. Lastly, the author discusses implications of the estimates of unobserved heterogeneity for the age pattern of mortality, mortality trends, and the degree to which centenarians are different from others. This chapter underlines the importance of obtaining data for small age groups.

CHAPTER 9. CAUSES OF DEATH AMONG THE OLDEST-OLD: VALIDITY AND COMPARABILITY

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Studies of the causes of death among the oldest-old are uncommon. And yet declining mortality means that the number of deaths at these ages is increasing all the time. Just after the Second World War, 36% of deaths in France occurred after age 75 and only 9% at over 85 years. In 1996, 56% of deaths occurred at over 75 years, and of these 33% were after age 85. Nearly half (46%) of all French female deaths occur at age 85+. Many of the readily available mortality statistics do not distinguish causes of death beyond age 85. The WHO database containing the cause of death series for all the countries for which statistics are available, combines all deaths at over 85 in a single age group (85 and over). Several reasons exist for this manifest indifference to a knowledge of causes of death among the oldest-old. One is that beyond a certain age death is seen as so inevitable that even health professionals do not perceive identification of its exact cause as a priority. Yet the highly favourable trend in mortality at advanced ages since the 1970s is probably due in part to changing attitudes among the medical profession towards these old people. The recognition that a person over 70 could suffer from known and treatable pathologies was in fact the prelude to a reduction in mortality at these ages (Meslé and Vallin 1998).

A further point is that many of those familiar with the pathologies of the oldest-old are sceptical about the reliability of the data. The cause of death often appears hard to identify at advanced ages, notably because it is not always possible to distinguish which among several coexisting conditions actually led to death. The selection of the underlying cause of death, on which most cause of death statistics are based, is thus of limited value in the case of very old people since a large part of the pathological process may thus be left out of the analysis. A more complete clinical picture can be built up by considering all the conditions recorded at the time of death through an analysis of multiple cause of death statistics. However, such data is seldom available and, even when it is, the analysis runs up against numerous methodological problems (Désesquelles and Meslé 2000, 2005).

In the first part of this study we attempt to evaluate the accuracy of cause of death reporting for old people using studies which compare the information recorded on death certificates with the content of medical records or autopsy results, and then focus more specifically on the contribution to oldest-old mortality of senility and of other ill-defined conditions in general. The second part takes the form of an analysis of multiple causes of death based

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on two examples, the United States and France. Lastly, in the third part, again using the example of France for which data since 1925 are available, we return to an analysis by underlying cause of death and try to identify the main patterns and trends in oldest-old mortality during the twentieth century.

I. Quality of Cause of Death Reporting

The accuracy of the cause of death reported by the medical examiner on the death certificate can be evaluated and compared between countries using two types of information—data from any autopsy that has been performed, and the relative importance of ill-defined causes.

A. Autopsies and Cause of Death Validation

The percentage of deaths for which autopsies are performed varies considerably between different countries and different ages (WHO 1998). Among the countries which supply the WHO with data on their autopsy practice, the percentage ranged in 1996 from, 4% in Japan to 49% in Hungary. However, autopsies are performed primarily for child deaths, and for violent deaths which are proportionally more numerous at younger ages. In the United states, for instance, only 5% of deaths occurring after age 65 resulted in an autopsy, as against 45% of deaths before age 15. This fall in the frequency of autopsies with rising age is observed in all the countries for which a breakdown by age group is available. For Denmark, where this is the most detailed, the percentage of deaths subject to autopsy fell from 65% at under one year to 17% at age 75 and over.

It would be premature to conclude from this data on autopsy practice alone that accuracy about cause of death declines with age. First, the higher proportion of autopsies carried out on young adults reflects primarily the structure of mortality by cause at these ages, which is dominated by violent deaths for which an autopsy is often a legal requirement. Second, the fact that an autopsy is performed is no guarantee that its findings will actually be included in the cause of death certification. In practice, these results are seldom known at the time medical certification is carried out, and there are few countries where they are communicated to the coding services for a possible correction of the diagnosis.

In contrast to this very crude data on the percentages of autopsied deaths, a number of studies have focused in detail on cause of death validation. Publications on the subject up to 1980 are covered in two English and French literature reviews published in the early 1980s (Gittelsohn and Royston 1982; Meslé and Vallin 1983). In what follows, attention is focused on subsequently published research. Drawing general lessons from these various studies is not straightforward. Most are concerned with particular groups in the population or with specific pathologies. Furthermore, differences in the study protocols are an obstacle to comparability of the results. Finally, it is unusual for the results to be analysed by age at death. A number of these studies are listed in the references.

However, the objective in this paper is not to provide a comprehensive review of the existing research. Attention will be limited here to studies that focus specifically on old people or that contain results by age.

When the age is specified, the authors usually report a decline in diagnostic accuracy with increasing age. For example, in a study comparing the reported cause of death with the hospital diagnosis, Alan Gittelsohn and John Senning (1979) found an exact match for 73% of deaths under age 60, but for only 69% for deaths at over 80 years.

An evaluation of Norwegian cause of death statistics carried out at the end of the 1970s (Glattre and Blix 1980) similarly found a poorer quality match between the reported cause of death and the medical diagnosis as can be established from other sources (cancer registry, hospital records, autopsy results, and the like). A mistake or inaccuracy in the cause of death reporting is observed in 6% of cases at 50–69 years, 8% at 70–79 years and 9.5% at 80 years and over.

Yutaka and Hasuo *et al.* (1989) compared the medical conditions reported on the death certificate with the autopsy results. The frequency of mismatches was again found to rise with age, notably for heart disease. In the same type of study conducted in Italy (Rossi *et al.* 1991), the quality of cause of death reporting appears to deteriorate appreciably as age increases (the match falls from 67% of cases at under age 60 to 57% at 61–80 years and to 50% for over 80 years). Unfortunately this study concerned too few cases (110 in total) for the result to be significant.

Comparing death certificates and medical records of cancer patients, George Myers and Kenneth Manton (1983) also show that the mismatch usually increases among the oldest patients. This is especially the case for cancers of the upper digestive and respiratory tract, for which the match at 60–74 years is 89% but only 69% at age 75 and over. Similarly, the proportion falls from 87% to 80% for prostate cancer and from 86% to 80% for lung cancer. Conversely, the diagnosis of some cancers appears to improve with increasing age. This is the case for stomach cancer, for which the match rises from 59% to 85% between ages 60–74 and age 75 and over, and to a lesser degree for intestinal cancer (from 78 to 81%).

The authors of a study on the quality of the reporting of breast cancer as cause of death in Sweden also found an increasing mismatch with age (Garne *et al*. 1996). Two sources, death certificates and the cancer register, were cross-tabulated for this study. As the authors correctly point out, however, the mismatch between these sources does not necessarily mean that one or the other is of inferior quality. An increase in this mismatch with age may simply reflect the coexistence of more numerous pathologies among elderly people which can lead to death independently of the breast cancer that has also been diagnosed.

Unfortunately, most of these studies do not cross-tabulate cause of death with age. The Norwegian study is the only one to publish such a table covering all causes of death (Glattre and Blix 1980). The two most important causes of death among old people, cardiovascular disease and cancer, are those for which the mismatch is smallest over age 80, at respectively 3.8% and 6.1%. For cardiovascular disease, a surprising decrease in the proportion of

mismatched cases with age is even observed, from 11.6% at 50–69 years to 7.1% at 70–79 years and to 3.8% at 80 years and over. Conversely, the quality of reporting of violent deaths deteriorates dramatically with age (from 8.1% of incorrect results at 50–69 years to 53% at over 80 years). Additional information with which to explain these large discrepancies is not available, though one possibility is that they originate in different selection criteria for the underlying cause, particularly in the case of accidental falls.

In sum, while it is true that most studies suggest a decline in the accuracy of cause of death reporting with age, this decline is usually not very large. Furthermore, it seems to vary with the cause of death and is less marked for the most important causes (cancers and cardiovascular disease). The loss of accuracy is probably due in part to the greater difficulty in identifying the underlying cause of death in the more complicated clinical picture often characteristic of old age. In this perspective, an analysis which considered all the illnesses and conditions reported on the death certificate could contribute to improved identification of the pathologies involved. We will return to this point in the second part of this paper.

B. Frequency of Ill-Defined Causes of Death

If the quality of cause of death reporting deteriorates with age, we could expect to observe an increase in the proportion of deaths whose cause cannot be clearly established. This hypothesis can be tested by examining the change with age of the percentage of deaths from ill-defined and unspecified causes, grouped in one chapter of the International Classification of Diseases (Chapter XVI, Symptoms, Signs and Ill-Defined Conditions, of ICD-9, or Chapter XVII, Symptoms, Signs and Abnormal Results of Clinical and Laboratory Findings, not Elsewhere Classified, of ICD-10). The loss of accuracy could also modify the distribution of deaths within the groups of specific causes, by increasing the proportion assigned to the less precisely defined items. We will examine this possibility for the two main groups of causes that are preponderant at advanced ages, namely cardiovascular disease and cancer.

1. Deaths from Ill-Defined and Unspecified Causes

The ninth and tenth revisions of the international classification both contain a whole chapter given over to ill-defined and unspecified causes. One of the items in this chapter is *senility*, considered to be an ill-defined cause. For the countries whose statistics were available in 1996, we have calculated the percentage of deaths assigned to this chapter (XVI or XVIII depending on the revision used) excluding senility, for which the figures are given separately (Table 1).

The proportion of deaths attributed to unspecified or ill-defined causes varies greatly between the countries considered, ranging from nearly 9% in Denmark to below 0.1% in Hungary. In nearly every country this proportion is particularly high at young ages, probably because of the poor quality of cause of death reporting for new-born babies. Figure 1 illustrates this diversity using the example of the four countries with the highest proportions.

Table 1. Proportions (%) of deaths from ill-defined and unspecified causes and deaths from senility in 1996 in some industrialised countries.

Ill-defined and unspecified causes (except senility)						Senility			
Country	**All ages**	**0–14**	**15–59**	**60–74**	**75+**	**Country**	**All ages**	**60–74**	**75+**
Denmark	8.92	5.35	9.41	8.27	9.16	Ukraine	5.44	0.40	14.20
Portugal	7.36	11.36	12.35	7.85	5.63	Poland	4.78	0.49	10.83
Greece	6.43	1.39	1.98	4.46	8.31	Portugal	4.48	0.48	7.83
France	4.31	15.87	6.12	3.29	4.08	Latvia	4.32	0.45	10.56
Poland	4.01	3.26	8.69	3.70	1.95	Estonia	3.71	0.11	9.04
Luxembourg	3.33	18.92	2.95	2.89	3.39	Russia	3.19	0.28	9.49
Netherlands	3.24	5.46	6.15	3.66	2.37	Bulgaria	2.42	0.00	5.46
Slovenia	2.17	1.92	4.70	1.82	1.36	Japan	2.33	0.10	4.15
Bulgaria	1.90	1.14	2.16	1.74	1.97	Denmark	1.84	0.12	3.09
Germany	1.83	14.66	4.28	1.90	1.05	France	1.79	0.16	2.91
Russia	1.26	2.81	2.46	0.78	0.50	Greece	1.65	0.06	2.74
United States	1.02	10.14	1.66	0.62	0.68	United Kingdom	1.53	0.03	2.51
Estonia	0.95	0.78	1.95	0.88	0.41	Sweden	1.20	0.02	1.75
Latvia	0.84	2.99	1.59	0.82	0.29	Pays-Bas	1.19	0.02	2.01
Sweden	0.59	7.13	1.33	0.60	0.42	Luxembourg	0.86	0.00	1.56
Ukraine	0.45	2.49	0.97	0.28	0.14	Germany	0.76	0.05	1.28
Japan	0.43	7.44	0.66	0.31	0.32	Slovenia	0.71	0.03	1.50
Lithuania	0.40	2.17	0.84	0.31	0.10	Austria	0.65	0.10	1.06
Czech Rep.	0.33	1.66	0.54	0.34	0.22	Lithuania	0.27	0.00	0.67
Finland	0.28	4.44	1.03	0.20	0.05	Czech Rep.	0.18	0.02	0.37
United Kingdom	0.24	8.28	0.61	0.11	0.10	United States	0.11	0.02	0.20
Austria	0.15	7.79	0.16	0.08	0.06	Finland	0.10	0.01	0.17
Hungary	0.06	2.29	0.06	0.03	0.02	Hungary	0.03	0.00	0.07

Sources: Author's figures, calculated from WHO data.

Of the four countries shown in Figure 1, Greece is the only one where the proportion of deaths from unspecified or ill-defined causes rises steadily with age. In Portugal, by contrast, this proportion is at its lowest after age 85. In France as in Denmark, the proportion of deaths attributed to these indeterminate causes is practically stable between ages 60 and 80. In both countries, however, an increase is observed at age 85 and over. So on the basis of deaths attributed to unspecified and ill-defined causes, there is certainly no evidence for a dramatic loss of accuracy in cause of death diagnosis at the highest ages. However, it is likely that the growth in inaccuracy has other explanations.

A first point to note is that the change in the proportion of deaths attributed to senility is indicative of a loss of accuracy in cause of death reporting. Once again the variations between countries are very large, ranging from 5.4% in Ukraine to 0.03% in Hungary

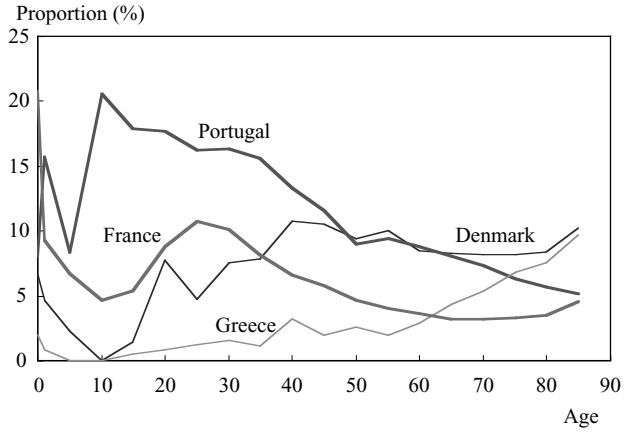


Figure 1. Percentage distribution by age of deaths from unspecified or ill-defined causes in four developed countries in 1996.

(Table 1). Calculating this percentage for all deaths is largely meaningless since the diagnosis of senility is hardly ever reported before age 60. It remains very rare between 60 and 75, concerning fewer than 0.5% of deaths in this age range. The dramatic increase occurs in some countries after age 75—in excess of 14% in Ukraine and 10% in Poland and Latvia, for instance. Predictably, the proportion of deaths attributed to senility rises sharply with age after 70 years (Figure 2); and this increase is observed in all the countries under review. Although diagnostic inaccuracy increases everywhere, the proportion of deaths affected by this inaccuracy still varies greatly between countries—thus at over 85 years it exceeds 22% in Ukraine but barely reaches 0.1% in Hungary. However, the relationship between

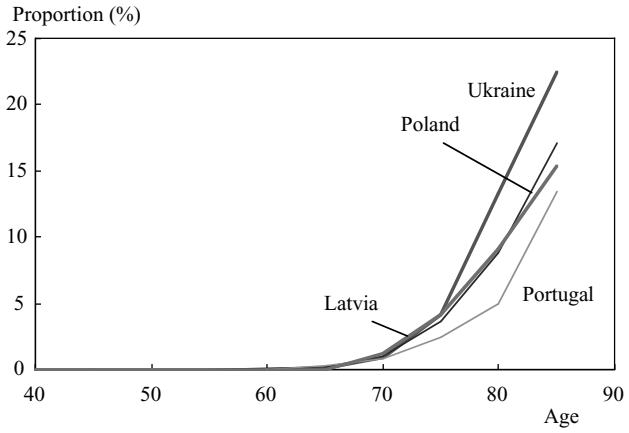


Figure 2. Percentage distribution by age of deaths from senility in four developed countries in 1996.

accuracy of statistics and proportion of deaths from senility is more complex than it appears at first sight. On this point the example of the countries of the former Soviet Union is particularly instructive. In 1996, these were among the countries where the proportion of deaths attributed to senility was the highest (Table 1). This had not always been the case. Indeed, on the contrary, prior to 1988, this cause was seldom reported. In Ukraine, for example, in 1987, the proportion at age 85 and over was only 0.24%. From 1989, however, new guidelines issued by the Ministry of Health recommended that any death after age 80 be registered as due to senility unless the medical records or autopsy report allowed a precise cause of death to be diagnosed or if the death appeared to have had violent causes (Meslé *et al*. 1996). The number of deaths at high ages attributed to senility promptly rose sharply; while that of deaths due to other causes, and indeterminate cardiovascular causes in particular, declined. Are we to conclude in this case that the accuracy of cause of death reporting has declined? Probably not. Rather, what has happened is a transfer to senility of some of the imprecise causes. Indeed, the decision could be seen as a first step by the Soviet health authorities to avoid the systematic use of catch-all categories, notably in the field of cardiovascular disease.

It is a fact that in addition to the items clearly intended for unspecified or ill-defined causes of death and that are grouped in a particular chapter of the ICD, each chapter that is given over to more precise causes also contains a certain number of these catch-all items whose relative importance also varies with age.

2. Vaguely Defined Items in Other Chapters

Each chapter of the ICD contains a number of items that are allocated to vaguely defined and indeterminate conditions. Mention can be made, for example, of item 136.9 in ICD-9, "other and unspecified infectious and parasitic diseases," in Chapter I, Infectious and Parasitic Diseases, or, from the same revision, item 519.9, "other diseases of respiratory system, unspecified," in Chapter VIII given over to diseases of the respiratory system. As age increases, do these indeterminate items also account for a growing proportion of the total deaths classified in the corresponding chapter? To facilitate observation of the variation with age in the relative importance of certain imprecise items, attention will be limited here to two large groups of causes, heart disease and cancers.

Unfortunately, the necessary information is not available for all the countries, or at least not in the WHO database. For the countries still using ICD-9, deaths are redistributed using an intermediate list, "the basic tabulation list," which does not allow us to isolate the three-digit items that are relevant to the present analysis. By contrast, for the countries that have already adopted the Tenth Revision, the WHO database supplies the maximum available detail. Consequently it is to these countries that we have had to limit attention in this initial analysis. In ICD-10, heart diseases are classified in the items I00 to I52. Items I50 and I51 regroup the especially vague causes of death: heart failure for item I50, complications and ill-defined descriptions of heart disease for item I51. Figure 3 illustrates the distribution by age of the deaths attributed to these two items as a proportion of total heart disease, for the seven countries using ICD-10 in 1996. Although this proportion also varies considerably between countries, in the majority of cases an increase with age is clearly discernible. Thus,

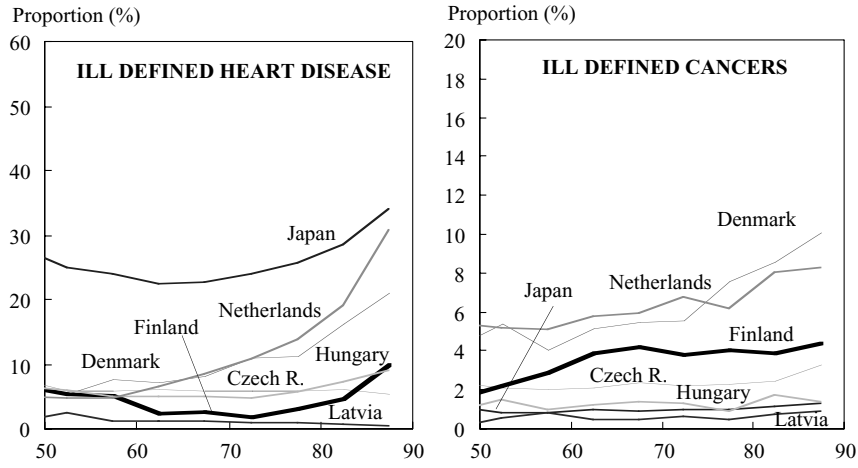


Figure 3. Distribution of ill-defined heart disease as a proportion of all heart disease, and of ill-defined cancers as a proportion of all cancers, in seven countries in 1996.

in Japan, which has the highest proportion at all ages, it rises from 22% at 65–69 years to 34% at over 85 years. The increase is still more spectacular in Denmark where between the same ages it rises from 8% to 21% and even more in the Netherlands (from 8 to 30%). However, the pattern is not universal: in Latvia and the Czech Republic the proportion of deaths assigned to these vaguely defined items appears to be independent of age.

The loss of accuracy with age is not quite so pronounced for cancers. A small increase in deaths attributed to item C80, "malignant neoplasm without specification of site," as a proportion of total cancer mortality, is observed in most of the countries considered. In Denmark and the Netherlands, however, this proportion rises strongly with age, doubling between 65–69 years and 85 years and over. At the higher ages, ill-defined cancers account for around 10% of cancer-related-deaths in these countries. Thus it would appear that this group of causes is less affected by imprecision than is heart disease, where the vaguely defined items account for up to 30% of deaths. The proportion is even larger when it can be calculated for ages over 85. In the case of France, for which detailed information is available up to age 100 (Figure 4), the items corresponding to ill-defined heart disease (item 428, "*heart failure*," and 429, "*ill-defined descriptions and complications of heart disease*," of ICD-9) are responsible for a considerable proportion of cardiac mortality above 85 years, even exceeding 50% at 100 years. As was seen in the other countries, the increase in diagnostic uncertainty with age is on a much smaller scale for cancers.

The question of cause of death validity concerns these two groups of causes in different ways. In the case of cancer, the problem is likely to be one of uncertainty in the cancer diagnosis. The pathology involved is correctly identified as a malignant tumour but this may prove harder to localize or is more likely to be considered multiple or generalized at advanced ages. In the case of heart disease, the increase in the proportion of deaths attributed to vaguely defined items, heart failure in particular, is evidence of a less effective

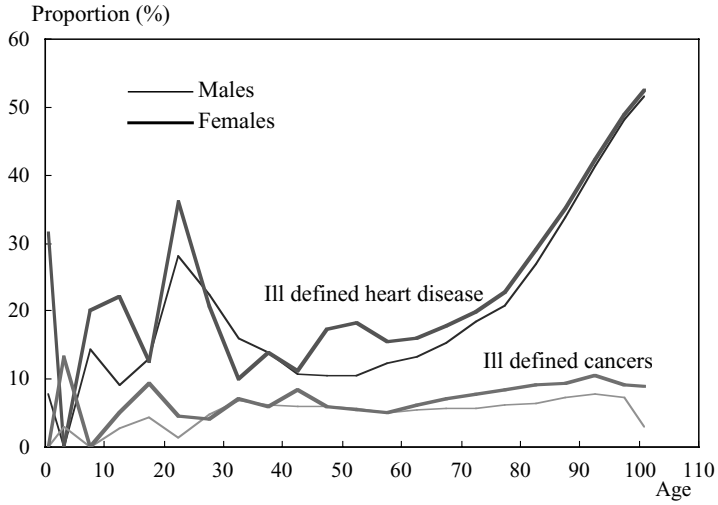


Figure 4. Distribution of ill-defined heart disease as a proportion of all heart disease, and of ill-defined cancers as a proportion of all cancers, by sex, France, 1996.

identification of the pathology in question, but doubtless also of a tendency to concentrate on the direct cause of death without seeking to identify the initial cause of the process. Improved diagnosis could well lead to a proportion of this ill-defined heart disease being redistributed to the chapter on cardiovascular disease, though probably also to some non-cardiac causes of death. At these very advanced ages, the pathological process sometimes appears too complex to the certifying doctor who thus reports merely the condition which finally leads to death; or the coder, not knowing which cause to choose, prefers to attribute the death to an indeterminate cardiovascular disease. In this case analysis could be clarified by an examination of the multiple causes of death.

II. Analysis of Multiple Causes of Death

Data on multiple causes of death remains extremely fragmented and is seldom available in published form. The analyses which have been conducted are usually of an ad hoc nature, with researchers aiming to describe the combination of conditions specific to a particular pathology rather than produce a general survey of mortality. Can the inclusion of these multiple causes improve the quality of cause of death statistics, for the oldest-old in particular? In what follows we use data for France and the United States to show that such an analysis encounters methodological problems which make it hard to interpret time-trends and international differences.

A. Variations in the Reporting of Multiple Causes by Age

Two sets of data are available for the study of multiple causes. For France, INSERM supplied us with computerized records for the period 1979–1996 that list for each death

the underlying cause, the direct cause and two associated causes. A maximum of four causes is thus available for each death. When more than four causes were recorded on the death certificate, the INSERM coders made a selection and retained only four. For the United States, on the other hand, we were able to use a CD-ROM prepared by the NCHS, which indicates for all deaths occurring in 1994 the full information recorded on the death certificate. This data allows up to 20 causes to be identified for each death. On the other hand, no information is given about the hierarchy of causes.

In both countries, and for all ages, deaths with two reported causes are the most frequent, representing 45% of total deaths in France and 29% in the United States. But the similarity between the two countries goes no further. In France, this two-cause profile is by far the most important, while deaths with just one reported cause account for only 28%, those with three causes for 20% and those with four causes for 7%. In the United States, on the other hand, a much more balanced distribution between the different profiles is observed (1 cause: 23%, 3 causes: 24%, and 4 or more causes: 24%). This reflects a major difference in statistical practice as regards multiple causes. The most common procedure in France is to record a direct cause in addition to the underlying cause, and that is all. It is rather unusual for the death certificate to indicate the associated causes, and in any case a maximum of two are recorded by INSERM. In the United States, by contrast, the recording of all the information contained in the death certificate and probably also a fuller completion of the certificate by medical doctors, results in the transmission of much fuller information.

The same contrast is observed in the age distribution of these different profiles (Figure 5). As age increases, so does the complexity of the pathological processes. Consequently we would expect the proportion of deaths for which more than one cause is reported to increase with age. This is indeed what is observed for the United States, where the proportion of deaths attributed to 3 or 4 causes increases substantially after age 60 up to over 85 years. In France, this proportion also increases at advanced ages up to around 80 years, but beyond this age it starts to decrease. More importantly, this relative increase in deaths attributed to three or four causes is very small compared with the very large decrease in deaths with two causes. After age 60, the proportion of these deaths declines sharply, from over 50% to under 35%; while that of deaths with a single cause reported increases by an identical proportion. This is probably an indication that the distinction between underlying and direct cause is gradually abandoned at higher ages.

This first step in comparing multiple cause statistics for France and the United States clearly shows how the very different conceptions on which these are based can make comparisons between them difficult. These conceptions can also change over time within the same country, thereby creating serious difficulties for a temporal comparison of the statistics.

B. Comparability Over Time of Multiple Cause of Death Statistics

For France a database going back to 1979 is available. This allows us to study the changes in the age distribution of deaths according to whether one or several causes have been attributed to them. As was seen above, the distinction is unclear in France between the direct cause, which is quite often recorded in addition to the underlying cause though

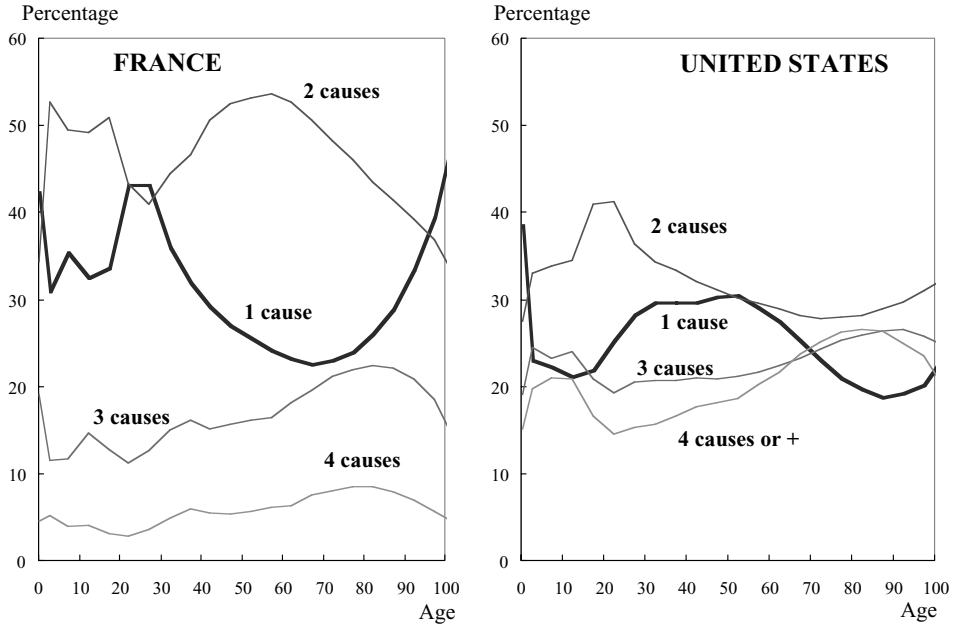


Figure 5. Variation in deaths by age and number of causes reported. United States, 1994 and France, 1996.

mainly at adult ages, and the associated causes, which are more frequently given as age increases. We have judged it useful to limit the present discussion to the associated causes and to study their changing distribution by age between 1979 and 1996 (Figure 6).

Restricting attention to the associated causes alone, in 1996, the pattern for France is closer to that for the United States, with the proportion of associated causes clearly increasing with age up to 85 years. Beyond this age, however, the proportion begins to fall. Strangely, by this measure, the quality of the statistics appears to have deteriorated between 1979 and 1996. In 1979, the proportion of deaths for which at least one associated cause was recorded increased up to age 95, while in 1996 the curve turned downwards from age 85. Plotting the same curve for the intermediate years reveals that its form changed as of 1983. This was in fact when INSERM modified its coding procedures and stopped encoding senility as an associated cause even when it was recorded on the medical death certificate. When 'senility' as an associated cause is excluded from the 1979 statistics (continuous thin grey line in Figure 6), the proportion of deaths reported with associated causes quickly stops rising with age, the downturn occurring at age 80, and it does seem that over time and at each age, there is an increase in the relative number of deaths for which at least one associated cause is reported. In this respect, then, the quality of the statistics has improved. On the other hand, this finding well illustrates the need to be extremely wary when studying time trends in multiple cause mortality. Such change owes much more to changes in coding practices than to genuine changes in pathologies.

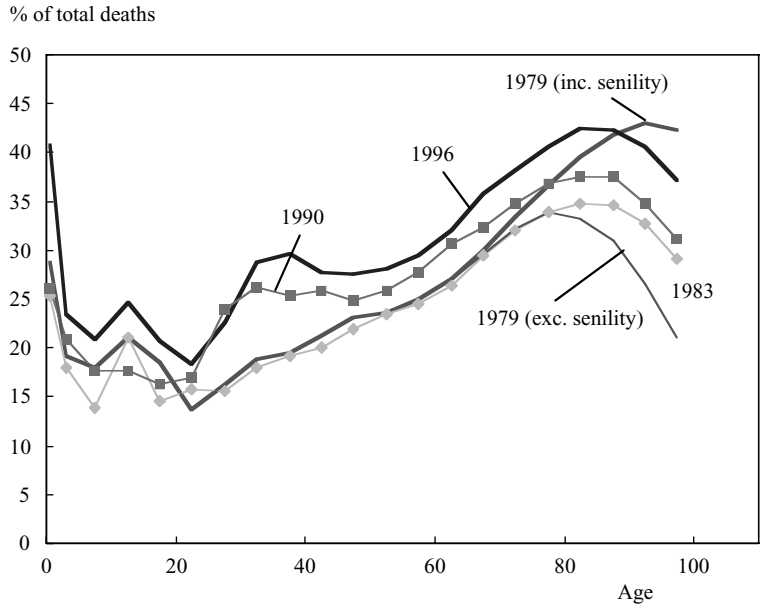


Figure 6. Change in the age distribution of associated causes of death in France, 1979–1996.
Source: Désesquelles and Meslé, 2000.

C. A 'SNAPSHOT' OF MULTIPLE CAUSE MORTALITY IN FRANCE AND THE UNITED STATES

Bearing all these qualifications in mind, and without attempting any direct comparisons, let us try to trace the broad outline of oldest-old mortality in France and the United States as it can be reconstructed from the multiple causes of death. Multiple correspondence analysis was used to test for the existence of strong interrelationships among certain causes of death.[1] For both France and the United States the causes were grouped into 52 items and the statistical analysis carried out separately for each sex on the individual records for deaths at over 75 years of age.[2] Only causes of death that account for at least 2% of all deaths are employed as active variables. Age is the illustrative variable. The results for the female sex alone are presented here (Figures 7 and 8).

The analysis carried out on the deaths of French women over 75 years of age reveals a clear contrast between cancers, situated in an extremely eccentric position on the first factor plan, and all the other causes of death, in particular diseases of the circulatory

[1] I would like to express special thanks to Bénédicte Garnier and Arnaud Bringé for their valuable help in this first exploratory research. The analysis was conducted using the SPAD software.

[2] The analysis concerned 489 429 male deaths and 690 180 female deaths in the United States, and 131 868 male deaths and 190 461 female deaths in France.

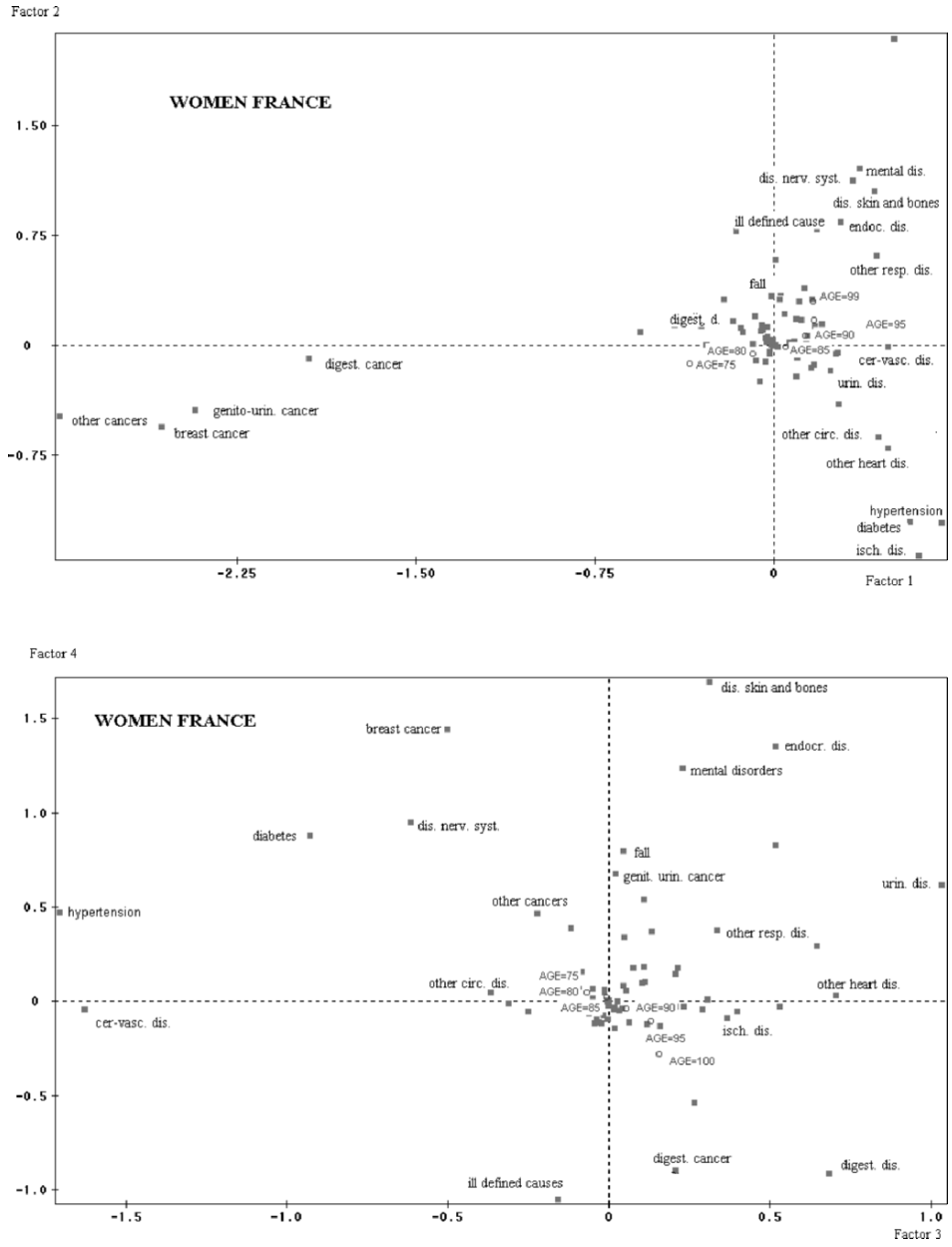
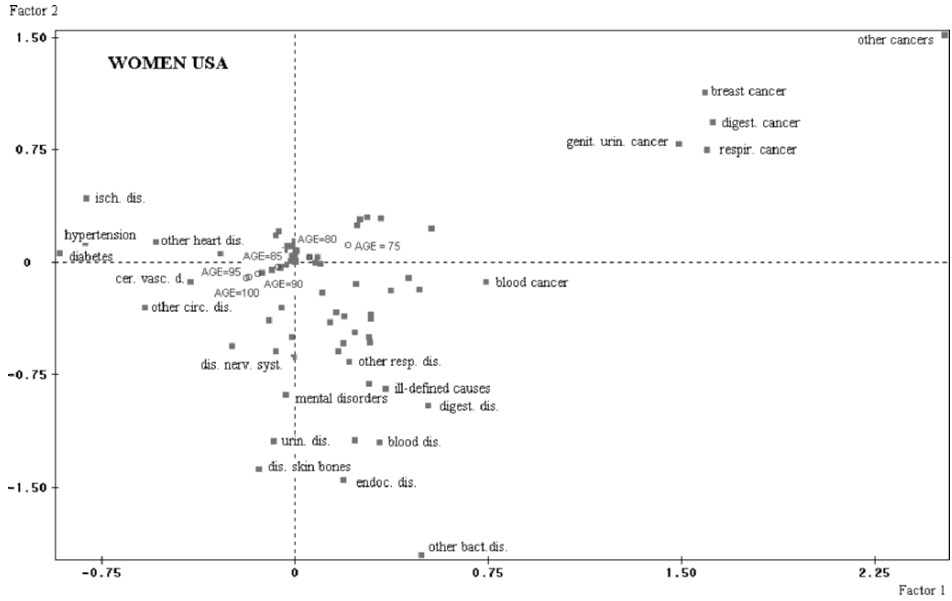


Figure 7. Position of causes of death and age groups on two factor plans. France, women 1996.



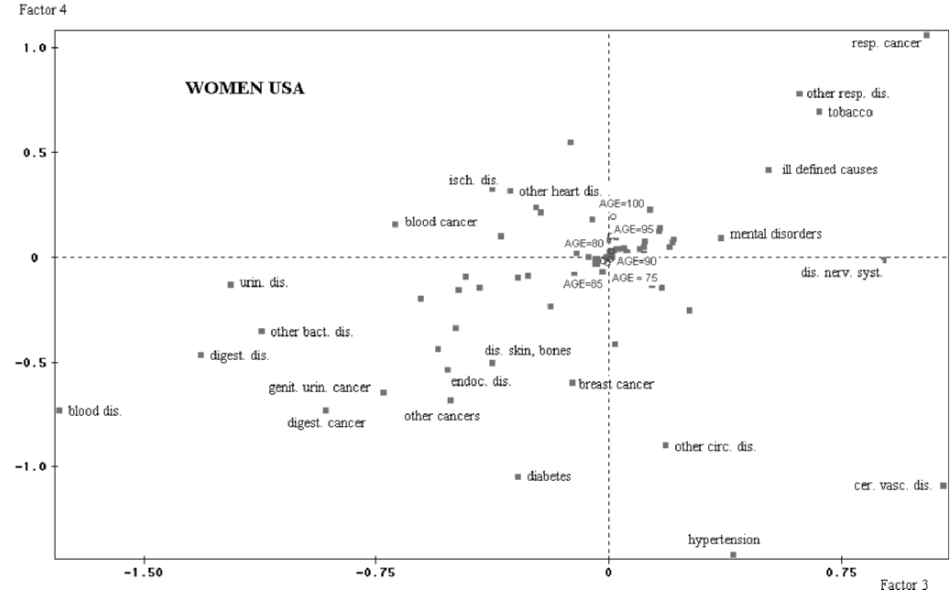


Figure 8. Position of causes of death and age groups on two factor plans. USA, women 1994.

system to which diabetes is strongly associated. The younger ages tend to be situated on the same side as the cancers, while the older ages are on the same side as cardiovascular disease.

The vertical axis in this first factor plan contrasts the diseases of the circulatory system—which as highly lethal causes of death are probably more often recorded as underlying causes—with the causes that less often lead directly to death (mental disorders, diseases of skin and bones, diseases of the nervous system) and which are more likely to be recorded as associated causes.

The second factor plan selected here displays another distribution of the causes of death, revealing in particular a contrast between cerebrovascular disease and hypertension, on one side, and heart disease on the other.

Although the American and French databases differ significantly in their conception, in particular because of the number of multiple causes that can be identified for a single individual (4 in France as against 20 in the United States), the multiple correspondence analysis for the United States gives results very similar to those obtained for France. Particularly noteworthy are the contrasts between malignant neoplasms and cardiovasular disease in the first factor plan, and between vascular diseases (including cerebrovascular) and heart disease in the second factor plan. For the United States a predictable correlation is also revealed between chronic diseases of the respiratory system, malignant tumours of the bronchus and lung, and excessive tobacco consumption.

In summary, multidimensional analysis is valuable for a preliminary exploration of the interrelationships between multiple causes of death. These initial findings show that despite differences in data collection procedures a number of broad trends are observed in both France and the United States. It would clearly be worthwhile extending this analysis to other databases.

III. Another Look at the Primary Cause of Death

Although analysis of mortality by multiple causes can improve our understanding of mortality among the oldest-old, it cannot at present be used to examine temporal variations, due to the lack of comparable time-series data. We propose to end this paper by going back to the primary cause and analysing the mortality evolution at advanced ages using the primary cause of death data for France available at INED (Vallin and Meslé 1988, 1998).

A. The Greater Role of Cardiovascular Diseases at Higher Ages

At all the higher ages, cardiovascular disease is seen to have a preponderant role in the mortality decline after age 70 (Figure 9). The reduction in the mortality associated with this category began in the 1920s and accelerated after the Second World War and again in the middle of the 1980s. These two accelerations have been sharper at the lower ages,

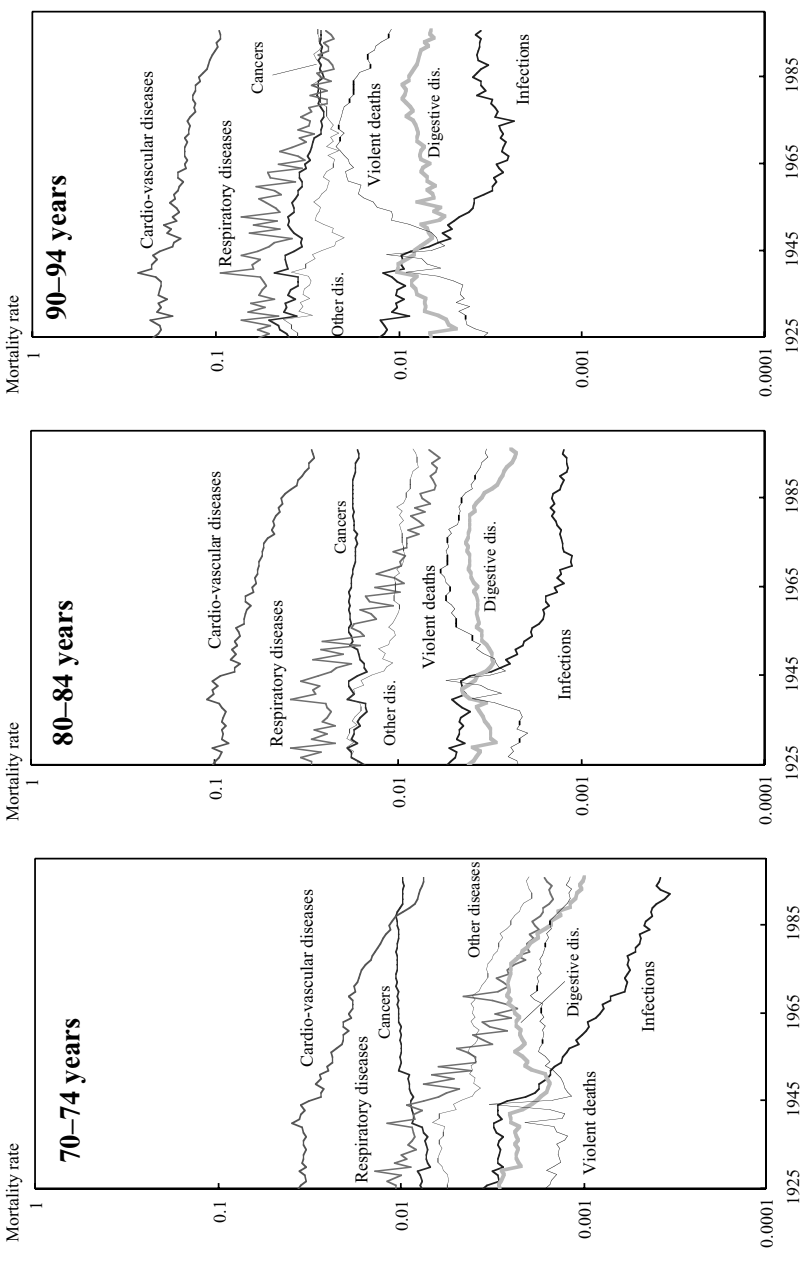


Figure 9. Mortality trends 1925–1996 for seven main categories of causes at 70–74, 80–84 and 90–94 years. France, both sexes.

to the extent that for 70–74 years cardiovascular mortality has actually fallen to second position, below cancer. This is not the case for the other two age groups shown on Figure 9, for which cardiovascular diseases still predominate to a large degree, although the decline is taking them close to the level of cancer at 80–84 years.

The growing importance of cancer mortality at increasingly high ages is the result of a much less favourable trend in this disease. Contrary to what is observed for cardiovascular mortality, this trend is slightly more favourable at the highest ages. It ranges from virtual stagnation at 70–74 years to a steady fall, at least until the start of the 1970s, at 90–94 years. However, this relative difference depending on age must be treated with caution. The proportion of female deaths in total deaths increases with age, so that any changes in female mortality have a growing influence on the mortality trend for both sexes combined. This is relevant given that cancer mortality is known to be evolving more favourably for women than for men. For this reason the trend in cancer mortality needs to be examined separately for each sex. This will be done shortly below.

The third main group of causes of death at advanced ages are diseases of the respiratory system. As was also observed for diseases of the circulatory system, their evolution has been more favourable at 70–74 years than at 80–84 years and especially at 90–94 years. In 1925, regardless of age, they were in second place behind the cardiovascular diseases. Although they have declined greatly at 70–74 years, the reduction is less pronounced at 80–84 years and weaker still at 90–94 years, whereas in 1996 mortality from this cause was still equal to that from cancer.

At much lower levels of mortality, the trend by age for infectious mortality is even more contrasted. Although at 70–74 years the reduction is continuous between 1945 and 1996, it stops in 1965 at 80–84 years and 90–94 years, and for the latter age there is even a slight increase in mortality. This relative failure to make progress against respiratory and infectious diseases at very advanced ages may seem surprising. These diseases frequently occur in the terminal stage of other diseases, and they could therefore be expected to be recorded as direct causes of death. But as was noted earlier, the distinction between underlying cause and direct cause becomes increasingly blurred at advanced ages; and the growing tendency, at least in France, is for the registering doctor to select just one cause. In other words, our improved control over cardiovascular diseases and, to a lesser degree, cancers, has been accompanied by a greater propensity to attribute death to a terminal complication of these diseases.

These less favourable changes are not enough to produce a reversal in a general downward trend caused primarily by the reduction in cardiovascular mortality, reinforced in recent years by the reduction in violent deaths and diseases of the digestive system.

B. Opposite Trends in Cerebrovascular Diseases and Ischemic Heart Disease

While cardiovascular mortality is the principal factor behind the mortality improvements obtained at advanced ages, its individual components contribute to these advances to very different degrees (Figure 10).

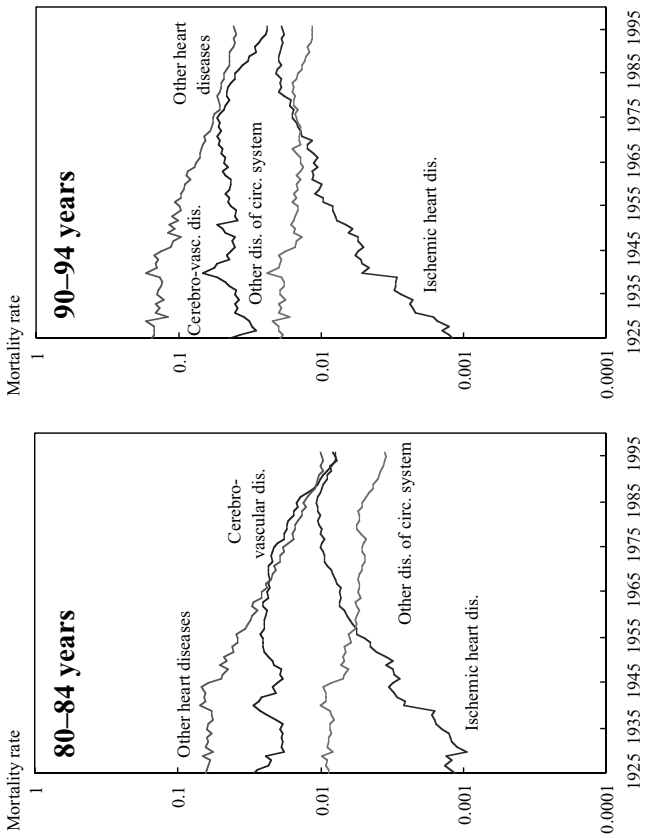


Figure 10. Mortality trends 1925–1996 for the principal diseases of the circulatory system at 70–74, 80–84 and 90–94 years. France, both sexes.

Mortality from other heart diseases and other diseases of the circulatory system has been declining significantly at all ages since the end of the Second World War. These two groups of causes cover disparate pathologies, a large proportion of which, however, are fairly imprecise. In addition to a genuine reduction in some pathologies, this decline is probably due mainly to better diagnosis, notably to the advantage of ischemic heart disease.

Some of the increase in mortality from these conditions (acute myocardial infarction, angina pectoris) from the mid-1920s to the mid-1970s can probably be ascribed to improved diagnostic practices. Nevertheless, the increase in mortality from ischemic heart disease has been very considerable and, as is the case for other diseases, is faster at higher ages. Recent years have seen this increase halted at all ages; but whereas the reversal of the trend at 70–74 years is very clear from the start of the 1980s, the stabilization of the mortality rate at 90–94 years is very recent.

At ages 70–74, cerebrovascular mortality has been on a downward trend throughout the period, while this did not begin until the start of the 1970s for ages 80–84 and at the start of the 1980s for ages 90–94. In more recent years, the acceleration in the decline in cerebrovascular mortality combined with the reversal in trend for ischemic disease mortality are the main factors responsible for the decline in diseases of the circulatory system.

C. The Diversity of Cancers

The fairly steady trend in total cancer mortality masks much more contrasted patterns of change depending on sex and cancer site (Figure 11).

Total male cancer mortality has been on the increase over almost the entire period. The exceptions to this pattern are a stabilization in recent years at ages 80–84 and 90–94, and a slight decline at 70–74 years. This increase is produced by the rise in lung cancer mortality at the younger ages and in prostate cancer mortality at the higher ages. The decline in stomach cancer mortality is not enough to counteract the dramatic increase in these other two cancers. However, it is their stabilization in recent years which has brought the rise in cancer mortality to a halt.

The overall trend in cancer mortality among women is downward regardless of age. For the main sites (stomach, intestine, uterus), mortality has been declining since the 1950s, and the pace of decline is particularly fast for stomach cancer. The slow increase observed for breast cancer is less favourable but is not enough to reverse the trend. Finally, lung cancer mortality, though on the increase, is as yet too low to influence the general trend.

D. Some Specific Diseases

We conclude this brief overview of cause of death mortality patterns among the oldest old by considering a number of specific diseases whose evolution is typical.

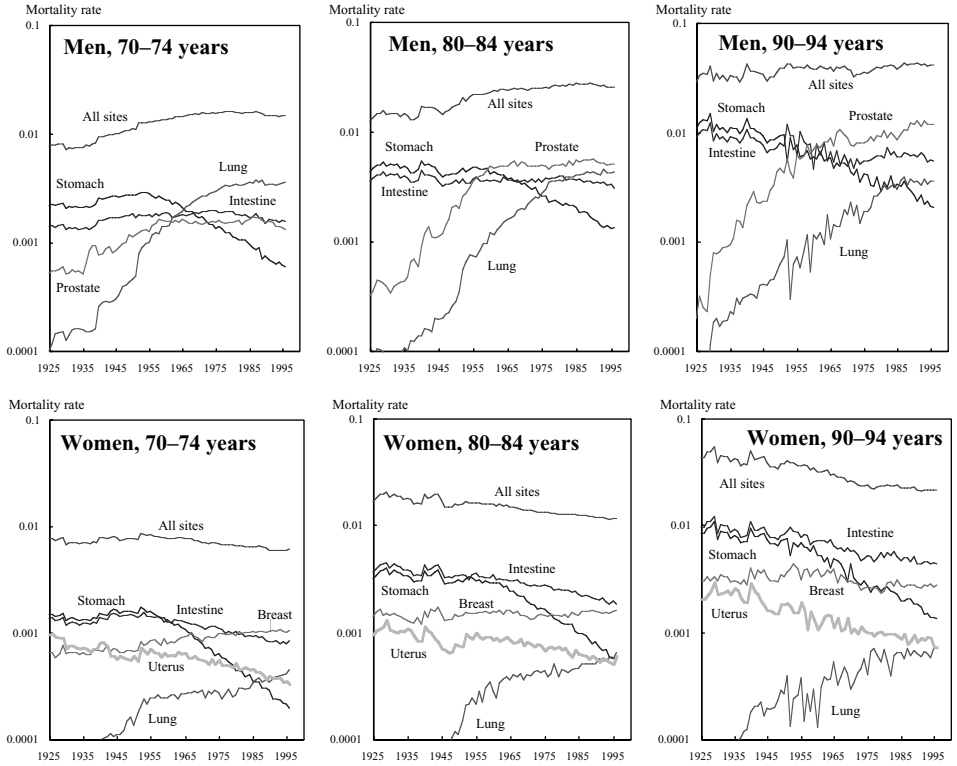


Figure 11. Mortality trends 1925–1996 for the main cancer sites at 70–74, 80–84 and 90–94, by sex. France.

Influenza mortality has changed in a spectacular fashion (Figure 12). Discounting the large fluctuations characteristic of this epidemic disease, mortality is observed to fall steeply from the start of the 1970s, corresponding to the development of the polyvalent vaccine and the free vaccination of elderly people (Vallin and Meslé 1999). In addition to the mortality reduction directly attributable to influenza, bringing this illness under control has helped to curb mortality from the secondary bacterial infections (pneumonia, bronchial-pneumonia, and the like) that commonly accompanied influenza epidemics.

Several phases can be identified in the evolution of liver cirrhosis mortality (Figure 12). This disease directly linked to excessive alcohol consumption is one of the few for which mortality is higher at 70–74 years than at 90–94 years. Following a sharp decline during the war years 1939–1945, due to the shortage of alcohol, liver cirrhosis mortality increased very rapidly in the 1950s and at the start of the 1960s. Only with the adoption of anti-alcohol measures in France at the end of the 1950s did alcohol consumption and, subsequently, liver cirrhosis mortality begin to regress. This decline was greater at younger ages, though not enough so for the level at 70–74 years to fall below those observed at the higher ages.

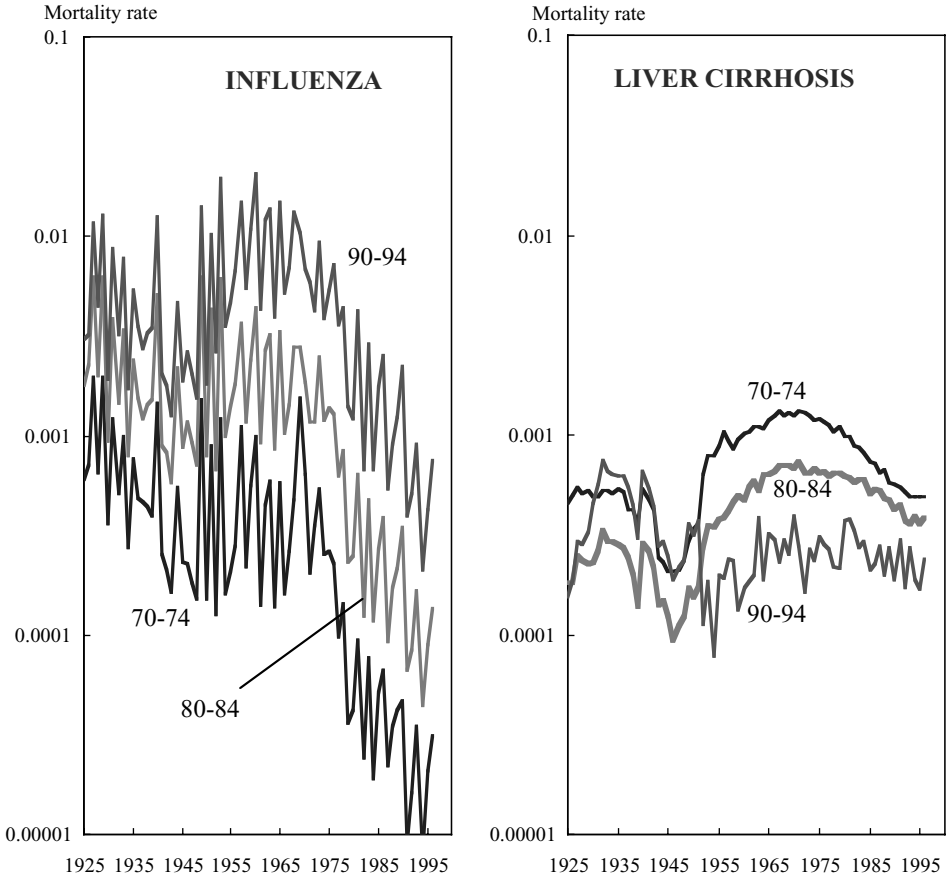


Figure 12. Mortality trends 1925–1996 for influenza and liver cirrhosis at 70–74, 80–84 and 90–94 years. France, both sexes.

A further two diseases have registered less favourable changes (Figure 13). After diminishing up to the end of the 1950s, bronchitis mortality began a sustained increase at the end of the 1960s. This increase, though quite rapidly halted and reversed at 70–74 years, is still continuing at 90–94 years. At the start of the period the majority of bronchitis deaths were in fact caused by acute bronchitis of infectious origin, and it was their reduction which brought about the fall in bronchitis mortality observed until the 1950s. Then, as a consequence of the spread of cigarette smoking, mortality from chronic bronchitis began to rise and contributed increasingly to overall mortality from this cause. It must be hoped that the new downturn in the trend that is clearly apparent at 70–74 years will gradually spread to the higher ages.

Finally, the evolution of suicide mortality presents few contrasts. The level not only varies little with age but has remained reasonably stable through time. Mention can be made,

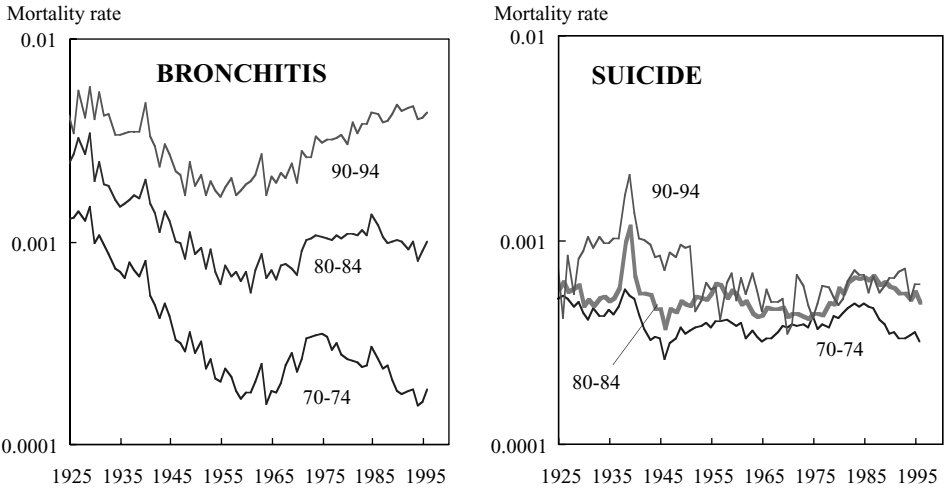


Figure 13. Mortality trends 1925–1996 for bronchitis and suicide at 70–74, 80–84 and 90–94 years. France, both sexes.

however, of the reversal since 1985, particularly at the younger ages, in the upward trend observed at the end of the 1970s. This relative lack of progress suggests that over and above the undeniable improvement in the physical health of the oldest-old, the state of their mental health warrants special attention.

Conclusion

The loss of quality in cause of death statistics at higher ages is indisputable. First, these statistics are often crude, seldom distinguishing between different age groups after age 85. Second, most validation studies have shown that when information on age is available, the accuracy of the diagnosis tends to fall as age increases. It is true that as age increases the growing complexity of the pathological processes that lead to death makes it harder to identify the underlying cause of death.

But this fact should not deter us from attempting an analysis of cause-specific mortality trends among the oldest-old. First, as regards the underlying cause of death, by reconstituting consistent causes of death series based on constant medical definitions it is possible to identify the main trends which inform us about the changing pattern of mortality at advanced ages. In France, for example, the analysis of these trends reveals that while advances are very clear for most causes of death at 70–74 years, the changes are progressively less favourable at the higher ages.

An analysis that took account of multiple causes could contribute to an improved understanding of the pathologies that lead to death among the oldest-old. Comparisons between the results obtained in different spatial and temporal contexts are difficult, however. For

these statistics to be fully comparable, a set of common rules needs to be elaborated governing the selection and classification of multiple causes, similar to those specified by the WHO for selection of the underlying cause of death. Only when this has been done will truly comparative studies become possible. It is towards this end that our efforts must be directed.

References

Désesquelles, A., and Meslé, F. (2000) "*First insight into the patterns and trends of old-age mortality using French multiple cause-of-death statistics.*" Paris, INED, p. 25. (Paper delivered to the Conference Reves 12 *Healthy Life Expectancy, Linking Policy to Science*, Los Angeles, 20–22 March, 2000).

Folsom, A. R., Gomez-Marin, O., Gillum, R. F., Kottke, T. E., Lohman, W., and Jacobs, D. R. (1987) "Out-of-hospital coronary death in an urban population-validation of death certificate diagnosis", *American Journal of Epidemiology*, 125(6):1012–1018.

Garne, J. P., Aspegren, K., and Balldin, G. (1996) "Breast cancer as cause of death", *Acta Oncologica*, 35(6):671–675.

Gittelsohn, A., and Senning, J. (1979) "Studies on the reliability of vital and health records: I. Comparison of cause of death and hospital record diagnoses", *American Journal of Public Health*, 69(7):680–689.

Gittelsohn, A., and Royston, P. N. (1982) *Annotated Bibliography of Cause-of-Death Validation Studies. 1958–1980*. Washington: National Center for Health Statistics, 42p. (Vital and Health Statistics, Series 2, no. 89).

Glattre, E., and Blix, E., (1980) *En vurdering av dodsarkaksstatistikken*. Oslo, Statistik sentralbyra, p. 73.

Hansluwka, H., (1988) "Mortality data in Europe—availability, validity and comparability". In: Charlotte, H., Wilfried, L., Rainer, M. (eds.), *Demographie in der Bundesrepublik Deutschland. Vier Jahrzehnte Statistik, Forschung und Politikberatung*, Boppard am Rhein, Boldt-Verlag, pp. 123–140.

Hasuo, Y., Ueda, K., Kiyohara, Y., Wada, J., Kawano, H., Kato, I., Yanai, T., Fujii, I., Omae, T., and Fujishima, M. (1989) "Accuracy of diagnosis on death certificates for underlying causes of death in a long-term autopsy-based population study in Hisayama, Japan; with special reference to cardiovascular diseases", *Journal of Clinical Epidemiology*, 42(6):577–584.

Höpker, W. W., and Burkhardt, H. U. (1984) Unsinn -und Sinn? Des Todesursachenstatistik, *Deutsche Medizinische Wochenschrift*, 109(34):1269–1274.

Mattsson, B., and Rutqvist, L. E. (1985) "Some aspects on validity of breast cancer, pancreatic cancer and lung cancer registration in Swedish official statistics", *Radiotherapy and Oncology*, 4:63–70.

Meslé, F., Shkolnikov, V., Hertrich, V., and Vallin, J. (1996) *Tendances Récentes de la Mortalité Par Cause en Russie, 1965–1994*. Paris, INED, 140p. +2 diskettes. (Données statistiques no.2).

Meslé, F., and Vallin, J. (1983) *Revue de la Littérature de Langue Française sur la Comparabilité des Classifications Successives des Causes de Décès et sur la Validité de la Déclaration des Causes de Décès*. Paris, INED, 25p. (Report written for the WHO).

Meslé, F., and Vallin, J. (1998) *Évolution de la Mortalité aux Ages Elevés en France Depuis 1950*. Paris, INED, 42p. (Dossiers et recherches no. 68).

Myers, G. C., and Manton, K. (1983) "Accuracy of death certification", In: *Proceedings of the Social Statistics Section, 1983*, American Statistical Association, pp. 321–330.

Office Fédéral de la Statistique. (1984) *Mortalité Cancéreuse: Qualité des Données en Suisse.* Berne: OFS, 67p.

OMS. (1998) *Annuaire de Statistiques Sanitaires Mondiales, 1996*. Genève: Organisation mondiale de la santé.

Rossi, S., Reale, D., and Grandi, E. (1991) "Correlation of clinical diagnosis with autopsy findings", In: Riboli, E., Delendi, M. (eds.), *Autopsy in Epidemiology and Medical Research*. Lyon: IARC, pp. 99–108.

Vallin, J., and Meslé, F. (1988) *Les Causes de Décès en France de 1925 à 1978*. Paris: INED,PUF, 608p. (Travaux et Documents, Cahier 115).

Vallin, J., and Meslé, F., (1998) "Comment suivre l'évolution de la mortalité par cause malgré les discontinuités de la statistique. Le cas de la France de 1925 à 1993". In: Gérard, P. (ed.), *Enjeux des Classification Internationales en Santé*, p. 113–156. Paris: Éditions INSERM, 220p. (Series 'Questions en santé publique').

Vallin, J., and Meslé, F., (1999) *Le Rôle des Vaccinations Dans la Baisse de la Mortalité*. Paris: INED, 16p. (Dossiers et recherches n°74).

CHAPTER 10. CAUSES OF DEATH AMONG THE OLDEST-OLD: AGE-RELATED CHANGES IN THE CAUSE-OF-DEATH DISTRIBUTION

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Introduction

In this chapter, age-related changes in the cause-of-death distribution are investigated. Vital statistics for the Caucasian population of the United States in 1991–1994 are analysed, with focus on differences between the oldest-old (85+) and the younger-old (65–84).

The distribution of deaths by cause reflects various characteristics of the population, including ecological environment, behaviour and life styles, genetic profiles of the population, availability of and accessibility to medical services, and the level of medical technology (Preston 1976; Vallin and Meslé 1988). The cause-of-death structure differs between males and females and varies substantially with age (Horiuchi 1999: Figure 2; National Institute of Population and Social Security Research 1999: Table 5.26).

Age-related changes in the cause-of-death distribution provide valuable information for ageing research for at least two reasons. First, the age variations should reflect physiological and behavioural changes with age. For example, if some organs of old persons tend to deteriorate faster than others, diseases of the organs are likely to be more prevalent causes of death at older ages. Second, age variations in the cause-of-death composition give important clues on individual differences in longevity. Suppose some persons are highly susceptible to particular diseases and they tend to die at younger ages from those diseases. Fewer of them are likely survive to older ages, thereby making those diseases less prevalent causes of death at older ages.

The cause-of-death distribution among the oldest-old is of particular importance for studying relationships between senescence and disease development. Causes of death that are prevalent at very old ages may be particularly strongly related to senescent processes.

The peculiar age pattern of mortality among the oldest-old adds to the importance of their cause-of-death structure. The age-associated increase of total (i.e., all-cause) mortality tends to slow down at very old ages in humans (Horiuchi and Wilmoth 1998; Thatcher, Kannisto, and Vaupel 1998) and a number of other species (Vaupel *et al*. 1998; Horiuchi

J.-M. Robine et al. (eds.), Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population, 215–235

2003). The mortality deceleration suggests that survivors to oldest ages may have genetic, environmental, and behavioural characteristics that are considerably different from those of the rest of the population. Observations of centenarians indicate that they are not the weakest segment of population but healthy people with special endowments (Perls, Silver, and Lauerman 2000). Characteristics of these special persons may be reflected in the cause-of-death profile of the oldest-old.

The age pattern of death rate at adult ages differs among major causes of death (Simms 1946; Kohn 1963; Horiuchi and Wilmoth 1997), suggesting that the cause-of-death structure of the oldest-old may be significantly different from those of the other age groups. Cause-specific death rates that rise with age steeply at ages 30–54 and cause-specific death rates that increase rapidly at ages 65–89 are considerably different, with only a few overlaps (Horiuchi *et al*. 2003).

The cause-of-death distribution among the oldest-old is important for medical economics as well. It has been found that the cost of medical services in the period preceding the death of an old patient tends to decline with age (Lubitz, Beebe, and Baker 1995; Scitovsky 1988, 1994; Temkin-Greener *et al*. 1992). This is partly because very old patients tend to be treated at less expensive hospitals and aggressive high-risk treatments are less likely to be applied to them. But the age-associated cost decline is also attributable to age differentials in the disease pattern (Perls and Wood 1996).

Causes of death reported in death certificates are not fully reliable (e.g., Crombie *et al*. 1995; reviewed in Manton and Stallard 1984: Chapter 2.3). Thus, a number of medical researchers studied autopsy findings and clinical records of old decedents and identified causes of death and other pathological conditions that are widely observed in very old persons. Puxty, Horan, and Fox (1983) reported that pneumonic diseases were the most common cause of death in old patients admitted acutely to hospital. Ishii, Hosoda, and Maeda (1980) listed bronchopneumonia, encephalomalacia (softening of the brain), myocardial infarction, gastric cancer, arteriosclerosis, and myocardial hypertrophy as the most prevalent diseases among the Japanese decedents who were 80 years or older. Klatt and Meyer (1987) examined autopsy and other medical records of 32 centenarians and concluded that atherosclerosis, neoplasia, and bronchopneumonia were common—but diabetes mellitus, obesity, hypertension, and cerebrovascular accident were absent or rare. Bordin *et al*. (1999) compared autopsy results between 114 extremely old decedents (97 years and older) and 151 younger ones (65–74) in Italy and found that extremely old persons tended to die of cardiovascular and respiratory diseases, and in most cases, of acute events.

Weinberg *et al*. (1989) indicated that infectious causes were the leading etiology for deaths in a nursing home. In another institutionalized population, the most common causes of death were bronchopneumonia, congestive heart failure, metastatic carcinoma, pulmonary embolism, myocardial infarction, and cerebrovascular event, in descending order (Gross *et al*., 1988). According to a study of centenarians in France (not based on autopsies), heart failure, respiratory failure, and chronic respiratory infection were among most prevalent diseases in morbid processes leading to 376 deaths (Allard *et al*., 1996). Hadley (1992) reviewed a number of autopsy studies and concluded that causes of death among the

oldest-old were generally characterized by a high proportion of deaths due to cerebrovascular diseases and pneumonia, a low proportion of deaths due to cancers, and a relatively high proportion of deaths from chronic ischemic heart disease in comparison with acute myocardial infarction.

As for identifiability of cause of death, Kohn (1982) reviewed autopsy results of more than 200 decedents at age 85 and over, and reported that a clear manifestation of specific diseases was lacking in at least 30 percent of the cases. He proposed, therefore, "senescence" should be accepted as a cause of death. This argument was not supported by later studies that identified specific causes for most deaths among the extremely aged (Puxty *et al*. 1983; Bordin *et al*, 1999).

Although these clinical and pathological reports provide substantially more detailed and more accurate data on causes of death than death certificates, they are not without limitations. The decedents are often limited to patients of a certain hospital or residents of a certain nursing home and do not necessarily represent a regional or national population. The number of deaths is small, making it difficult to study age trajectories of the cause-of-death distribution, particularly with respect to less prevalent diseases. Thus, in research on causes of death, clinical reports and vital statistics based on death certificates should complement each other. An examination of death certificates of centenarians in Minnesota showed that congestive heart failure, atherosclerosis, neurological/mental conditions, and poorly defined conditions were major reported causes of deaths of centenarians (Gessert, Elliott, and Haller 2002). The present study uses U.S. vital statistics for investigating age-related changes in the distribution of causes of death among old persons in the large national population, with special attention to the oldest-old.

Data

Vital statistics on deaths in the U.S. from 1991 to 1994 are used in this study. Selected information on each death certificate is available on CD-ROMs published by the National Centre for Health Statistics (NCHS) of the USA (1997, 1998). The analysis is limited to White U.S. residents, because the focus of this study is on age variations in the cause-of-death structure in the elderly population, and reported ages among the Black elderly in the U.S. are not highly accurate (Preston *et al*. 1996, 1998). Data in the four calendar years are pooled together, in order to increase the statistical reliability of results for relatively uncommon causes of death.

The four calendar years (1991–1994) fall in the ICD9 period. Causes of death in the period were recorded according to the Ninth Revision of the International Classification of Diseases (ICD9). Although the data set includes multiple cause-of-death information, this study focuses on the "underlying cause of death," which is "(a) the disease or injury which initiated the train of events leading directly to death, or (b) the circumstance of the accident or violence which produced the fatal injury" (World Health Organization 1977:763). Multiple cause-of-death data are complicated and may require development of innovative statistical methodologies, which is beyond the scope of this paper.

It is well known that causes of death reported on death certificates are not highly accurate. A number of studies comparing death certificates and autopsy findings in several countries (including Australia, Germany, Iceland, Italy, Japan, and U.S.A.) have indicated errors in death certificates (Asnaes, Frederiksen, and Fenger 1983; Engel *et al*. 1980; Gloth and Burton 1990; Hasuo *et al*. 1989; Kircher *et al*. 1985; Kiyohara *et al*. 1989; Lee 1989; Maclaine, Macarthur, and Heathcote 1992; McKelvie 1993; Modelmog, Rahlenbeck, and Trichopoulos 1992; Mollo *et al*. 1986; Nielsen, Bjornsson, and Jonasson 1991; Poli *et al*. 1993). The number of deaths for each cause of death in vital statistics should not be automatically accepted at its face value. Nevertheless, if used with caution, cause-of-death statistics are an important source of information on health and mortality. Suppose similar age patterns of mortality are found for certain diseases that have some common pathological, physiological, or epidemiological characteristics. Then the age patterns may be related to the characteristics, possibly providing some clues on interactions between senescent processes and development of those diseases.

Method

For each age–sex category and each selected cause of death, the proportion of all deaths in the age–sex group that are attributable to the cause can be calculated. Age patterns and sex differentials of those proportions are compared among different causes of death. In this study, the proportion is denoted by $d_{ijk} = D_{ijk}/D_{\bullet jk}$, where D_{ijk} is the number of deaths due to the underlying cause i for the age group j and sex category k; and $D_{\bullet jk}$ is the number of all deaths for the age group j and sex category k.

Five-year age intervals from 0–4 to 95–99, and 100+, are used in the analysis of 35 selected cause-of-death categories (Figure 3). Although age variations in the cause-of-death distribution are examined for the entire age range, the focus of this study is on old ages. Hereafter, "old age" indicates 65 years and over, "oldest-old age" 85 years and over, and "younger-old age" 65–84 years.

The 95% confidence interval of the proportion is estimated using the standard procedure of Gaussian-distribution approximation. This approximation should be appropriate for most of the proportions in old age, because the data set is large and the selected causes of death are generally prevalent at old ages. (However, for several proportions computed from very small numbers of deaths, the approximation is not necessarily appropriate, so that confidence interval estimates for the proportions may not be accurate and the lower boundaries of the intervals may even become negative.)

There are a few different statistical approaches to mortality variations by age and cause. Age trajectories of *death rate* were previously compared among various causes of death (Simms 1946; Kohn 1963; Vallin and Meslé 1988: Chapter 10). This type of study includes age patterns of cause-specific life table ageing rate (Horiuchi and Wilmoth 1997, 1998) and calculation of cause-specific Gompertzian slopes (Horiuchi *et al*. 2003). Another type of statistics is the proportional distribution of deaths, which can be obtained in at least two ways: the distribution of deaths *by age for each cause*, as investigated by Vallin and Meslé (1988: Chapter 7), and the distribution of deaths *by cause within each age group*,

as examined in this study. The distribution of deaths by age for each cause and sex is computed as $D_{ijk}/D_{i\bullet k}$, and the distribution of deaths by cause within each age–sex group is computed as $D_{ijk}/D_{\bullet jk}$.

Thus at least three different types of analysis must be distinguished: (a) age trajectories of cause-specific death rates, (b) age-distributions of cause-specific deaths, and (c) age variations in the cause-of-death structure. They are closely interrelated but have different strengths and limitations, thus complementing each other. In (a), it is not always easy to compare age patterns of cause-specific mortality. Death rates for most degenerative diseases rise steeply with age, making their age trajectories appear fairly similar. This problem applies to (b) as well. Age distributions of deaths for many degenerative diseases may look similar, with peaks concentrating in the narrow age range between 70 and 85. In contrast, age trajectories of (c) tend to be clearly distinguishable from each other, because the cause-of-death distribution measures *relative* differences in the prevalence of causes of death, independently of age-related changes in the total mortality and the total number of deaths. In (c), however, if the proportion of deaths from a certain cause declines with age, it is not clear whether the mortality from the cause decreases or increases with age (unless additional information is provided). The decline of the proportion may be due to an age-related decrease of the cause-specific mortality, or its relatively slow increase with age.

Selection of Causes of Death

Two sets of cause-of-death categories, nine broad categories (Figures 1 and 2) and thirty-five more specific categories (Figure 3) are used. Their definitions in terms of ICD9 codes are listed in Tables 1 and 2.

The thirty-five causes are mutually exclusive but not exhaustive. The set of thirty-five categories was developed through a trial-and-error process of combination, division, and elimination. Initially, the 282-category system prepared by NCHS (1998) was used, and

Table 1. ICD9 codes of the broad cause-of-death categories for Figures 1 and 2.

Broad cause-of-death category	ICD9 code
Infectious and parasitic diseases	001–139
Neoplasms	140–239
Heart diseases	390–398, 402, 404–429
Cerebrovascular diseases	430–438
Other diseases of the circulatory system	401, 403, 440–459
Diseases of the respiratory system	460–519
Congenital and perinatal disorders	740–779
Other diseases	240–389, 520–739, 780–799
External Injuries	E800–E999

Table 2. ICD9 codes of causes of death selected for Figure 3.

Cause of death	ICD9 code
septicemia	038
malignant neoplasms	140–208
diabetes mellitus	250
nutritional deficiencies	260–269
anemias	280–285
mental disorders	290–319
Parkinson's disease	332
multiple sclerosis	340
chronic rheumatic heart disease	393–398
hypertensive disease	401–404
acute myocardial infarction	410
coronary atherosclerosis	414
pulmonary embolism	415.1
heart failure	428
haemorrhagic stroke	430–432
infarctive stroke	433–434
other cerebrovascular diseases	435–438
atherosclerosis	440
aortic aneurysm	441
pneumonia	480–486
influenza	487
chronic bronchitis	491
emphysema	492
peptic ulcer	531–533
hernia of abdominal cavity	550–553
intestinal obstruction without mention of hernia	560
chronic liver disease and cirrhosis	571
renal failure	584–586
diseases of the integumentary system	680–709
senility without mention of psychosis	797
motor vehicle accidents	E810–E825
accidental falls	E880–E888
inhalation and ingestion accidents	E911–E912
suicide	E950–E959
homicide	E960–E978

categories with small numbers of deaths at old ages (less than 0.3% of all deaths at ages 65 and over) were mostly eliminated. (However, several cause-of-death categories which seemed important for ageing research were not eliminated even though their proportions were less than 0.3%.)

Some categories appeared to be heterogeneous mixtures of diseases. For example, the 282-category system includes "renal failure, disorders resulting from impaired renal function,

and renal sclerosis, unspecified" as a single category. An apparently heterogeneous category like this one was, if possible, divided into subcategories, and the d_{ijk} pattern was examined for each subcategory.

In general, a category whose major subcategories exhibited similar age patterns in old age was not divided. Such categories include malignant neoplasms, nutritional deficiencies, anemias, mental disorders, chronic rheumatic heart disease, hypertensive disease, hemorrhagic stroke, infarctive stroke, pneumonia, ulcer of stomach and duodenum, chronic liver disease and cirrhosis, diseases of the integumentary system, motor vehicle accidents, suicide, and homicide.

A few remarks are needed about some of the cause-of-death categories. Diseases grouped together as "infectious and parasitic diseases" in ICD9 (001–139) constitute a less comprehensive category than the name usually implies. This group does not include some infectious diseases that are common in old age, such as influenza and kidney infections, as well as many types of pneumonia, bronchitis, chronic hepatitis, rheumatism, and various inflammations in the heart. In ICD9, these diseases are classified according to the organ systems (circulatory, respiratory, digestive, genitourinary, etc.) The ICD9 category of "infectious and parasitic diseases" mainly consists of highly contagious diseases that are prevalent in economically underdeveloped countries, such as cholera, diphtheria, tetanus, measles, typhus, and malaria.

"Hypertensive disease" (ICD9 code 401–404) and "atherosclerosis" (ICD9 code 440) are essentially "residual" categories after major diseases related to hypertension and atherosclerosis are placed in other categories (e.g., acute myocardial infarction, coronary atherosclerosis, haemorrhagic stroke, infarctive stroke). "Hypertensive disease" does not include those involving vessels of the heart, brain, or eye; and "atherosclerosis" does not include atherosclerosis of cerebral, coronary, mesenteric, or pulmonary arteries. Data on deaths that are reported as due to "diabetes mellitus" may be difficult to interpret, partly because Type 1 diabetes and Type 2 diabetes are not distinguished in ICD9, and partly because, when a person dies from a heart disease that was caused by diabetes mellitus, the underlying cause of death tends to be reported as heart disease, rather than diabetes mellitus, possibly deviating from WHO's definition of the "underlying cause of death." Special caution is also needed for "pulmonary embolism", which tends to be seriously under-diagnosed (Bordin *et al*. 1999; Green and Donald 1976; Poli *et al*. 1993).

Distribution of Deaths by Broad Cause-of-Death Categories

Figure 1 displays age variations in the number of deaths for both sexes combined in the U.S. White population during the four-year period from 1991 to 1994. The deaths are divided into nine broad cause-of-death categories. The figure indicates that the distribution is peaked in the age range of 80–84 and that heart diseases and neoplasms are the most dominant causes. However, it is difficult to draw more detailed information from the figure.

Figure 2 shows age variations in the proportional distribution of deaths by cause. Congenital and perinatal disorders are the main cause of death in the first year of life but their proportion

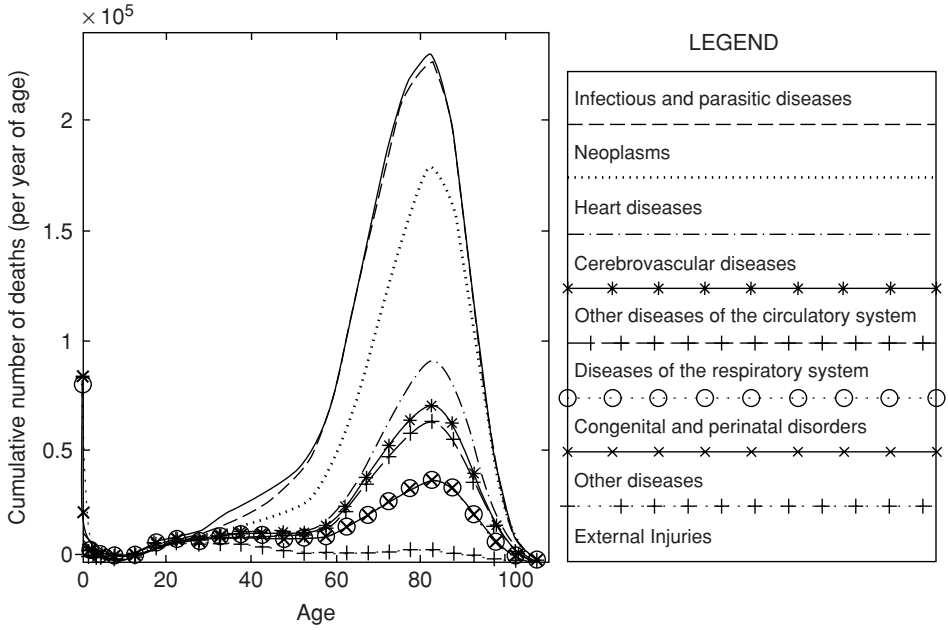

Figure 1. Cumulative number of deaths by cause, U.S. Whites, 1991–1994 combined. Each cause-of-death category corresponds not to a curve, but to the area between the two adjacent curves. For example, the number of deaths from heart diseases is represented by the vertical distance between the dotted line and the dash-dot line.

becomes almost negligible in adult years. The dominant cause of death at young ages is external injuries, which include accidents, poisoning, suicide, and homicide. About three-quarters of deaths around age 20 are due to external injuries. The proportion of deaths due to infectious and parasitic diseases remains low in both childhood and old age, but is notably high between the late 20s and the late 40s because of HIV infection.

The proportion of deaths from neoplasms rises steeply between ages 20 and 60. About 40 percent of deaths around age 60 are attributed to neoplasms. The proportion declines steeply after age 60, to only a few percent of deaths among centenarians. The proportion of deaths due to heart diseases increases with age throughout adult years. Also the proportion of deaths from cerebrovascular diseases rises with age up to around 90. About one-tenth of deaths at old ages is attributable to diseases of the respiratory system. The proportion of deaths due to respiratory diseases increases gradually with age.

Distribution of Deaths by Specific Causes

Figure 3 shows age patterns of the proportion of deaths for thirty-five selected causes. Vertical dotted lines are drawn at ages 65 and 85, indicating the lowest boundaries of "old

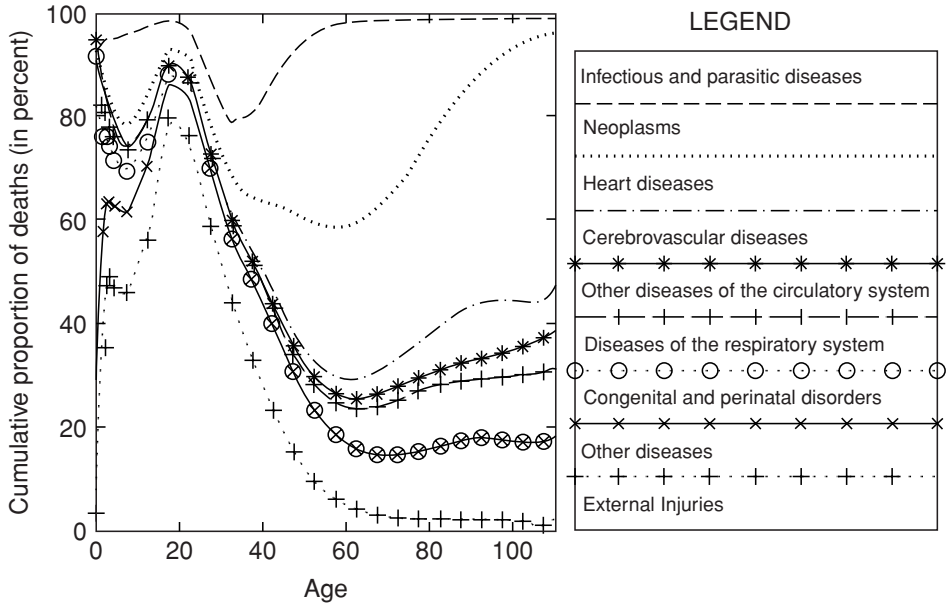

Figure 2. Age-related changes in the distribution of deaths by cause, U.S. Whites, 1991–1994 combined. Each cause-of-death category corresponds not to a curve, but to the area between the two adjacent curves. Namely, the proportion of deaths at the given age that are attributable to the cause-of-death category is indicated by the vertical distance between two adjoining curves. For example, the proportion of deaths from heart diseases is represented by the distance between the dotted line and the dash-dot line. The dotted line shows the proportion of all deaths at the given age from causes *other than* infectious and parasitic diseases and neoplasms. At age 60, the dotted line indicates 59 percent. The dash-dot line shows the proportion of all deaths from causes *other than* infectious and parasitic diseases, neoplasms, and heart diseases. At age 60, the dash-dot line indicates 29 percent. Thus, the difference (i.e., the vertical distance) between the two curves is the proportion attributable to heart diseases, which is 30 (59 minus 29) percent at age 60. (In this example, age 60 is chosen for simplicity, but actually the proportions are not given for single-year ages but for five-year age intervals, and points placed at the middle of the intervals are linked by curves.)

age" and "oldest-old age", respectively. The age trajectories in old age can be classified into three patterns: upward, downward, and bell-shaped. The proportion of deaths due to a certain cause may ascend with age (upward), descend with age (downward), or ascend then descend with age (bell-shaped). (There was no reversed bell-shaped pattern or consistently flat pattern.) We limit the label "bell-shaped" to those with peaks near age 85, and consider those with peaks near the beginning or end of the old-age range ("left-hooked" or "right-hooked") as special versions of "downward" or "upward", respectively. Only three curves in Figure 3 are identified as bell-shaped: Parkinson's disease for males and females, and

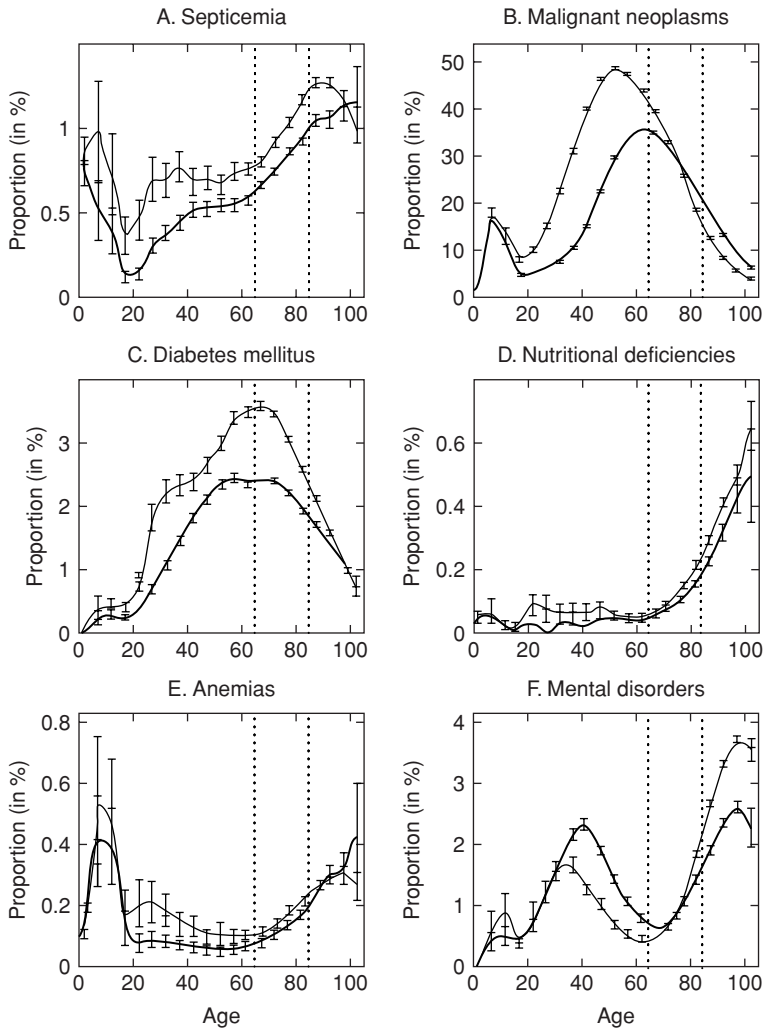

Figure 3. Age-related changes in the distribution of deaths by cause, for selected causes, U.S. White males (thicker line) and females (thinner line), 1991–1994 combined. The vertical axis indicates the proportion of all deaths at the given age that is attributable to the cause of death. The short bars show 95% confidence intervals. The two dotted vertical lines indicate age 65 and age 85.

acute myocardial infarction for females. Thus, most of the curves are classified as upward or downward in old age.

The proportion of deaths due to a given cause rises with age if the death rate from the cause increases with age faster than the total mortality (the death rate for all causes combined).

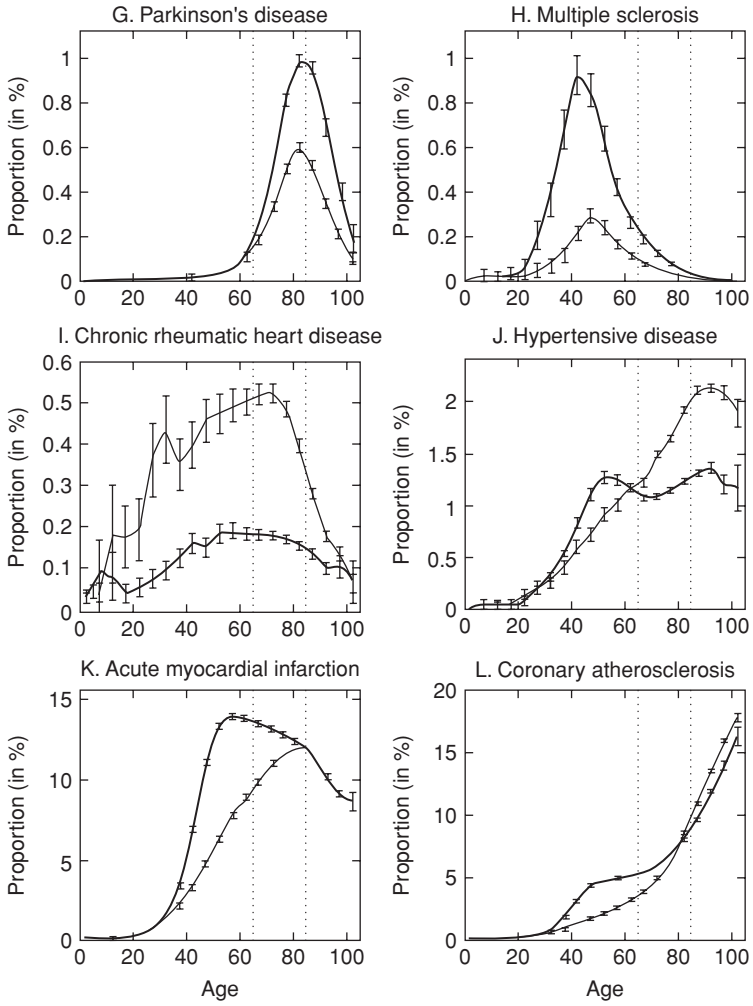

Figure 3. (*Continued***)**

The proportion of deaths falls with age if the cause-specific death rate increases with age more slowly than the total mortality, or if the death rate decreases with age.

The age pattern differs notably among major degenerative diseases. The proportion of deaths due to malignant neoplasms declines steeply in old age (Figure 3B). All cancers are grouped together in Figure 3, because their patterns were similar: steep downward curves after peaks in the 40s, 50s or 60s of age, except for the late peak of prostate cancer in 75–79.

The downward patterns of cancers are consistent with the observation that deaths from cancers are infrequent among the oldest-old (Hadley 1992) and rare among centenarians

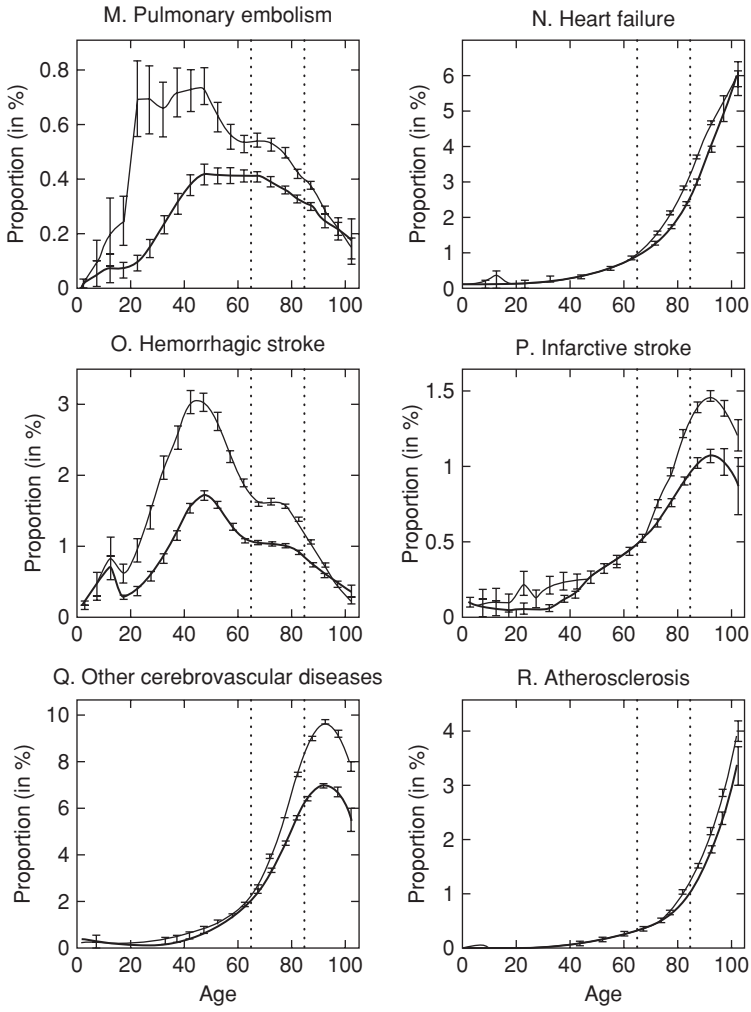

Figure 3. (*Continued***)**

(Allard *et al*. 1996; Gessert *et al*. 2002). This seems partly due to selection: persons who are less likely to have cancers tend to survive to older ages. It may also be due to age-related changes in cancer development. Generally, cancers at older ages are slower, less aggressive/virulent, and less metastatic (Sarma 1987; reviewed in Bordin *et al*. 1999). It is difficult to determine which one of the two effects is the more dominant reason for the downward patterns of cancers.

For heart diseases, a sharp contrast is observed between acute myocardial infarction (Figure 3K)—which is downward for males and bell-shaped for females—and coronary atherosclerosis (Figure 3) and heart failure (Figure 3N), both of which are steeply upward. Another

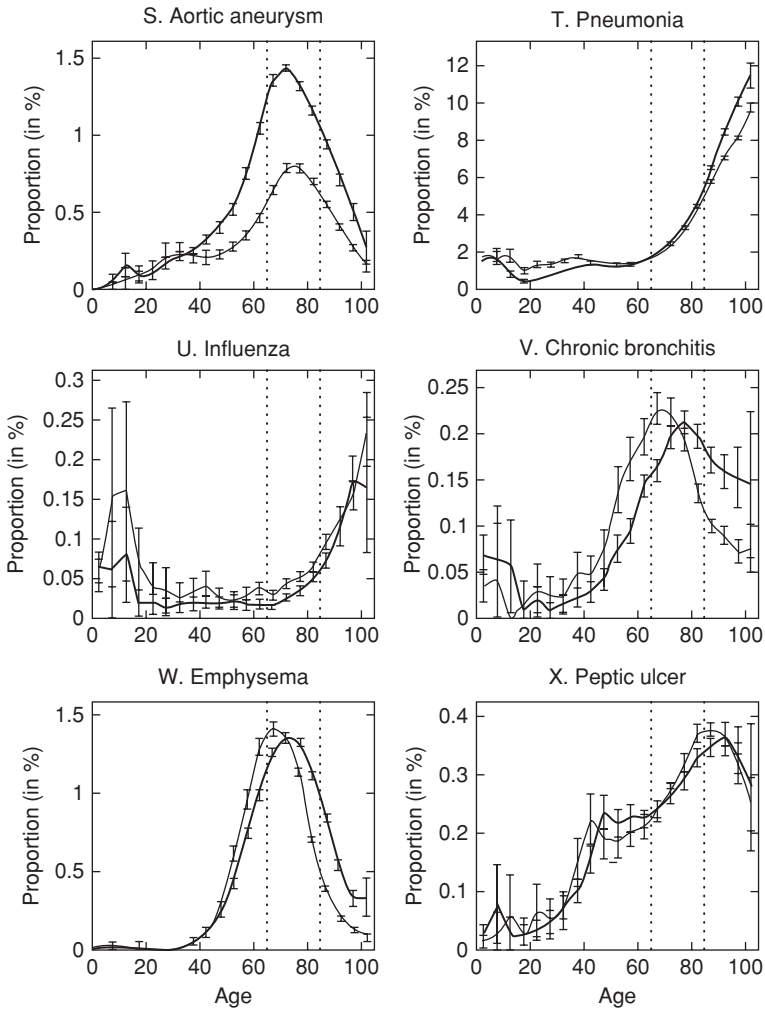

Figure 3. (*Continued*)

sharp contrast is observed for cerebrovascular diseases, between the downward pattern of haemorrhagic stroke (Figure 3O) and the upward pattern (with a peak in oldest-old age) of infarctive stroke (Figure 3P). Although the majority of deaths due to stroke fall in the "other cerebrovascular diseases" category, their collective pattern (Figure 3Q) is similar to that of infarctive stroke. Thus, deaths classified in "other cerebrovascular diseases" may be predominantly infarctive.

The proportion of deaths due to pneumonia rises sharply from about 2 percent around age 60 to about 10 percent among centenarians (Figure 3T). Influenza, though less prevalent as a cause of death than pneumonia, follows a similar trajectory of steep increase (Figure 3U).

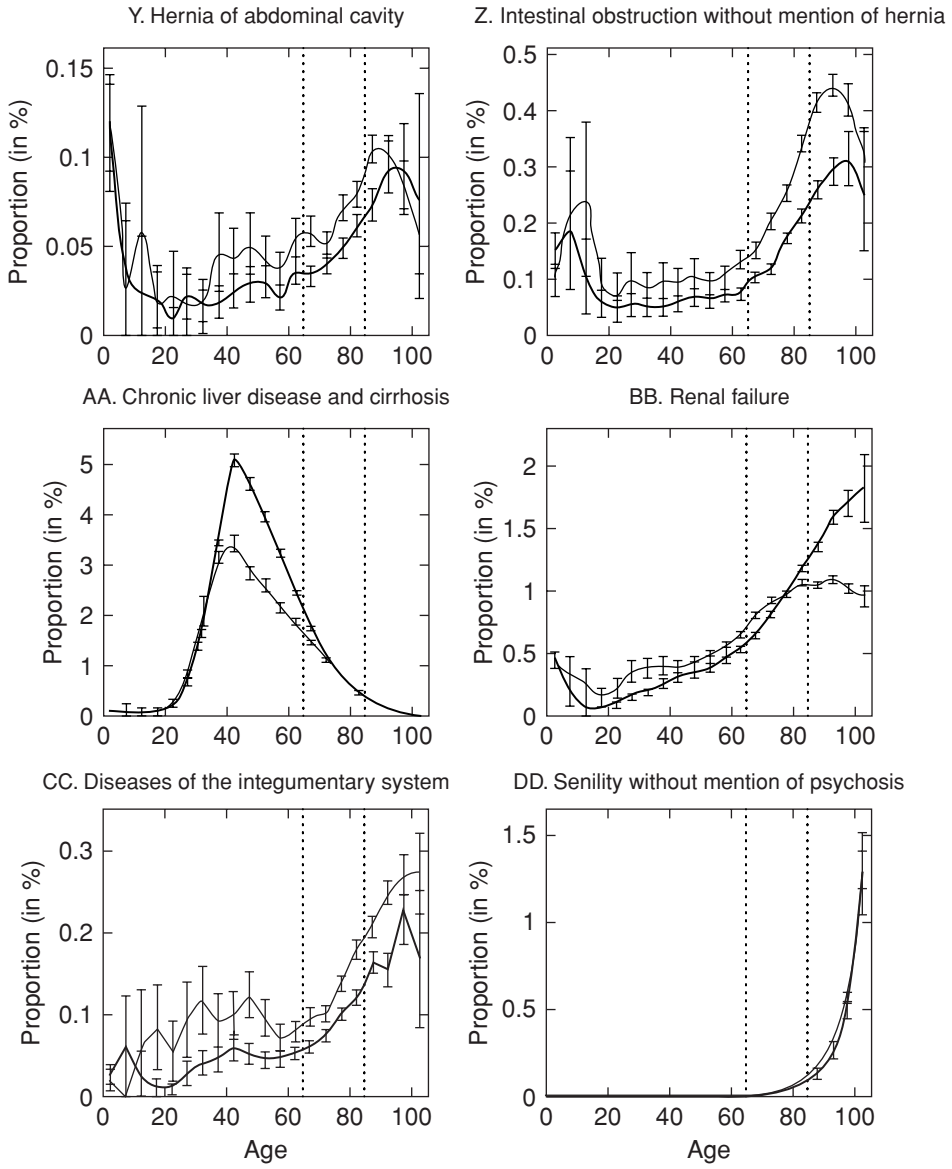

Figure 3. (*Continued***)**

Most "infectious and parasitic diseases" (which, as described earlier, do not include many infectious diseases that are common among the elderly) have a very small number of deaths at old ages in the U.S. White population. The notable exception is septicemia, which constitutes about 70 percent of all deaths in this group and shows a clear upward pattern (Figure 3A).

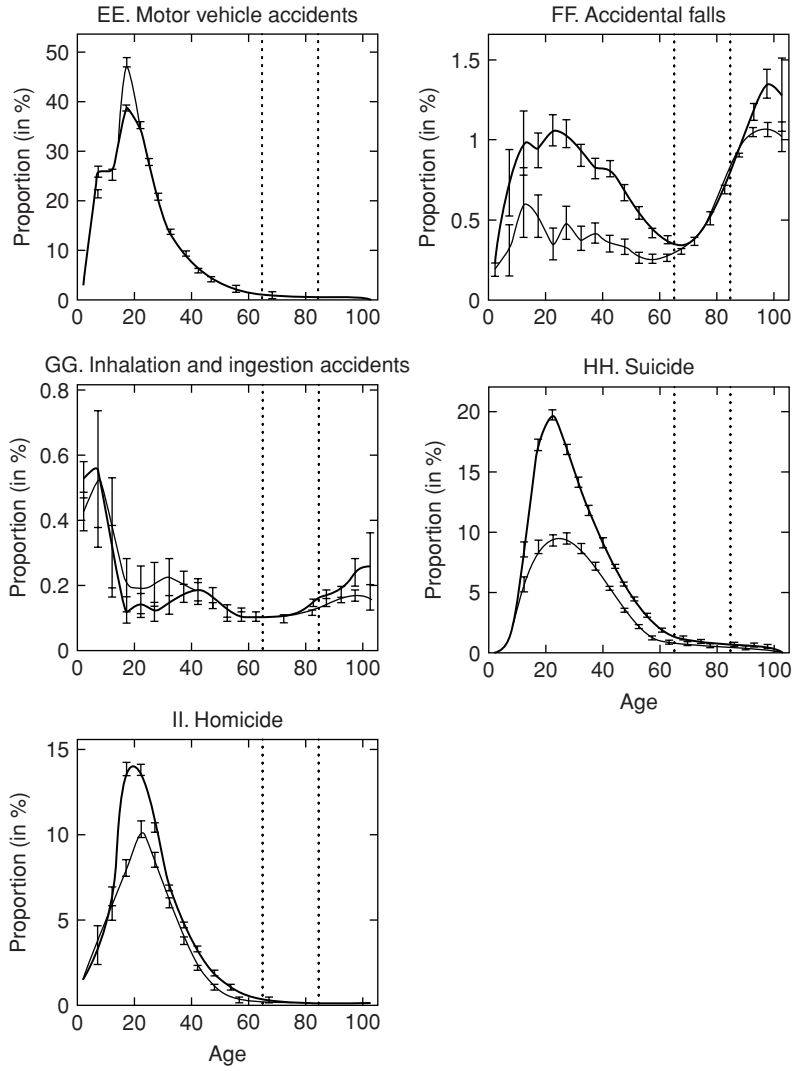

Figure 4. (*Continued***)**

The trajectory of Parkinson's disease is bell-shaped (Figure 3G). Although some effects on Parkinson's disease of heredity, estrogen and folate levels, and exposure to insecticides and herbicides were found, risk factors of the disease have not been well established yet. However, its steep downward slope at oldest-old ages seem to suggest that the disease may be highly selective, too.

The proportions of deaths due to motor vehicle accidents, suicide, and homicide are substantially smaller at old ages than at young adult ages (Figures 3EE, 3HH and 3II). The

Table 3. Selected list of causes of death that characterize the oldest-old population.

More prevalent in 85+ than in 65–84[a]
septicemia
nutritional deficiencies
anemias
mental disorders
hypertensive disease (females)
coronary atherosclerosis
heart failure
infarctive stroke
other cerebrovascular diseases
atherosclerosis
pneumonia
influenza
peptic ulcer
hernia of abdominal cavity
intestinal obstruction without mention of hernia
renal failure
diseases of the integumentary system
senility without mention of psychosis
accidental falls
inhalation and ingestion accidents
Less prevalent in 85+ than in 65–84[b]
malignant neoplasms
diabetes mellitus
multiple sclerosis
chronic rheumatic heart disease
acute myocardial infarction (males)
pulmonary embolism
haemorrhagic stroke
aortic aneurysm
chronic bronchitis
emphysema
chronic liver disease and cirrhosis

[a] The proportion of deaths in 85+ due to the cause is higher than in 65–84.
[b] The proportion of deaths in 85+ due to the cause is lower than in 65–84.

downward patterns of motor vehicle accidents and homicide seem attributable to the declining exposure to risk, although older drivers have high risks when they drive (Bilban 1997; Dulisse 1997; Sjogren *et al*. 1993). In spite of the age-related increase of the death rate from suicide, the proportion of suicidal deaths declines notably in old age, because death rates from many diseases rise faster with age than the suicide death rate.

Table 3 shows two groups of causes of death: those for which the proportion of deaths is significantly higher among the oldest-old (85+) than among the younger-old (65–84), and

those for which the order is reversed. As for the causes that are relatively more prevalent among the oldest-old, the following points seem noteworthy. First, the group includes some common diseases and injuries that seldom cause deaths at younger adult ages but become serious threats at very old ages (anemia, influenza, hernia of abdominal cavity, other types of intestinal obstruction, skin diseases, and inhalation and ingestion accidents). Secondly, a few diseases in the group are always or usually caused by infection (septicemia, pneumonia, and influenza). Thirdly, some are related to a frail musculoskeletal system and/or inappropriate neural control (accidental falls, inhalation and ingestion accidents, intestinal obstruction). Fourthly, debilitation and weakening of two major organs (heart failure and renal failure) are included. Lastly, the group seems pathologically more diverse than the other group, including diseases of the urinary, integumentary, and musculoskeletal systems as well as such causes as nutritional deficiencies and mental disorders.

These characteristics seem to reflect senescent processes that eventually make almost all individuals vulnerable to multiple pathologies. At middle ages and younger-old ages, deaths are largely limited to certain diseases such as malignant neoplasm, acute myocardial infarction, stroke, and liver cirrhosis. However, with the advancing age, various causes of death that are uncommon at younger ages become increasingly common. The resulting diversification of causes of death seems to reflect the long-term accumulation of unrepaired damage, leading to simultaneous deterioration of many physiological functions. The general ability to maintain homeostasis declines, making the person vulnerable to various kinds of physiological stress (Gavrilov and Gavrilova 1991). Particularly notable are the weakening of immune functions as well as the frail musculoskeletal system and the compromised ability to control physical movements of internal organs. Some major organs (such as the heart and the kidney) that have been severely debilitated by previous diseases and/or chronic problems may become too weak to function properly. The increasing proportion of deaths reported as "senility" (Figure 3DD) indicates the difficulty of determining the primary cause of death for a very old person with multiple weaknesses and limited reserve capacities.

Most causes of death that are relatively more prevalent among the younger-old than among the oldest-old seem to be diseases that tend to develop selectively and prematurely in some high-risk individuals at middle ages and younger-old ages. These diseases are known to be strongly associated with certain risk factors. They include malignant neoplasms (heredity, smoking, exposure to toxic materials), diabetes mellitus (heredity, diet, obesity, inactivity), multiple sclerosis (heredity), chronic rheumatic heart disease (acute rheumatic fever earlier in life), acute myocardial infarction (diet, smoking, heavy drinking, mental stress), haemorrhagic stroke (hypertension), chronic bronchitis (smoking), emphysema (smoking), and chronic liver disease and cirrhosis (chronic hepatitis and heavy alcohol consumption). Causes of death that are dominant at oldest-old ages have risk factors as well; but overall, their risk factor effects do not seem as strong as those of the diseases that are dominant at younger old ages.

Death rates from those diseases increase with age, partly because the diseases or conditions leading to the diseases tend to develop over decades. However, the proportions of deaths from those diseases decrease with age, probably because senescent processes do not necessarily make all individuals highly vulnerable to those diseases; and persons who

have the risk factors are less likely to survive to older ages. Thus, the causes of death that are more prevalent among the younger-old do not seem to be associated with senescent processes as strongly as those that are more prevalent among the oldest-old.

Conclusion

In summary, causes of death that are more prevalent among the oldest-old than among the younger-old include heart failure, pneumonia, influenza, coronary atherosclerosis, infarctive stroke, septicemia, mental disorder, nutritional deficiency, and accidental fall. They seem to be strongly associated with senescent processes that eventually raise the general vulnerability of almost all individuals to multiple pathologies. Causes of death that are more prevalent among the younger-old than among the oldest-old include malignant neoplasms, acute myocardial infarction (particularly for males), haemorrhagic stroke, chronic liver disease and cirrhosis, diabetes mellitus, and multiple sclerosis. These diseases tend to develop selectively and prematurely in some high-risk individuals at middle ages and younger-old ages.

In textbooks of pathology and epidemiology, many degenerative diseases and some types of external injuries have been described, fairly uniformly, as having age-associated increases in incidence, prevalence, and mortality. Because death rates from most degenerative diseases increase with age, their age trajectories may appear similar. However, death rates from some diseases and injuries rise significantly faster with age than others, and those differences are clearly reflected in age variations of the proportional cause-of-death distribution. The simple analysis of the age variations in this study helps us to unambiguously distinguish major causes of death that are more prevalent among the oldest-old and those that are more prevalent among the younger-old and demonstrates the usefulness of information on age-related changes in the cause-of-death structure for gerontological research.

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References

Allard, M., Vallin, J., Andrieux, J.-M., and Robine, J.-M. (1996) "In search of the secret of centenarians: A demographic and medical survey about centenarians in France". In: Caselli, G., Lopez A.D., (eds.), *Health and Mortality Among Elderly Populations*. Oxford: Clarendon Press, pp. 61–86.

Asnaes, S., Frederiksen, V., and Fenger, C. (1983) "The value of the hospital autopsy: A study of causes and modes of death estimated before and after autopsy", *Forensic Science International*, 21(1):23–32.

Bilban, M. (1997) "Road traffic accidents caused by elderly drivers", *Collegium Antropologicum*, 21(2):573–583.

Bordin, P., Da Col, P.G., Peruzzo, P., Stanta, G., Guralnik, J. M., and Cattin, L. (1999) "Causes of death and clinical diagnostic errors in extreme aged hospitalized people: A retrospective clinical-necropsy survey", *The Journals of Gerontology: Medical Sciences*, 54A(11):M554–M559.

Crombie, D. L., Fleming, D. M., Cross, K. W., and Lancashire, R. J. (1995) "Concurrence of monthly variations of mortality related to underlying cause in Europe", *Journal of Epidemiology and Community Health*, 49(4):373–378.

Dulisse B. (1997) "Older drivers and risk to other road users", *Accident Analysis and Prevention*, 29(5):573–582.

Engel, L. W., Strauchen, J. A., Chiazze Jr., L., and Heid, M. (1980) "Accuracy of death certification in an autopsied population with specific attention to malignant neoplasms and vascular diseases", *American Journal of Epidemiology*, 111(1):99–112.

Gavrilov, L. A., and Gavrilova, N. S. (1991) *The Biology of Life Span: A Quantitative Approach*. New York: Harwood.

Gessert, C. E., Elliott, B. A., and Haller, I. V. (2002) "Dying of old age: An examination of death certificates of centenarians", *Journal of the American Geriatric Society*, 50(9), pp.1561–1565.

Gloth, F. M. 3rd, and Burton, J. R. (1990) "Autopsies and death certificates in the chronic care setting", *Journal of the American Geriatrics Society*, 38(2):151–155.

Green, A., and Donald, K. J. (1976) "Necropsy as a control of death certification: Some unexpected findings", *Medical Journal of Australia*, 2(4):131–132.

Gross, J. S., Neufeld, R. R., Libow, L. S., Gerber, I., and Rodstein, M. (1988) "Autopsy study of the elderly institutionalized patient: Review of 234 autopsies", *Archives of Internal Medicine*, 148(1):173–176.

Hadley, E. (1992) "Causes of death among the oldest-old". In: Suzman, R. M., Willis, D.P., Manton, K.G. (eds.), *The Oldest Old*. Cambridge: Oxford University Press, pp. 183–196.

Hasuo, Y., Ueda, K., Kiyohara, Y., Wada, J., Kawano, H., Kato, I., Yanai, T., Fujii, I., Omae, T., and Fujishima, M. (1989) "Accuracy of diagnosis on death certificates for underlying causes of death in a long-term autopsy-based population study in Hisayama, Japan; with special reference to cardiovascular diseases", *Journal of clinical epidemiology*, 42(6):577–584.

Horiuchi, S. (1999) "Epidemiological transitions in human history". In: *Health and Mortality: Issues of Global Concern*. New York: United Nations, pp. 54–71.

Horiuchi, S. (2003) "Interspecies comparison of life span distribution: Humans versus invertebrates". In: Carey, J., Tuljapurkar, S. (eds.), *Life Span: Evolutionary, Ecological and Demographic Perspectives, (Population and Development Review, Special Supplement to Volume 29*), pp. 127–151.

Horiuchi, S., Finch, C., Meslé, F., and Vallin, J. (2003) "Differential patterns of age-related mortality increase in middle age and old age", *The Journals of Gerontology: Biological Sciences*, 58A(6):495–507.

Horiuchi, S., and Wilmoth, J. R. (1997) "Age patterns of the life-table aging rate for major causes of death in Japan, 1951–1990", *The Journals of Gerontology: Biological Sciences*, 52A:B67–B77.

Horiuchi S., and Wilmoth, J. R. (1998) "Deceleration in the age pattern of mortality at older ages", *Demography*, 35(4):391–412.

Ishii, T., Hosoda, Y., and Maeda, K. (1980) "Cause of death in the extreme aged–a pathologic survey of 5106 elderly persons 80 years old and over", *Age and Ageing*, 9(2):81–89.

Kircher, T., Nelson, J., and Burdo, H. (1985) "The autopsy as a measure of accuracy of the death certificate", *New England Journal of Medicine*, 313(20): 1263–1269.

Kiyohara, Y., Ueda, K., Hasuo, Y., Wada, J., Kawano, H., Kato, I., Sinkawa, A., Ohmura, T., Iwamoto, H., and Omae, T. (1989) "Incidence and prognosis of subarachnoid hemorrhage in a Japanese rural community", *Stroke*, 20(9):1150–1155.

Klatt, E. C., and Meyer, P. R. (1987) "Geriatric autopsy pathology in centenarians", *Archives of Pathology and Laboratory Medicine*, 111(4):367–369.

Kohn, R. R. (1963) "Human aging and disease", *Journal of Chronic Diseases*, 16:5–21.

Kohn, R. R. (1982) "Cause of death in very old people", *Journal of the American Medical Association*, 247(20):2793–2797.

Lee, P. N. (1994) "Comparison of autopsy, clinical and death certificate diagnosis with particular reference to lung cancer: a review of the published data", *APMIS supplementum*, 45:1–42.

Lubitz, J., Beebe, J., and Baker, C. (1995) "Longevity and medicare expenditures", *New England Journal of Medicine*, 332 (15):1027–1029.

Maclaine, G. D., Macarthur, E. B., and Heathcote, C. R. (1992) "A comparison of death certificates and autopsies in the Australian capital territory", *Medical Journal of Australia*, 156(7):462–463, 466–468.

Manton, K. G., and Stallard, E. (1984) *Recent Trends in Mortality Analysis*. Orlando: Academic Press.

McKelvie, P. A. (1993) "Medical certification of causes of death in an Australian metropolitan hospital: Comparison with autopsy findings and a critical review", *Medical Journal of Australia*, 158(12):816–818, 820–821.

Modelmog, D., Rahlenbeck, S., and Trichopoulos, D. (1992) "Accuracy of death certificates: A population-based, complete-coverage, one-year autopsy study in East Germany", *Cancer Causes and Control*, 3(6):541–546.

Mollo, F., Bertoldo, E., Grandi, G., and Cavallo, F. (1986) "Reliability of death certifications for different types of cancer: an autopsy survey", *Pathology, Research and Practice*, 181(4):442–447.

National Center for Health Statistics. (1997) *1991 Multiple Cause-of-Death File. CD-ROM Series 20, no. 9*. Hyattsville, Maryland.

National Center for Health Statistics. (1997) *1992 Multiple Cause-of-Death File. CD-ROM Series 20, no. 10*. Hyattsville, Maryland.

National Center for Health Statistics. (1997) *1993 Multiple Cause-of-Death File. CD-ROM Series 20, no. 11*. Hyattsville, Maryland.

National Center for Health Statistics. (1998) *1994 Multiple Cause-of-Death File. CD-ROM Series 20, no. 12*. Hyattsville, Maryland.

National Institute of Population and Social Security Research. (1999) *Latest Demographic Statistics 1999*. Tokyo.

Nielsen, G. P., Bjornsson, J., and Jonasson, J. G. (1991) "The accuracy of death certificates: Implications for health statistics", *Virchows Archives - A, Pathological Anatomy and Histopathology*, 419(2):143–146.

Perls, T. T., Silver, M. H., and Lauerman, J. F. (2000) *Living to 100: Lessons in living to your maximum potential at any age*. New York: Basic Books.

Perls, T. T., and Wood, E. R. (1996) "Acute care costs of the oldest old: They cost less, their care intensity is less, and they go to nonteaching hospitals", *Archives of Internal Medicine*, 156(7):754–760.

Poli, L., Pich, A., Zanocchi, M., Fonte, G., Bo, M., and Fabris, F. (1993) "Autopsy and multiple pathology in the elderly", *Gerontology*, 39(1):55–63.

Preston, S. H. (1976) *Mortality Patterns in National Populations: With Special Reference to Recorded Causes of Death*. New York: Academic Press.

Preston, S. H., Elo, I. T., Foster, A., and Fu, H. (1998) "Reconstructing the size of the African American population by age and sex, 1930–1990", *Demography*, 35(1):1–21.

Preston, S. H., Elo, I. T., Rosenwaike, I., and Hill, M. (1996) "African-American mortality at older ages: Results of a matching study", *Demography*, 33(2):193–209.

Puxty, J. A., Horan, M. A., and Fox, R. A. (1983) "Necropsies in the elderly", *Lancet*, 1(8336):1262–1264.

Simms, H. S. (1946) "Logarithmic increase in mortality as a manifestation of aging", *Journal of Gerontology*, 1:13–26.

Sarma, D. P. (1987) "Lung cancer in men aged 75 or older", *Journal of Surgical Oncology*, 34(1):19–21.

Scitovsky, A. A. (1988) "Medical care in the last twelve months of life: The relation between age, functional status, and medical care expenditures", *Milbank Quarterly*, 66(4):640–660.

Scitovsky, A. A. (1994) "The high cost of dying revisited", *Milbank Quarterly*, 72(4):561–591

Sjogren, H., Bjornstig, U., Eriksson, A., Sonntag-Ostrom, E., and Ostrom, M. (1993) "Elderly in the traffic environment: analysis of fatal crashes in northern Sweden", *Accident Analysis and Prevention*, 25(2):177–188.

Temkin-Greener, H., Meiners, M. R., Petty, E. A., and Szydlowski, J. S. (1992) "The use and cost of health services prior to death: a comparison of the medicare-only and the medicare-medicaid elderly populations", *Milbank Quarterly*, 70(4):679–701.

Thatcher, A. R., Kannisto, V., and Vaupel, J. W. (1998) *The force of mortality at ages 80 to 120*. Odense: Odense University Press.

Vallin, J., and Meslé, F. (1988) *Les causes de décès en France de 1925 a 1978*. Paris: Institut National d'Études Démographiques Presses Universitaires de France.

Vaupel, J. W., Carey, J. R., Christensen, K., Johnson, T. E., Yashin, A. I., Holm, N. V., Iachine, I. A., Kannisto, V., Khazaeli, A. A., Liedo, P., Longo, V. D., Zeng, Y., Manton, K. G., and Curtsinger, J. W. (1998) "Biodemographic trajectories of longevity", *Science*, 280(5365):855–860.

Weinberg, A. D., Engingro, P. F., Miller, R. L., Weinberg, L. L., and Parker, C. L. (1989) "Death in the nursing home: senescence, infection and other causes", *Journal of Gerontological Nursing*, 15(4):12–16.

World Health Organization (1977) *International classification of diseases, 1975 revision*. Vol 1, Geneva.

CHAPTER 11. GENETIC FACTORS ASSOCIATED WITH INDIVIDUAL LIFE DURATION: HERITABILITY

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Lifespans cluster to some degree in families, and in recent years long-lived families have become the focus of many research efforts aiming at understanding the underlying aetiology for the variation in lifespan. Socioeconomic status is clearly associated with lifespan, but genetic factors are also believed to play a substantial role. Heritability is a useful estimate of the overall influence of genetic factors in a population. This chapter will cover the formal definition of heritability, describe design options to obtain heritability estimates, and summarize estimates of the heritability of various measures of human life duration such as lifespan per se, early and late death, and age-specific susceptibility to death ('frailty').

Heritability is defined as the proportion of the total variance in a population that is attributable to genetic differences between individuals. Hence, a high heritability for a trait indicates that a large proportion of the individual differences in the trait is caused by genotypic or allelic differences; while a low heritability suggests that the reasons for the phenotypic differences are primarily to be sought in differences in environmental exposures or in stochastic processes. In this way heritability estimates are useful in pointing towards the potentially most fruitful research directions.

However, the heritability concept has a number of limitations. First of all it is time- and population-specific and sensitive to changes in the overall and environmental variances as well as to violations of underlying assumptions. E.g., if the environmental variance goes down due to more homogeneous living conditions and the genetic variance stays the same, then the total variance goes down and therefore the heritability goes up despite absence of change in the genetic variance. If, on the contrary, the environmental variance goes up dramatically (as seen for lifespan during famine or epidemics) this may overshadow the influence of genetic variance.

Despite these limitations, a heritability estimate is very useful because it can outline the potentials for identifying specific genetic or environmental factors of importance for a trait in the population from which the heritability estimate was derived.

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Definition of Heritability

The heritability concept is based upon the assumption that a quantitative phenotype (P) can be expressed as the additive linear function of genetic and environmental components.

$$P = \text{Genes} + \text{Environment} \tag{1}$$

Genetic effects can be divided into:

1. Additive genetic effects (A), which are the effects of genes taken singly and added over loci, i.e., the genetic effects that do not interact.
2. Genetic dominance effects (D), which are non-additive genetic effects due to intralocus interaction. i.e., interaction within one gene locus (the allele inherited from the mother interact with the allele inherited from the father).
3. Epistasis (I) which is non-additive genetic effects due to interlocus interactions, i.e., interaction between several genes. Non-additive genetic factors may contribute to similarities between sibs, but not to similarities between parents and offspring. Only additive genetic factors are leading to similarities from generation to generation.

Environmental effects can be divided into:

1. Shared environmental effects (C), which are environmental effects shared by family members and contributing to family member similarity.
2. Non-shared environmental effects (E), which are environmental effects not shared by family members but contribute to family member dissimilarity.

This leads to the following decomposition of P:

$$P = A + D + I + C + E \tag{2}$$

Measurement error is not explicitly included in the model, but will be part of E. This means that non-shared environment and stochastic processes are confounded—a point which may be important considering the emerging evidence that stochastic processes play an important role for ageing and lifespan (Finch and Kirkwood 2000). The phenotypic variance (VP) can similarly be decomposed as:

$$VP = VA + VD + VI + VC + VE \tag{3}$$

with VA, VD, VI, VC, and VE being the variance of the respective genetic and environmental factors.

Standardizing the variance yields:

$$1 = VA/VP + VD/VP + VI/VP + VC/VP + VE/VP \tag{4}$$

or

$$1 = a^2 + d^2 + i^2 + c^2 + e^2 \tag{5}$$

where a^2 is the proportion of the variance attributable to additive genetic factors; d^2 and i^2 the proportion of the variance attributable to non-additive genetic factors; c^2 the proportion of the variance attributable to shared environment; and e^2 the proportion of the variance attributable to non-shared environment and stochastic processes.

Heritability is the proportion of phenotypic variance due to genetic variance. Narrow sense heritability includes only additive genetic variance:

$$h^2 = VA/VP = a^2 \tag{6}$$

while broad sense heritability includes both additive and non-additive genetic factors:

$$H^2 = VA/VP + VD/VP + VI/VP = a^2 + d^2 + i^2 \tag{7}$$

Designs to Obtain Heritability Estimates

TRADITIONAL FAMILY STUDIES

Traditional family studies of parent–offspring, sibs etc. determine whether or not there is familial resemblance for the phenotype being studied, but they do not indicate whether this resemblance is due to genetic or shared environmental factors. Uncertain paternity, comparisons of individuals from different generations, and the fact that non-additive genetic factors are not transmitted from generation to generation may also make the interpretation of the results difficult. As families not only share genes but also the environment, traditional family studies can only provide the upper limit for heritability. Additional constraints in the study design is needed to estimate the heritability, and such constraints are provided by twin and adoption studies.

ADOPTION STUDIES

Adoption studies are much fewer and smaller than other kinds of family studies. Nevertheless, adoption studies have had a very big impact on the nature–nurture debate for a number of traits, because these studies have produced remarkable results, and the design is easily understood and interpreted. Adoption studies use the fact that adoptees share genes, but not environment, with their biological families: they share environment, but not genes, with their adoptive families. The adoption studies are, however, not without weaknesses. In particular a bias can be introduced by selective placement of adoptees (i.e. the adoptees are preferably placed with adoptive parents who resemble the birth parents in some ways). It can be shown that selective placement tends to overestimate the effect of both genetic and shared family environment (Plomin *et al.* 2001). Furthermore, similarity among offspring and biological parents may not only be due to genetic factors, but also to environmental factors during pregnancy or early childhood (if adoption took place later rather than immediately after birth).

TWIN STUDIES

The fact that twinning is relatively common, and nationwide twin registers exist in several countries, has made twin studies the most important tool for estimating the heritability of life duration in humans. Therefore this section will provide details about the model and the assumption behind the heritability estimates obtained in twin studies.

In humans two types of twinning occur: monozygotic (MZ) twins share all their genetic material and dizygotic (DZ) twins, like ordinary siblings, share, on average, 50% of their genes. In the classical twin study, MZ and DZ correlations for a trait are compared. A significantly higher correlation in monozygotic twins indicates that genetic factors play an etiological role.

Figure 1 is a path diagram showing the relationship between the different latent genetic and environmental components in an MZ twin pair and in a DZ twin pair. The double-headed arrows represent expected correlations between the latent variables in a pair of twins reared together. The single-headed paths express the extent to which genetic and environmental deviations cause phenotypic deviations. MZ twins are genetically identical and share all additive and non-additive genetic effects. DZ twins are correlated, but not identical, as they represent the results of meiosis in the parental germ lines. DZ twins share on average 1/2 of all additive effects and 1/4 of genetic dominance effects. Shared

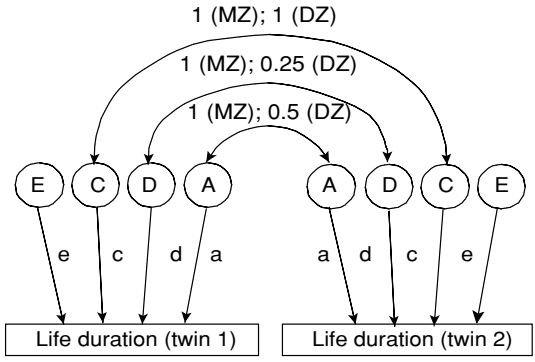

Figure 1. Path model. The figure illustrates a model for causes of longevity. Latent etiologic factors are divided into additive genetic factors (A), genetic dominance factors (D), shared (C), and non-shared (E) environment. Additive genetic factors and genetic dominance factors are both perfectly correlated in MZ twins, whereas in DZ twins, the correlation between additive genetic factors equals 1/2, and the correlation between genetic dominance factors equals 1/4. Shared environment is assumed to contribute equally to the correlation in MZ and DZ twins. The proportions of variance attributable to the latent factors are the square of the respective standardized path coefficients (e.g. the proportion of additive genetic variance equals a^2), which are estimated through maximum likelihood procedures. Heritability equals genetic variance divided by total phenotypic variance. (Modified after Herskind *et al.* 1996).

environment is assumed to be perfectly correlated within both MZ twin pairs and DZ twin pairs.

Thus,

$$r_{MZ} = a^2 + d^2 + c^2 \quad (8)$$

$$r_{DZ} = 1/2a^2 + 1/4d^2 + c^2 \quad (9)$$

The correlations (r) for MZ and DZ twins can be estimated using the following equation:

$$r_{twin1,twin2} = cov_{twin1,twin2}/(var_{twin1} * var_{twin2})^{1/2} \quad (10)$$

which for large sample sizes is an estimate of the intraclass correlation.

The 'Classical' Estimate of Heritability (Falconer)
The 'classical' estimate of heritability is calculated as twice the difference between the MZ and the DZ correlation (Falconer 1989):

$$h^2 = 2 * (r_{MZ} - r_{DZ}) \quad (11)$$

This approach is very simple, but has several limitations. In deriving the heritability estimate it is assumed that only additive genetic effects and shared environment influence intra-pair similarity. In the presence of genetic dominance this estimate will be subject to bias. Furthermore, the method cannot test competing hypotheses about the nature of genetic and environmental influences on the trait, i.e., whether twin similarity is a result of additive genetic effects, genetic dominance, or shared environmental effects, or whether more than one of these effects is required to explain the data.

Model Fitting
A major improvement has been the use of structural equation modelling (path analysis), which has been described in detail by Neale and Cardon (1992). Here different hypotheses (models) of the nature of genetic and environmental influences on the trait are fitted to observed summary statistics (twin variances and intra-pair covariances for MZ and DZ pairs).

Models are represented by different modifications of Equations 5, 8–9. Given three equations with three observables only three of the four unknown parameters (a, d, c and e) can be estimated at any one time. First, the full model ACE including parameters for additive genetic variance, shared and non-shared environment is fitted to the observed data for MZ and DZ twins. In this case the parameter d is equal to zero in the model:

$$1 = a^2 + c^2 + e^2 \quad (12)$$

$$r_{MZ} = a^2 + c^2 \quad (13)$$

$$r_{DZ} = 1/2a^2 + c^2 \quad (14)$$

Three alternative, reduced models, AE, CE, and E, are then fitted and compared with the full model. The AE model includes parameters for additive genetic variance and non-shared environment; the CE model includes shared and non-shared environment assuming that twin similarity is the result of shared environment only; the E model includes only non-shared environment assuming no similarity among twins. Finally, models which include genetic dominance (ADE and DE) are fitted. Model fitting is typically carried out by the method of maximum likelihood. The procedure results in a χ^2 test statistic which is used to assess the goodness of fit for the models. The hypothesis (model) will be rejected if the goodness of fit test is significant. To select the most parsimonious model for any given data set (i.e. the model that best explains data with the fewest parameters), χ^2 of the full and reduced models is compared for the appropriate degrees of freedom. When models are not nested, Akaike's Information Criterion (AIC), which is χ^2 minus twice the degrees of freedom, is used to compare models. The model with the lowest AIC reflects the best balance between goodness of fit and parsimony (Akaike 1987). Structural equation modelling is often carried out using the statistical software Mx (Neale 1999), which has been developed especially to handle path analysis for twin data.

When the phenotype of interest is qualitative (e.g. early death), the approach takes on a slightly different form. It is still possible to use the general model described above, but since it is only observed whether an individual is either affected or not (in the case of two categories), the continuous phenotype P is unobserved. Traditionally, categorical data are analysed assuming that the ordered categories reflect an imprecise measurement of an underlying normally distributed liability with one or more thresholds depending on the number of categories ('the multiple threshold model') (Neale and Cardon 1992). An increasing liability reflects an increasing risk of being affected. In this case expectations in terms of genetic and environmental parameters are fitted to summary statistics in the form of different types of correlations (tetrachoric correlations, polychoric correlations etc.). Parameter estimation is by weighted least squares.

Assumptions Underlying the Heritability Estimates Obtained in Twin Studies
The approach above is based on several assumptions:

1. No gene-environment interaction

Gene-environment interaction refers to cases in which an environmental factor may have a greater effect on some genotypes than on others, or in which a genotype may be expressed differently in some environments than in others. Gene-environment interaction can be detected using the model-fitting approach, if individuals can be scored for the presence or absence of a particular environmental variable. However, large sample sizes are needed (Neale and Cordon 1992). The effect of gene-environment interaction on the estimates is not at all clear, but will probably lead to underestimation of genetic and shared environmental effects.

2. No gene-environment correlation

Gene–environment correlation refers to a non-random distribution of environments among different genotypes, e.g. the individual's rearing environment is provided by the parents who are genetically related to the individual, and/or the individual creates an environment

which is a function of its genotype. A positive correlation will increase while a negative correlation will decrease estimates of all genetic components.

3. No assortative mating

Assortative mating (the tendency to 'like marrying like', either with respect to the trait under study or to a correlated trait) tends to increase the similarity of DZ twins relative to MZ twins and will therefore deflate estimates of genetic effects and inflate estimates of shared environment.

4. No epistasis

Epistasis (I) is non-additive genetic effects due to interaction between alleles at different loci. These genetic effects are perfectly correlated in MZ twins, whereas in DZ twins the correlation is $0 < k < 1/4$, depending on the number of genes involved. This type of genetic interaction could have been included in equations 12–14, but would have introduced two more unknown parameters (k, i). Epistasis tends to increase the similarity in MZ twins relative to DZ twins.

5. The equal environments assumption

The twin method assumes that a similarity greater between MZ than between DZ twins can be attributed to a greater genetic similarity alone and not in part to a greater environmental similarity (the 'equal environments assumption' [EEA]). In the case of an environmental similarity greater among MZ pairs than among DZ pairs, heritability estimates in studies of twins might be inflated. However, since both MZ and DZ twins share the same uterus at the same time, are of the same age, and are reared in the same family at the same time, it seems reasonable to assume an equal environment. In addition, studies of twins who have been misclassified showed that having been labelled as MZ or DZ had little effect on their behavioural similarity. Some studies, however, have found a need to control for possible environmental differences in MZ and DZ, because MZ twins spend more time together (e.g., Fabsitz *et al*. 1978). Others have found that MZ twins tend to be treated slightly more alike in childhood than DZ twins; but the question is, whether parents create or respond to differences in the twins. A further question is whether these environmental differences affect the trait under study (Plomin *et al*. 2001).

Limitations

It has been suggested that MZ twins have an increased incidence of certain diseases, such as cardiovascular diseases and Alzheimer's which could pose a potential threat to the validity of the twin method (Philips 1993; Räihä et al. 1996). Danish surveys among elderly twins have, however, shown similar patterns of general health for MZ and DZ twins (Christensen *et al*. 1996, 1999, 2000). These findings also agree with Danish and Swedish observations of similar mortality trajectories throughout adult life for MZ twins, DZ twins, and singletons (Vågerö and Leon 1994; Christensen *et al*. 1995), which suggests that twin studies of adult mortality can be generalized to the background population. Based on the fetal origins hypothesis which suggests that adverse intrauterine conditions increase the risk of cardiovascular diseases (Barker 1998), it could be expected that twins had an increased occurrence of cardiovascular diseases. However, a Danish study of more than 19,000 twins followed for more than 40 years showed similar death rates due to cardiovascular diseases in twins and singletons (Christensen *et al*. 2001).

As mentioned above, the twin approach described is based on a number of assumptions, some of which can be taken into account in more extensive twin analyses. In addition, when a specific model fits, it is not thereby proved that the hypothesis is correct in some ultimate sense: it only indicates that a given set of genetic and environmental assumptions adequately account for the data. Furthermore, the results relate to a particular population of genotypes at a specific time. Studies based on other types of relatives have their own as well as some of the above-mentioned assumptions and limitations.

Thus, all three types of studies, traditional family studies, adoption studies, and twin studies, have distinct assumptions and limitations that have to be taken into account in the interpretation of the data. However, a convergence of evidence from family, adoption, and twin studies provides a very convincing argument.

Life Duration Measurements in Heritability Studies

Studies of life duration can focus on different phenotypes from lifespan per se, early or late death to age-specific susceptibility to death ('frailty').

LIFESPAN

The most obvious individual life-duration measurement is lifespan. However, the heritability of lifespan can only be studied directly in cohorts born 100 years or more ago as the twin cohort has to be (at least nearly) extinct. In studies of lifespan one is usually interested in excluding the effect of sex and cohort from the calculations—the similarity in lifespan for e.g. two same-sexed twins that arises from the fact that the twins have the same sex and the same year of birth is not the focus. Therefore, in the calculation of the heritability of lifespan, the deviation from the sex and cohort specific mean is often used.

EARLY DEATHS

Early deaths (e.g., adult deaths before age 50 or 65) are of great concern because they represent a loss of many years of life and often have big social consequences. Based on the existence of several genetic diseases such as hypercholesterolemia that are associated with early-onset cardiovascular diseases, one may expect a stronger genetic component to early death compared to older ages. On the other hand, accidents may comprise a higher proportion of early deaths than later deaths, and this could reduce the genetic component.

LATE DEATHS

Late deaths (e.g. death after age 90 or 100) are of interest because they may be a marker of successful ageing. The existence of a few families with many extreme longlivers has facilitated the impression of a familial clustering of late deaths, but the data to document this is still very sparse. A prevailing assumption in gerontology is that the accumulation of unique environmental exposures during a long life is the key determinant of health at older ages and lifespan (Harris *et al*. 1992). Alternatively, evolutionary biologists have argued that there is less selective pressure against deleterious genetic mutations first expressed late

in life than against mutations expressed early in life. This hypothesis predicts an increase in genetic variance among the oldest (Charlesworth 1990).

AGE-SPECIFIC SUSCEPTIBILITY TO DEATH (FRAILTY)

It may seem more likely that age-specific susceptibility to death, rather than lifespan, is inherited. The concept of age-specific susceptibility can be modelled by using 'frailty models' (Vaupel *et al.* 1979). The frailty model is parameterized as follow:

Let $\mu(x, z)$ be the force of mortality for an individual at age x and with a 'frailty' of z. The inclusion of the variable z allows for individual differences in mortality rates. This 'frailty' variable is defined by the following relationship:

$$\mu(x, z)/\mu(x, z') = z/z' \tag{15}$$

or, alternatively,

$$\mu(x, z) = z \cdot \mu(x, 1) = z \cdot \mu_0(x) \tag{16}$$

An individual with a frailty of 1 might be called a 'standard' individual. Then, an individual with a frailty of 2 is twice as likely to die, at any particular age, as the standard individual; an individual with a frailty of $\frac{1}{2}$, on the other hand, is only one-half as likely to die. One of the advantages of the frailty model is that censored data can be used in the analyses: it is not necessary to use extinct cohorts in order to get heritability estimates of frailty. Furthermore, it provides opportunities for semiparametric analysis (Yashin and Iachine 1995).

Estimates of the Heritability of Human Lifespan Duration

LIFESPAN

Traditional Family Studies

Studies of relatives suggest that there is a within-family correlation in lifespan. However, studies have generally found only small correlations in lifespan between parents and offspring (0.01–0.15) (Pearl 1931; Cohen 1964; Wyshak 1978), whereas correlations between siblings tend to be higher (0.15–0.35) (Cohen 1964; Wyshak 1978). Heritability estimates based on regression analysis were in the range of 0.10–0.33 for parents–offspring and 0.33–0.41 for siblings, constant over a period of 300 years (Meyer 1991); but as mentioned these estimates comprise both genetic factors and shared environmental factors. Some family studies have found a stronger maternal than paternal effect (Abbott *et al*. 1974), but not all (Wyshak 1978). The lower correlation found for parents and offspring than for siblings suggests that genetic non-additivity (genetic effects due to gene interaction which are not passed from one generation to the next) is present, although it may also reflect a higher degree of shared environment among siblings than among parents and offspring, the latter being a comparison between two generations of people living under sometime very different conditions.

Twin Studies

Twin studies are designed to separate the effects of additive and non-additive genetic, as well as shared and non-shared environmental factors. However, most of the early twin studies had methodological problems due to left-truncation of the cohorts included, selection bias, lack of zygosity diagnosis, or heavy right-censoring. Carmelli and Andersen (1981) included a sample of 2,242 Mormon twin pairs born 1800–1899 in which both co-twins had died, corresponding to 60% of the original sample. Wyshak (1978) followed 972 Mormon twin pairs (possibly included in the study of Carmelli and Andersen) until death. Unfortunately, both studies lacked zygosity diagnosis, and so heritability estimates could not be provided. However, similarity in length of life was found—more pronounced for like-sexed twins (which include both MZ and like-sexed DZ twins) than for opposite-sexed twins (including only DZ twins)—suggesting genetic influences on lifespan. Jarvik *et al*. (1960) followed a sample of 853 twin pairs for 12 years including only pairs with at least one of the twins surviving to the age of 60. At the end of the follow-up period both co-twins had died out of only 35% of the twin pairs. The mean intra-pair difference in lifespan was found to be higher in DZ than in MZ twins suggesting genetic influences on lifespan. Hrubec and Neel (1981) followed a sample of 31,848 male twin veterans born 1917–27 for 30 years to ages 51–61. Around 10% were deceased at the time of analysis. To avoid censoring problems, longevity was analysed as a categorical variable (dead/alive), and heritability of 'liability' to death was estimated to be 0.5.

The first non-censored and population-based twin study that could provide an estimate of the magnitude of genetic influences on lifespan was conducted by McGue *et al*. (1993). A total of 600 Danish twin pairs born 1870–1880 was included. Using path analysis a heritability of 0.22 was found, with genetic influences being mainly non-additive. Later this study was expanded by Herskind *et al*. (1996) to include more than 2800 twin-pairs with known zygosity born 1870–1900. These cohorts were followed from age 15 to death. This study confirmed that approximately a quarter of the variation in lifespan in this population could be attributed to non-additive genetic factors while the remaining three-quarters were due to non-shared environmental factors (Figure 2).

Ljungquist *et al*. (1998) studied the 1886–1900 Swedish twin cohorts and concluded that a maximum of around a third of the variance in longevity is attributable to genetic factors. Hence, it seems to be a rather consistent finding in the Nordic countries that approx. 25% of the variation in lifespan is caused by genetic differences. It is interesting that animal studies have revealed similar estimates for a number of species not living in the wild (Curtsinger *et al*. 1995; Finch and Tanzi 1997).

EARLY AND LATE DEATHS

Both twin and adoption studies have demonstrated a substantial genetic component to premature death. The only larger adoption study published shows a correlation between Danish adoptees and their biological parents, especially for death due to infection and vascular causes. In contrast, death due to cancer appeared to be influenced by the family environment (Sørensen *et al*. 1988). A Swedish twin study showed that death from coronary heart diseases was influenced by genetic factors in both women and men but that the

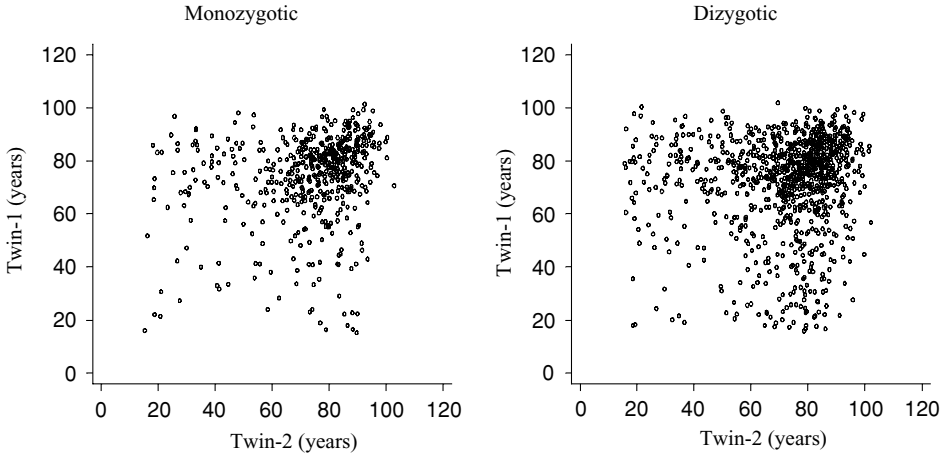

Figure 2. Lifespan for 2872 pairs of like-sex twins born in Denmark in the period 1870–1900. The raw correlation in lifespan for monozygotic twins was 0.19, while the corresponding number for dizygotic twins was 0.07. The mean difference in lifespan for MZ twins were 15.2 years and 18.2 years for dizygotic twins. The heritability of longevity was estimated to be 0.26 for males and 0.23 for females. (Herskind *et al*. 1996).

influence of genetic effects on cardiovascular mortality was strongest at younger ages (Marenberg *et al*. 1994).

There is some evidence that extreme longevity does cluster in some families: a few families with a high proportion of extreme longlivers have been identified, and results from a few studies suggest a modest 'recurrence risk' for exceptional longevity. Perls and co-workers found that the risk ratio of survival for siblings of centenarians versus siblings of 73-year-olds was about 4 for ages 80–94 (Perls *et al*. 1998). Kerber *et al*. (2001) also found, based on Mormon genealogies, an increased recurrence risk for siblings for surviving to extreme ages, although the estimate was somewhat lower than Perls'. Gudmundsson and colleagues (2000), using the population-based genealogy in Iceland, found that the first-degree relatives of the probands who live to an extreme old age ($\geq$95 percentile) are twice as likely as the controls to survive to the same age. However, as mentioned, such studies can only provide an upper limit for the heritability, because the clustering can be due to both genetic factors and family environment.

Twin studies of late death are hampered by the lack of data. Combining two rather rare events, twinning and late death, makes even the obtainable sample sizes in nationwide comprehensive twin registers such as the Danish and Swedish twin registry limited. Furthermore, Yashin and Iachine (1999) have demonstrated that changes in heritability with age can simply be an artefact of the bivariate survival relation between two twins. The size and possible impact of this artefact is, however, not clear. Based on the combination of

scarce data and potential methodological problems it is at present not certain whether the heritability of lifespan goes up, goes down, or stays the same with increasing age.

AGE-SPECIFIC SUSCEPTIBILITY TO DEATH (FRAILTY)

A frailty model applied to the Danish cohorts suggests that about 50% of the variation in human lifespan after age 30 can be attributed to survival attributes which are fixed for individuals by the time they are 30; a third to a half of this effect is due to genetic factors, and a half to two-thirds to non-genetic survival attributes (related to, for example, socioeconomic status or nutritional and disease history). The model suggests that the importance of survival attributes may increase with a person's life expectancy (Vaupel *et al*. 1998).

Iachine *et al*. (1998) used correlated frailty models of bivariate survival on more than 31,000 pairs of Danish, Swedish, and Finnish twins and found similar results for the three countries. The heritability of frailty, i.e. the age-specific susceptibility to death, was estimated to be approximately 50%.

Conclusion

The current evidence based primarily on Nordic contemporary populations suggests that approx. a quarter of the variation in adult lifespan can be attributed to genetic factors, i.e., the heritability of lifespan is about 25%. The age-specific susceptibility to death ('frailty') has a heritability of about 50%. It is to be expected that the heritability of 'frailty' is higher than the heritability of lifespan because it is more plausible that one inherits a 'frailty' or 'susceptibility' level than a fixed lifespan.

References

Abbott, M. H., Murphy, E. A., Bolling, D. R., and Abbey, H. (1974) "The familial component in longevity: A study of offspring of nonagenarians. II. Preliminary analysis of the completed study", *John Hopkin Medical Journal*, 134(1):1–16.

Akaike, H. (1987) "Factor analysis and AIC", *Psychometrika*, 52:317–332.

Barker, D. J. (1998) *Mothers, Babies, and Health in Later Life*. Edinburgh: Churchill Livingstone.

Carmelli, D., and Andersen, S. (1981) "A longevity study of twins in the Mormon genealogy", *Progress in Clinical and Biological Research*, 69 Pt C:187–200.

Charlesworth, B. (1990) "Mutation-selection balance and the evolutionary advantage of sex and recombination", *Genetic Research*, 55(3):199–221.

Christensen, K., Vaupel, J. W., Holm, N. V., and Yashin, A. I. (1995) "Mortality among twins after age 6: Fetal origins hypothesis versus twin method [see comments]", *British Medical Journal*, 310(6977):432–436.

Christensen, K., Holm, N. V., and Vaupel, J. W. (1996) "Alzheimer's disease in twins [letter; comment]", *Lancet*, 347(9006):976.

Christensen, K., Holm, N. V., McGue, M., Corder, L., and Vaupel, J. W. (1999) "A Danish population-based twin study on general health in the elderly", *Journal of Aging and Health*, 11:49–64.

Christensen, K., McGue, M., Yashin, A. I., Iachine, I. A., Holm, N. V., and Vaupel, J. W. (2000) "Genetic and environmental influences on functional abilities among Danish twins aged 75 years and older", *Journal of Gerontology: Series A Biological Sciences and Medical Sciences*, 55A(8): M446–M452.

Christensen, K., Wienke, A., Skytthe, A., Holm, N. V., Vaupel, J. W., and Yashin, A. I. (2001) "Cardiovascular mortality in twins and the fetal origins hypothesis", *Twin Research*, 4(5):344–349.

Cohen, B. H. (1964) "Family pattern of mortality and life-span", *Quarterly Review of Biology*, 39:130–181.

Curtsinger, J. W., Fukui, H. H., Khazaeli, A. A., Kirscher, A., Pletcher, S. D., Promislow, D. E., and Tatar, M. (1995) "Genetic variation and aging", *Annual Review of Genetics*, 29:553–575.

Fabsitz, R. R., Garrison, R. J., Feinleib, M., and Hjortland, M. (1978) "A twin analysis of dietary intake: Evidence for a need to control for possible environmental differences in MZ and DZ twins", *Behaviour Genetics*, 8(1): 15–25.

Falconer, D. S. (1989) *Introduction to Quantitative Genetics*. (3rd edn.) Essex: Harlow, Longman.

Finch, C. E., and Kirkwood, T. B. L. (2000) *Chance, Development, and Aging*. Oxford: Oxford University Presss.

Finch, C. E., and Tanzi, R. E. (1997) "Genetics of aging", *Science*, 278(5337):407–411.

Gudmundsson, H., Gudbjartsson, D. F., Frigge, M., Gulcher, J. R., and Stefansson, K. (2000) "Inheritance of human longevity in Iceland", *European Journal of Human Genetics*, 8(10):743–749.

Harris, J. R., Pedersen, N. L., McClearn, G. E., Plomin, R., and Nesselroade, J. R. (1992) "Age differences in genetic and environmental influences for health from the Swedish Adoption/Twin Study of Aging", *Journal of Gerontology*, 47(3):213–220.

Herskind, A. M., McGue, M., Holm, N. V., Sorensen, T. I., Harvald, B., and Vaupel, J. W. (1996) "The heritability of human longevity: A population-based study of 2872 Danish twin pairs born 1870–1900", *Human Genetics*, 97(3):319–323.

Hrubec, Z. and Neel, J. V. (1981) "Familial factors in early deaths: Twins followed 30 years to ages 51–61 in 1978", *Human Genetics*, 59(1):39–46.

Iachine, I. A., Holm, N. V., Harris, J. R., Begun, A. Z., Iachina, M. K., Laitinen, M., Kaprio, J., and Yashin, A. I. (1998) "How heritable is individual susceptibility to death? The results of an analysis of survival data on Danish, Swedish and Finnish twins", *Twin Research*, 1(4):196–205.

Jarvik, L., Falek A, Kallmann, F. J., and Lorge, I. (1960) "Survival trends in a senescent twin population", *American Journal of Human Genetics*, 12:170–179.

Kerber, R., O'Brien, E., Smith, K., and Cawthon, R. (2001) "Familial excess longevity in Utah genealogies", *Journal of Gerontology, A Biological Sciences Medical Sciences*, 56(3):B130–B139.

Ljungquist, B., Berg, S., Lanke, J., McClearn, G. E., and Pedersen, N. L. (1998) "The effect of genetic factors for longevity: A comparison of identical and fraternal twins in the Swedish Twin Registry", *Journal of Gerontology: Series A Biological Sciences*, 53(6): M441–M446.

Marenberg, M. E., Risch, N., Berkman, L. F., Floderus, B., and de Faire, U. (1994) "Genetic susceptibility to death from coronary heart disease in a study of twins", *New England Journal of Medicine*, 330(15):1041–1046.

McGue, M., Vaupel, J. W., Holm, N., and Harvald, B. (1993) "Longevity is moderately heritable in a sample of Danish twins born 1870–1880", *Journal of Gerontology*, 48(6): B237–B244.

Meyer, P. J. (1991) "Inheritance of longevity evinces no secular trend among members of six New England families born 1650–1874", *American Journal of Human Biology*, 3:49–58.

Neale, M. C., and Cardon, L. R. (1992) *Methodology for Genetic Studies of Twins and Families*. (1st edn.) Dordrecht: Kluwer Academic Publishers.

Neale, M. C. (1999) *Mx: Statistical Modeling*: (3rd edn.), Box 710 MCV, Richmond, VA: Department of Psychiatry.

Pearl, R. (1931) "Studies on human longevity IV. The inheritance of longevity", *Human Biology*, 3:245–269.

Perls, T. T., Bubrick, E., Wager, C. G., Vijg, J., and Kruglyak, L. (1998) "Siblings of centenarians live longer [letter]", *Lancet*, 351(9115):1560–1957.

Phillips, D. I. (1993) "Twin studies in medical research: Can they tell us whether diseases are genetically determined? [see comments]", *Lancet*, 341(8851):1008–1009.

Plomin, R., DeFries, J. C., McGuffin, P., and McClearn, G. E. (2001) *Behavioural Genetics*. (4th Ed.), New York: Freeman.

Räihä, I., Kaprio, J., Koskenvuo, M., Rajala, T., and Sourander, L. (1996) "Alzheimer's disease in Finnish twins", *Lancet*, 347(9001):573–578.

Sørensen, T. I., Nielsen, G. G., Andersen, P. K., and Teasdale, T. W. (1988) "Genetic and environmental influences on premature death in adult adoptees", *New England Journal of Medicine*, 318(12):727–732.

Vågerö, D., and Leon, D. (1994) "Ischaemic heart disease and low birth weight: A test of the fetal-origins hypothesis from the Swedish Twin Registry [see comments]", *Lancet*, 343(8892):260–263.

Vaupel, J. W., Manton, K. G., and Stallard, E. (1979) "The impact of heterogeneity in individual frailty on the dynamics of mortality", *Demography*, 16(3):439–454.

Vaupel, J. W., Carey, J. R., Christensen, K., Johnson, T. E., Yashin, A. I., Holm, N. V., Iachine, I. A., Kannisto, V., Khazaeli, A. A., Liedo, P., Longo, V. D., Zeng, Y., Manton, K. G., and Curtsinger, J. W. (1998) "Biodemographic trajectories of longevity", *Science*, 280(5365):855–860.

Wyshak, G. (1978) "Fertility and longevity in twins, sibs, and parents of twins", *Social Biology*, 25(4):315–330.

Yashin, A. I., and Iachine, I. A. (1995) "Genetic analysis of durations: Correlated frailty model applied to survival of Danish twins", *Genetic Epidemiology*, 12(5):529–538.

Yashin, A. I., and Iachine, I. A. (1999) "What difference does the dependence between durations make? Insights for population studies of aging", *Lifetime Data Analysis*, 5(1):5–22.

CHAPTER 12. MORTALITY AMONG THE LEAST FRAIL: LESSONS FROM RESEARCH ON THE APOE GENE

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Until recently, most research on the factors associated with mortality among adults was limited to the ages under 85. Now we find that mortality is declining rapidly over age 85 (Wilmoth *et al*. 2000) and the number of centenarians is increasing at a surprising rate. These trends have led to uncertainty about the prospects for further improvements in survival at the oldest ages. Recent research on health and mortality over age 85 suggests that the oldest-old may be different in many ways from the younger-old. Some of the physiological risk factors that are well established for those under age 85 may not work in the same way at the oldest ages. One reason for this is that survivors to the oldest ages are on average more robust (less frail) than average. That is, they have a lower frequency of risk factors for causes of premature mortality. Studying how risk factors change with age introduces several methodologically difficult issues. It requires new demographic and statistical approaches that model changes in the relative risks with age. It may also require different approaches to data collection and publication of results. Since few studies will be large enough to answer these questions, there is an increasing need for meta-analyses that combine data from numerous studies.

There are few risk factors that have been studied extensively through a wide range of adult ages. One such factor is the APOE gene which is the only gene known to have effects that are important at the population level (Ewbank 2001; Ewbank 2004). The APOE e4 allele is associated with excess risk of ischemic heart disease (Wilson *et al*. 1996) and Alzheimer's disease (Corder *et al*. 1993; Farrer *et al*. 1997) as well as with excess total mortality (e.g., Ewbank 2002; Tilvis, Strandberg, and Juva 1998). It is perhaps the most thoroughly studied genetic risk factor for chronic disease. For example, there are over 200 studies on the prevalence of the APOE e4 allele in different populations. There are also a number of studies of APOE and mortality which serve as a case study for the development of demographic models for research on risk factors among the oldest-old. In particular, APOE serves as a useful example of the way that unobserved heterogeneity can lead to changes in relative risks with age.

Data on genotype have certain advantages for developing demographic models. In particular, they are measured consistently at all ages; they don't change with age (although the expression of genes can change with age); and they are not affected by concurrent disease

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or disability (in contrast to activity levels and mood). Although genotype often interacts with environment, it may generally be easier to compare the effects of genotypes across populations than it is for many social characteristics.

Models developed for studying the effects of genes at the oldest ages can provide insights into the likely effects of other risk factors. For example, some non-genetic traits are fixed after a certain age such as sex, birth weight, childhood living conditions, and education. In addition, many behaviours change only rarely or have such long-lasting effects that changes can be ignored. For example, it may be that the characteristic of ever having been a smoker or having certain dietary tendencies (to eat meat, drink caffeinated beverages, etc.) could be usefully treated as fixed risk factors in some populations.

A second characteristic of APOE genotype as a risk factor is that there is no evidence of antagonistic pleiotropy in its effect among adults. In other words, there is no evidence that APOE genotypes have one effect on mortality among young adults and a different effect at older ages. It appears that the APOE e4 allele is a risk factor for chronic disease and excess mortality at all ages over age 40. There have not been any studies of differences in overall mortality by APOE genotype among younger adults. However, there are several studies showing strong associations of APOE genotype with the markers of coronary heart disease and risk factors for disease under age 40. For example, pathological indicators of atherosclerosis have been found to be associated with APOE genotype in men who died at ages 15–34 (Hixson 1991). APOE genotype was associated with several cardiovascular risk factors (such as total cholesterol and LDL cholesterol levels) in children aged 8–17 in the Bogalusa Heart Study (Srinivasan *et al*. 1996). In an Australian study, men under age 40 who were referred for coronary angioplasty were 16 times more likely to carry the riskiest APOE genotype (e4/4) than men in the general population (van Bockxmeer and Mamotte 1992).

In addition to serving as a model for the study of mortality at the oldest ages, research on APOE provides estimates of the amount of heterogeneity in the risk of death. The models described below provide several insights into the nature of heterogeneity and estimates of the amount of variation. Estimates of the magnitude and distributional form of heterogeneity can provide insights into the age pattern of mortality and the changing pattern of risks at the oldest ages.

The following section provides a brief summary of the literature on APOE as a risk factor for chronic disease and mortality. The second section outlines a demographic model of the effects of unobserved heterogeneity on relative risks of death. The model is applied to data on changes in APOE gene frequencies by age and prospective studies of mortality by genotype. It provides new estimates of the association of APOE with mortality and the amount of unobserved heterogeneity.

The final section discusses the implications of the estimates of unobserved heterogeneity for the age pattern of mortality, research on mortality trends and the degree to which centenarians are different from others. This leads to speculation about the nature of heterogeneity in the risk of death.

Table 1. Odds ratios by APOE genotype for the risk of ischemic heart disease (IHD) and Alzheimer's disease (AD).

	Odds ratio by APOE genotype			
	e3/3	**e3/4**	**e4/4**	**e2/3**
IHD	1.0	1.44		0.96
AD	1.0	2.7	12.5	0.6

Sources: IHD risks from Wilson *et al*. (1996); AD risks from Corder *et al*. (1993) and Farrer *et al*. (1997).

APOE and the Risk of Chronic Disease and Mortality

The APOE gene codes for apolipoprotein-E which plays a central role in lipid transport. It has three common polymorphisms labelled e2, e3, and e4.[1] Therefore, individuals have one of six possible genotypes: e2/2, e2/3, e2/4, e3/3, e3/4, or e4/4. The e3/3 is the most common genotype comprising about 60–70% in all populations. Table 1 presents estimates of the risks of ischemic heart disease (IHD) and Alzheimer's disease (AD) by APOE genotype. The e3/4 and e4/4 genotypes are associated with increased risk of both IHD (Wilson *et al*. 1996) and AD (Corder *et al*. 1993; Farrer *et al*. 1997).[2] The e2/2 and e2/3 genotypes are associated with reduced risk of AD. Heart disease and AD are both chronic diseases that are best studied through prospective research designs. Since APOE is an important risk factor for both IHD and AD, a number of epidemiological studies have examined mortality rates or AD incidence rates by APOE genotype.

The APOE gene frequency differs among populations (Gerdes 1992). The proportion of the population with the e3/4 genotype varies from 11% among Chinese to 40% among Nigerians. When combined with the large relative risks of ischemic heart disease and Alzheimer's disease associated with the e4 allele, this wide range has the potential to explain substantial differences in mortality across populations.

Stengård, Weiss, and Sing (1998) have compared the APOE gene frequencies and coronary heart disease (CHD) mortality rates for nine populations in the WHO MONICA Project. The populations include U.K. (Glasgow and Belfast), Finland (Kuopio and Turku-Loimaa), France (Strasbourg, Lille, and Toulouse), Iceland and China (Beijing). The CHD mortality rates for middle-aged men range from 50 per 100,000 to 400 per 100,000; the APOE e4 allele frequency ranged from 7% to 20%. The variation in the frequency of the e4 across these populations explains about 75% of the variation in CHD mortality. This is much higher than the proportions explained by differences in average serum total cholesterol

[1] There are numerous other mutations of the APOE gene (Fullerton *et al*. 2000). However, there has been no research examining the effects of these mutations.

[2] The e4 allele is associated with an increased risk of ischemic heart disease in both sexes (Wilson 1996). However, its role in mortality to ischemic heart disease is less clear in females than in males.

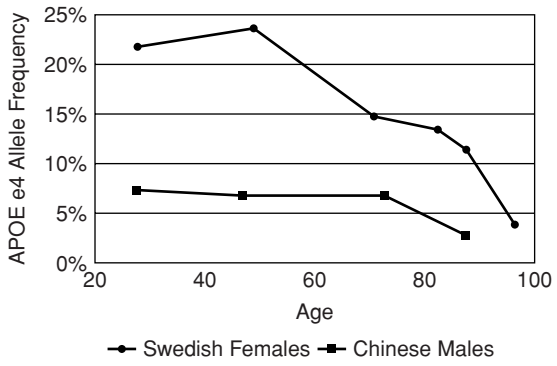

Figure 1. APOE e4 allele frequencies by age, Swedish females and chinese males.

(33%), variations in average systolic blood pressure (15%), and the average body mass index (18%) in univariate comparisons. Differences in smoking rates and diastolic blood pressure did not explain any of the variance. In their analysis, Stengård *et al*. also found that controlling for differences in the frequency of the e2 allele did not help to explain CHD mortality differences once the e4 allele frequency was controlled.

Evidence of excess mortality associated with the e4 allele also comes from cross-sectional studies in several countries that have examined changes in the APOE allele frequencies by age. The data are strongly suggestive of substantial differences in survival by APOE genotype. Figure 1 shows data from Sweden (Corder *et al*. 1996; Eggersten *et al*. 1993) and a Chinese population (Jian-Gan *et al*. 1998). The Swedish data show noticeable declines in the e4 frequency after age 60.[3] The decline becomes noticeable in China at an older age.

Data from Denmark provide some evidence that the e4 allele may not be an important risk factor for mortality at extreme ages. Gerdes *et al*. (2000) report no decline in the e4 allele frequency between those aged 100 (7.2%) and those aged 105 (10.5%). Although the study included only 19 individuals aged 105, the lack of a decline in the e4 allele frequency is impressive given the very high mortality rates among centenarians. Gerdes *et al*. also review the evidence on APOE and mortality from numerous other studies, but they made no attempt to compare or combine the estimates of relative risks derived from different studies.

Prospective Studies of Overall Mortality

Prospective studies of mortality by genotype provide direct information about mortality differentials. However, even many very large cohort studies have limited power to detect mortality differences by genotype. Although most studies of mortality by APOE genotype

[3] The first three data points are from Eggersten *et al*. (1993), the latter three from Corder *et al*. (1996). Corder *et al*. do not provide the frequency of the e4/4 genotype by age. However, the decline in the e4 allele frequency is not sensitive to assumptions about the number of individuals with the e4/4 genotype.

show excess mortality associated with the e4 allele, the observed differences often do not reach statistical significance. For example, Skoog *et al*. (1998) found differences for a Swedish cohort of 85-year-olds that were not significant. Similarly, Fillenbaum *et al*. (2000) studied a population in North Carolina and found differences in the right direction that were not significant. Lee *et al*. (2001) report that in Hispanics and white non-Hispanics there was reduced mortality associated with the e2 allele, but no higher mortality associated with the e4 allele. Juva *et al*. (2000) report higher mortality for e4 carriers in a sample of individuals over age 85 in Finland. However, once again the difference was not significant.

Several studies suggest that the effect of the e4 allel may decline with age. Tilvis, Strandberg, and Juva (1998) provide data on survival by APOE genotype for three cohorts in Finland. These data suggest that the risk associated with the e4 allele declines with age. For those initially aged 75, the relative risk for the e4 was 1.85 (95% C.I.: 1.06–3.21). This declined to 1.52 (1.07–2.14) for those initially aged 80 and to 0.98 (0.74–1.30) for those aged 85. Although the observed decline with age is not significantly different, the decline is consistent across the age groups. Some of this decline is attributable to the fact that the odds ratio is probably based on a larger proportion of e4/4 carriers at the younger ages. A similar decline in the risk associated with e4 is shown by Vogt, Cauley, and Kuller (1997). They report a relative risk for the e4 allele of 2.0 (1.1–4.0) among American women aged 65–69 compared to 1.1 (0.7–1.7) among those aged 70–93. The decline with age is even stronger for the relative risk of death to cardiovascular diseases: from 2.8 (1.0–8.3) to 0.8 (0.4–1.7). Corder *et al*. (1996) found differences by genotype in Sweden that were significant among those over age 85, but not significant among those aged 75–84.

Demographic Estimates of the Association of APOE Genotype with Mortality

To examine the association of APOE with longevity, we need to estimate life tables for cohorts of individuals with each genotype. We can estimate mortality by APOE genotype by fitting a demographic multi-state model to both the data on APOE genotype by age from cross-sectional studies and the data from longitudinal studies on survival by genotype. The model, an extension of the "RR" method proposed by Yashin *et al*. (1999), is described in detail in Ewbank (2002). It is fitted by maximizing the likelihood of observing all of the available data, including cross-sectional and longitudinal data from numerous studies.

The RR model is extended in four major ways. First, it is fitted to data from fourteen studies in seven countries (Denmark, Finland, France, Italy, the Netherlands, Sweden, and the U.S.) rather than to data from a single population. Therefore, it functions much like a meta-analysis in summarizing the results of numerous studies.

Second, rather than using a current life table, the model uses different life tables for each cohort in each population. This is important since the change in e4 allele frequency depends both on the relative risks associated with the genotypes and on the level of mortality. The differences in the proportion surviving to each age are a result of differences in the cumulated mortality rates. In particular, the ratio of the population with e3/4 genotype to

the e3/3 population at age x is:

$$\frac{{}^{3/4}\mathrm{l}_x}{{}^{3/3}\mathrm{l}_x} = \frac{b_{3/4}\mathrm{e}^{-\int \mu_{\mathrm{y},3/4}\mathrm{dy}}}{b_{3/3}\mathrm{e}^{-\int \mu_{\mathrm{y},3/3}\mathrm{dy}}} = \frac{b_{3/4}}{b_{3/3}}\mathrm{e}^{-\int (\mu_{\mathrm{y},3/4}-\mu_{\mathrm{y},3/3})\,\mathrm{dy}}$$

where $b_{3/4}$ and $b_{3/3}$ are the numbers born into the population with each genotype. If the gene frequencies at birth remain constant across cohorts, differences across ages (cohorts) depend solely on the cumulative difference between the mortality rates for the two genotypes, $\mu_{3/4}$ and $\mu_{3/3}$. Since the oldest cohorts have generally experienced higher mortality rates at each age, they will have experienced a larger decline in their e4 allele frequencies. Using the appropriate cohort life tables rather than a recent period life table changes the estimated relative risks for e2/3 and e3/4 by about 5%. Although this is well within the confidence intervals for the estimates, it is an avoidable bias.

Third, the model is fitted to data from both cross-sectional and longitudinal data sets. Longitudinal studies provide important information about the relative risks at specific ages and therefore provide a firm basis for estimation of the amount of unobserved heterogeneity. The estimation includes longitudinal data on almost 6,000 individuals including data for about 1,500 over the age of 85.

Finally, the model incorporates the effects of heterogeneity of risk. This turns out to be very important. APOE is not the only difference among individuals that affects their survival chances. Those individuals with the e4/4 genotype who survive to the oldest ages probably have other characteristics that countered the excess risk associated with the e4/4 genotype. As mortality weeds out those with the highest risks within each genotype, the relative risks associated with each genotype move towards 1.0.

Demographers use the word "frailty" to denote the combined effect of all of the characteristics of an individual that affect their risk of death (or other adverse outcome). Since it is not possible to measure all of the factors that affect risk, it is not possible to measure an individual's frailty. Therefore, we assume a functional form for the distribution of frailty in a population. When studying the effects of a number of measured characteristics (such as education or genotype), the distribution applies to the combined effects of all unmeasured risk factors. Then it is possible to control statistically for the effects of all unmeasured characteristics.

Yashin *et al*. (1999) suggest a model based on functional forms for the age pattern of mortality (usually a Gompertz curve) and for the distribution of frailty (often a gamma distribution). I have tested two models that do not require assumptions about the age pattern of mortality. Both models are based on the assumption of proportional hazards. The mortality rate, $\mu_{i,x}$, of individuals at age x with a given level of frailty is a constant multiple of the rate among individuals with a frailty of 1. That is:

$$\mu_{i,x} = \mu_{1,x} z_i$$

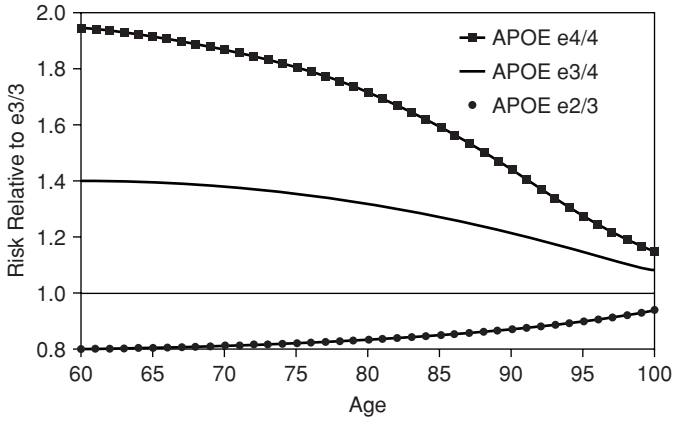

Figure 2. Estimates of the relative risks of death associated with APOE e2/3, e3/4 and e4/4 genotypes relative to genotype e3/3, by age, Swedish females born 1890–1894.

Following Manton, Stallard, and Vaupel (1986) I have tested models that assume that z is distributed according to either a gamma distribution or an inverse Gaussian distribution using a general family of distributions that encompasses both the gamma and the inverse Gaussian. This model shows that within a wide range of distributions of frailty, the data are most consistent with a model that is virtually identical to the gamma distribution and significantly different from the inverse Gaussian (Ewbank 2002).

I have fitted the model to gene frequencies and prospective mortality estimates from 14 cohorts of European origin (Ewbank 2004). Figure 2 shows the estimates of relative risk for the e2/3, e3/4 and e4/4 genotypes relative to the e3/3 for Swedish females born in 1900 based on a gamma distribution of frailty.[4] The APOE genotype is associated with large differences in mortality at the middle and older ages. The e3/4 genotype is associated a risk of death that is 1.40 times as high as the e3/3 genotype at ages 65–69 (95% confidence interval: 1.25–1.61). The relative risk for the e4/4 is not significantly different from the square of the risk for the e3/4, 1.95. The relative risk associated with e4/4 drops to about 1.69 at age 80 and to 1.15 at age 100. The risk for the e3/4 is only 1.08 at age 100. Since very few e4/4 survive to age 100 and the relative risks have declined, the effect of APOE genotype on mortality has virtually disappeared among centenarians.

[4] The model provides estimates of the relative risks at the youngest ages for the e2/3 and e3/4 genotypes relative to the e3/3 genotype and the coefficient of variation in frailty. The rare e2/2 is combined with the e2/3 and the e2/4 with the e3/3. I have assumed that at age 60 the relative risk associated with the e4/4 genotype is the square of the relative risk for the e3/4 genotype. This assumption has been tested using likelihood ratio tests (Ewbank 2002). Between ages 20 and 60 the relative risks change to reflect the increasing importance of IHD as a cause of death (Ewbank 2004).

Extensive analyses reveal no significant differences in the parameter estimates across populations or by sex. For example, there is no evidence that at age 60 the excess mortality among the e3/4 genotype differs between men and women or between Scandinavia and France and Italy.

If frailty is distributed according to a gamma distribution after age 60 (as these data suggest), then the relative risk at age x for genotype j relative to genotype 1 is

$$r_{j,x} = r_{j,60} \frac{1 + \gamma^2 \int_{60}^{x} \lambda(t)\, dt}{1 + r_{j,60}\gamma^2 \int_{60}^{x} \lambda(t)\, dt}$$

where $\lambda(t)$ is the baseline mortality rate for individuals with mean frailty among those with APOE genotype e3/3 and γ is the coefficient of variation at age 40. The model leads to an estimated coefficient of variation in frailty of 0.52 (95% C.I. of 0.29–0.73) within each APOE genotype.

In populations with higher mortality rates over age 60, that is, higher values of $r_{j,60}$, the relative risks will decline more rapidly. For example, Figure 3 shows the estimated relative risks for the e3/4 genotype for two cohorts. It also includes the relative risks that would occur if the 1995–1999 life table for Swedish females remained constant for the lifetime of a cohort. The model assumes that all populations have the same relative risks at age 60. The differences by sex and cohort in the level of mortality lead to differences in the relative risks at later ages. The relative risk at age 85 for males born in 1890–1894 is

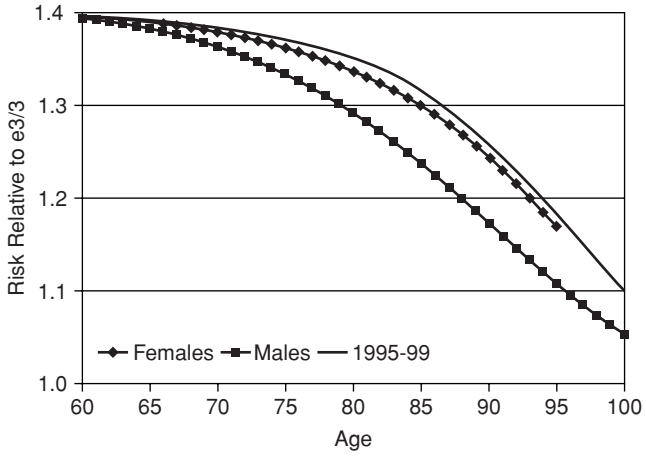

Figure 3. Estimated relative risks of death for APOE e3/4 genotype relative to the e3/3 genotype based on Swedish cohorts of men born in 1890–1894 and women born in 1910–1914 and the life table for Swedish females in 1995–1999.

1.24 compared to 1.28 for females in the cohort of 1910–1914. The life table for Swedish females in 1995–1999 would lead to a relative risk of 1.32 at age 85.

APOE and the Variation in Mortality and Longevity

The usual summary measure of mortality is the value of life expectancy at a given age, e_x. Life expectancy varies by APOE genotypes at every age (Ewbank 2004). However, e_x does not adequately capture either the concept of longevity or the contribution of a factor to variation in age at death. Longevity is better measured by the age beyond which only 1% of the population survives. Since ω is often used as the highest or oldest age, we can use the second to last letter in the Greek alphabet, ψ, to denote the age at which only 1% are still alive. If we ignore infant, child and adolescent mortality, we can define ψ_{20} as the age at which ${}_{(x-20)}p_{20}$, the survival rate from age 20 to age x, is equal to 0.01. Differences in ψ_{20} by APOE genotype would then indicate the contribution of APOE to longevity among adults.

The estimates of ψ_{20} for the Swedish cohort born in 1890–1894 show substantial differences in longevity by APOE genotype (Table 2). Among men, ψ_{20} is 6.5 years lower for the e4/4 genotype than for the e2/3 genotype. Among women, the difference is 6.0 years. The differences between genotypes are larger than the differences by sex (3.0 years).

APOE and the Variation in the Age at Death

Despite large differences in longevity among genotypes, APOE explains only a small fraction of the variation in age at death among individuals in a given population. For example, for the cohort born in Denmark in 1895–1899 APOE genotype explains only about 0.9% of the variation among individuals in age at death over age 15 and 1.8% of the variation over age 50 (Ewbank 2004). There are two reasons for this. First, the extreme survival differences are between the rarest genotypes. Even though the e4 allele is more common in Denmark than in most European populations, about 81% of the population at age 20 is e3/3 or e3/4. Second, there is a large overlap between the distributions of age at death within each cohort. Some individuals with the e2/2 genotype die before age 20 and some with the e4/4 genotype survive to 90.

Herskind *et al*. (1996) estimated from twin data from Denmark that about 25% of the variation in age at death after age 15 is attributable to genetic differences. Therefore, about 3.5% of the variation attributable to genetics can be ascribed to APOE (Ewbank 2004).

Table 2. The age to which only 1% survive from age 20, Swedish cohort born in 1890.

Sex	Age at which only 1% of those alive at age 20 are still alive			
	e2/3	e3/3	e3/4	e4/4
Males	97.8	96.4	93.9	91.3
Females	100.7	99.4	97.1	94.7

Effect of Heterogeneity on Observed Trends in Mortality

The estimated amount of heterogeneity is based on the assumptions of the model. In particular, the model assumes that for individuals with a given level of frailty the effects of APOE genotype are constant across all ages over age 60. Although this is a relatively strong assumption, the estimate of frailty appears to be quite plausible. First, the implied distribution in frailty is very consistent with a gamma distribution, which has been assumed by many writers to be reasonable. Second, the lack of significant differences in the effect of APOE across populations with very different levels of cardiovascular mortality (e.g., Italian females and Finnish males) suggests that the effect of APOE on mortality is not limited to one cause of death which varies in importance across ages.

A third approach to considering the plausibility of the estimated amount of variation is to calculate the implications of this estimate for trends in mortality by level of frailty. Vaupel, Manton, and Stallard (1979) noted that in the presence of heterogeneity, trends in mortality rates understate the declines in the mortality rate of individuals. The mean frailty of survivors changes with age according to the formula:

$$\bar{z}_x = \frac{\bar{z}_0}{1 + \gamma^2 \int \lambda(t)\, dt}$$

where $\bar{z}_x$ is the mean frailty of survivors to age x, γ is the coefficient of variation in frailty, and $\lambda(t)$ is the mortality rate for the index frailty at age t. Therefore, the mean frailty declines as cumulative mortality increases with age. Then the mortality rate at age x of an individual with average frailty is higher than the mortality rate of the average survivor to age x. Reductions in mortality tend to save the lives of individuals with relatively high frailty. In other words, the difference between the mean frailty of survivors and the mean frailty at birth declines. Therefore the rate of mortality decline in the total population is smaller than the rate of decline among individuals with average frailty. We can use the equation for the mean frailty of survivors to calculate the mortality rate at any age for individuals of a given level of (relative) frailty. If the estimate of γ is too large, the rate of decline will be implausibly large.[5]

Table 3 presents estimates of the decline in ${}_5M_{80}$ and ${}_5M_{90}$ between the Swedish cohorts born 1890–1894 and 1908–1910. The declines estimated for the baseline hazard rates are more rapid than for the population as a whole. For example, the mortality rate at ages 80–85 among Swedish males declined at an annual rate of about 1.2% per year between the cohorts born in 1898–1902 and those born in 1908–1910. This corresponds to mortality declines during the 1980s. However, for individuals with a given level of frailty mortality declined by 1.5% per year. At age 90–95 the reported decline was 0.1% per year whereas the decline for individuals with a given level of frailty was 0.5% per year. The rates of decline for individuals of fixed frailty are reasonable. This suggests that the estimate of γ derived from the model of APOE and mortality are not implausibly large.

[5] For this calculation, the value of γ must include both variation in mortality by APOE genotype and other (unobserved) heterogeneity

Table 3. Mortality reductions between Swedish cohorts born in 1890–1894, 1898–1802, and 1908–1910 with estimated declines for individuals of average frailty, by sex for ages 80–85 and 90–95.

	Annual average rate of decline in mortality			
	Males		Females	
Age group, cohorts	Actual	Individuals with mean frailty	Actual	Individuals with mean frailty
80–85, 1890–1894 to 1898–1902	0.5%	0.7%	1.8%	2.2%
80–85, 1898–1902 to 1908–1910	1.2%	1.5%	1.5%	1.8%
90–95, 1890–1894 to 1898–1902	0.1%	0.5%	0.3%	1.0%

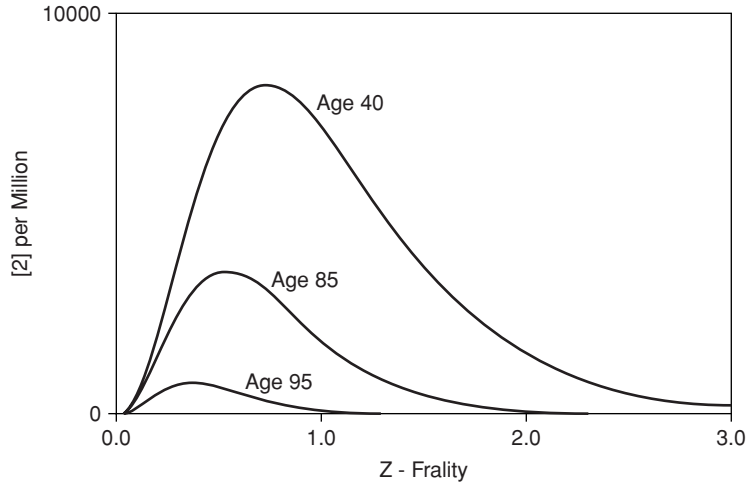

Figure 4. The estimated distribution of frailty at age 40 and among survivors to ages 85 and 95 among one million individuals alive at age 40, Swedish females born 1890–1894.

The Distribution of Frailty among Survivors to the Oldest Ages

Figure 4 shows the distribution of frailty among the survivors of one million individuals alive at age 40 among Swedish females born in 1890–1890.[6] The 30% of individuals still alive at age 85 have a mean frailty that is 71% of the mean at age 40. By age 100 less than 1% of those alive at age 40 are still alive. They have a mean frailty that is 39% of the mean

[6] The life table was derived from period mortality rates from the Berkeley Mortality Database (http://www.mortality.org/).

at age 40. This low level of frailty among survivors to age 100 is what underlies the effect of unobserved differences in mortality on studies of risk factors for death and disease.

Implications of Heterogeneity for the Age Pattern of Mortality

The estimates presented here do not depend on an assumed age pattern of mortality—only on an assumed distribution of frailty. Therefore, we can explore the implications of the frailty estimate for the age pattern of mortality among individuals of a given frailty. The age pattern of mortality is best described using the LAR, the rate of increase in the log of the mortality rate with age. Figure 5 plots the LAR for Swedish females born in 1890–1894. At age 65 the LAR for the cohort is 0.091. It then increases to about 0.106 at age 73 when it starts declining slowly to 0.073 at age 100.

Figure 5 also shows the LAR for the same cohorts for individuals with a given frailty. The LAR starts slightly higher than the curve for the population. It then increases rather consistently to 0.13 at age 98. This age pattern for individuals of a given frailty does not match the Gompertz curve which has a constant LAR.

Implications for Research on Other Risk Factors at the older Ages

The study of APOE as a risk factor for mortality leads to several conclusions that are generalizable to other risk factors. First, the effects of traits fixed at young ages on relative risks for all-cause mortality are apt to change the relative risks for any risk factor after about age 85. Even characteristics with moderate relative risks (like APOE e3/4) can be affected by unobserved heterogeneity. For characteristics associated with relative risks in

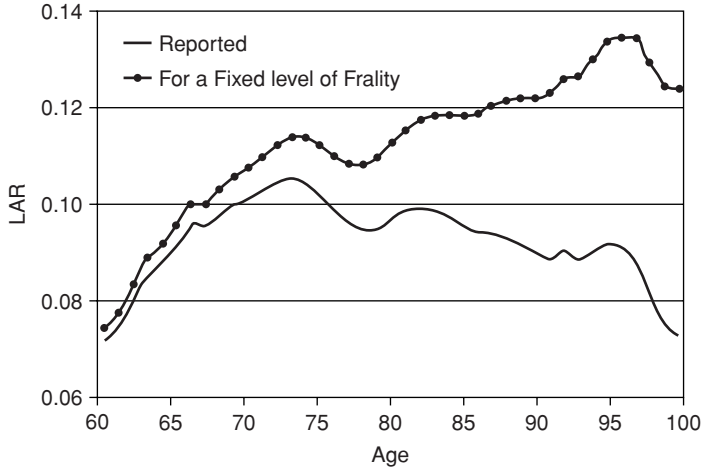

Figure 5. The rate of increase in the log of the mortality rate with age (LAR) for the cohort of females born in Sweden in 1890–1894 and the estimated values for individuals of a fixed level of frailty.

the range of 2 or more, heterogeneity becomes important for all-cause mortality by age 70. Higher relative risks and effects on more common conditions would cause the effects of frailty to become apparent at even younger ages.

Research on risk factors for mortality should therefore consider the possible effects of unobserved differences in frailty. One way to incorporate changing risk ratios would be to include interactions of each covariate with age in logistic regressions or Cox regressions. However, this is inefficient since it does not incorporate the fact that the changes in the risk ratios for different risk factors are all affected by the same unobserved heterogeneity. In addition, the decline in the relative risks is not linear. An alternative would be to develop simple models based on Equation (1). However, it requires a substantial amount of data over a wide age range to estimate the amount of unobserved heterogeneity. Therefore, it may be necessary to apply Bayesian estimation procedures that incorporate prior expectations about the value of γ.

A second conclusion suggested by the APOE example is that the gamma distribution of frailty appears to fit better than the inverse Gaussian. Although this conclusion must be considered preliminary until it is verified by similar studies of other risk factors, the strength of the evidence for the gamma distribution is surprisingly strong. At a minimum, this research suggests that changes in relative risks with age can provide important information about the nature of unobserved heterogeneity.

A third conclusion, is that data on mortality by genotype (or other risk factors) should be published for relatively small age groups (e.g., five year age groups) even if the sample sizes get small. This provides important information about changes in the age pattern of risk which reflect heterogeneity. The same is true for cross-sectional data on the prevalence of risk factors at the oldest ages. The importance of data for small age groups increases with the option of using models similar to those presented here which produce meta-analytic type estimates.

This research suggests new lines of research into the effects of risk factors for mortality at the oldest ages. By combining data from numerous studies (with appropriate tests for homogeneity of effects), it is possible to clarify the exact nature of the changes in relative risks with age and to gain insights into the nature of heterogeneity. This type of research could provide important insights into the risks associated with other fixed characteristics such as education, childhood environment, and pregnancy histories.

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References

Corder, E. H., Saunders, A. M., Strittmatter, W. J., Schmechel, D. E., Gaskell, P. C., Small, G. W., Roses, A. D., Haines, J. L., and Pericak-Vance, M. A. (1993) "Gene dose of apolipoprotein E type 4 allele and the risk of Alzheimer's disease in late onset families", *Science*, 261(5123):921–923.

Corder, E. H., Lannfelt, L., Viitanen, M., Corder, L. S., Manton, K. G., Bengt, W., and Hans, B. (1996) "Apolipoprotein E genotype determines survival in the oldest old (85 years or older) who have good cognition", *Archives of Neurology*, 53(5):418–422.

Eggertsen, G., Tegelman, R., Ericsson, S., Angelin, B., and Berglund, L. (1993) "Apolipoprotein E polymorphism in a healthy Swedish population: variation of allele frequency with age and relation to serum lipid concentrations", *Clinical Chemistry*, 39(10):2125–2129.

Ewbank, D. C. (2001) "Demography in the age of genomics: A first look at the prospects". In Finch: C. E., Vaupel, J. W., and Kinsella, K. (eds.), *Cells and Surveys*. Washington, D.C.: National Academy Press, pp. 64–109.

Ewbank, D. C. (2002) "Mortality differences by APOE genotype estimated from demographic synthesis", *Genetic Epidemiology*, 22(2):146–155.

Ewbank, D. C. (2004) "The APOE gene and differences in life expectancy in Europe", *Journal of Gerontology: Series A Biological Science and Medical Science*, 59A(1):8–12.

Farrer, L. A., Cripples, L. A., Haines, J. L., Hyman, B., Kukull, W. A., Mayeux, R., Myers, R. H., PericakVance, M. A., Risch, N., van Duijn, C. M., and APOE and Alzheimer Disease Meta Analysis Consortium (1997) "Effects of age, sex, and ethnicity on the association between apolipoprotein E genotype and Alzheimer disease", *JAMA*, 278(16):1349–1356.

Fillenbaum, G. G., Landerman, L. R., Blazer, D. G., Saunders, A. M., Harris, T. B., and Launer, L. J. (2001) "The relationship of APOE genotype to cognitive functioning in older African-American and Caucasian community residents", *Journal of the American Geriatrics Society*, 49(9):1148–1155.

Fullerton, S. M., Clark, A. G., Weiss, K. M., Nickerson, D. A., Taylor, S. L., Stengård, J. H., Salomaa V., Vartiainen, E., Perola, M., Boerwinkle, E., and Sing, C. F. (2000) "Apolipoprotein E variation at the sequence haplotype level: Implications for the origin and maintenance of a major human polymorphism", *American Journal of Human Genetics*, 67(4):881–900.

Gerdes, L. U., Klausen, I. C., Sihm, I., and Færgeman, O. (1992) "Apolipoprotein E polymorphism in a Danish population compared to findings in 45 other study populations around the world", *Genetic Epidemiology*, 9:155–157.

Gerdes, L. U., Jeune, B., Ranberg, K. A., Nybo, H., and Vaupel, J. W. (2000) "Estimation of Apolipoprotem E genotypespecific relative mortality risks from the distribution of genotypes in centenarians and middle-age men: Apolipoprotein E gene is a 'frailty gene', not a 'longevity gene"', *Genetic Epidemiology*, 19(3):202–210.

Hixson, J. E. (1991) "Apolipoprotein E polymorphisms affect atherosclerosis in young males. Pathobiological Determinants of Atherosclerosis in Youth (PDAY) research group", *Arteriosclerosis and Thrombosis*, 11(5):1237–1244.

Jian-Gang, Z., Yong-Xing, M., Chuan-Fu, W., Pei-Fang, L., Song-Bai, Z., Nui-Fan, G., Guo-Yin, F., and Lin, H. (1998) "Apolipoprotin E and longevity among Han Chinese population", *Mechanisms of Ageing and Development*, 104:159–167.

Juva, K., Verkkoniemi, A., Viramo, P., Polvikoski, T., Kainulainen, K., Kontula, K., and Sulkava, R. (2000) "APOE epsilon 4 does not predict mortality, cognitive decline, or dementia in the oldest old", *Neurology*, 54(2):412–415.

Lee, J. H., Tang, M. X., Schupf, N., Stern, Y., Jacobs, D. M., Tycko, B., and Mayeux, R. (2001) "Mortality and apolipoprotein e in Hispanic, African-American, and Caucasian elders", *American Journal of Medical Genetics*, 103(2):121–127.

Manton, K. G., Stallard, E., and Vaupel, J. W. (1986) "Alternative models for the heterogeneity of mortality risks among the aged", *JASA*, 81(395):635–644.

Skoog, I., Hesse, C., Aevarsson, O., Landahl, S., Wahlstrom, J., Fredman, P., and Blennow, K. (1998) "A population study of apoe genotype at the age of 85: Relation to dementia, cerebrovascular disease, and mortality", *Journal of Neurology, Neurosurgery and Psychiatry*, 64(1):37–43.

Srinivasan, S. R., Ehnholm, C., Wattigney, W. A., Bao, W., and Berenson, G. S. (1996) "The relation of apolipoprotein E polymorphism to multiple cardiovascular risk in children: The Bogalusa Heart Study", *Atherosclerosis*, 123(1–2):33–42.

Stengård, J. H., Weiss, K. M., and Sing, C. F. (1998) "An ecological study of association between coronary heart disease mortality rates in men and the relative frequencies of common allelic variations in the gene coding for apolipoprotein E", *Human Genetics*, 103(2):234–41.

Tilvis, R. S., Strandberg, T. E., and Juva, K. (1998) "Apolipoprotein E phenotypes, dementia and mortality in a prospective population sample", *Journal of the American Geriatrics Society*, 46(6):712–715.

van Bockxmeer, F. M., and Mamotte, C. D. (1992) "Apolipoprotein E4 homozygosity in young men with coronary heart disease", *Lancet*, 340(8824):879–880.

Vaupel, J. W., Manton, K. G., and Stallard, E. (1979) "The impact of heterogeneity on individual frailty on the dynamics of mortality", *Demography*, 16:439–454.

Vogt, M. T., Cauley, J. A., and Kuller, L. H. (1997) "Apolipoprotein A phenotype, arterial disease, and mortality among older women: The study of osteoporotic fractures", *Genetic Epidemiology*, 14(2):147–156.

Wilson, P. W. F., Schaefer, E. J., Larson, M. G., and Ordovas, J. M. (1996) "Apolipoprotein E alleles and risk of coronary disease: A meta-analysis", *Arteriosclerosis, Thrombosis, and Vascular Biology*, 16:1250–1255.

Wilmoth, J. R., Deegan, L. J., Lundrstrom, H., and Horiuchi, S. (2000) "Increase of maximum life-span in Sweden, 1861–1999", *Science*, 289(5488):2366–2368.

Yashin, A. I., De Benedictis, G., Vaupel, J. W., Tan, Q., Andreev, K. F., Iachine, I. A., Bonafe, M., DeLuca, M., Valensin, S., Carotenuto, L., and Franceschi, C. (1999) "Genes, demography and life span: The contribution of demographic data in genetic studies of aging and longevity", *American Journal of Human Genetics*, 65:1178–1193.

Section 4

Sex, Gender, and Social Determinants and Consequences of Mortality

SECTION 4. SEX, GENDER, AND SOCIAL DETERMINANTS AND CONSEQUENCES OF MORTALITY

The next section starts with a chapter on the social determinants of mortality. Indeed in the first part of Chapter 13, Marja Jylha and Tiina Luukkaala discuss the theoretical perspectives and empirical findings concerning social factors as determinants of longevity. The most convincing evidence of the importance of social factors is the gradient for higher mortality with lower socioeconomic position. Recently, the concept of "allostatic load" has been provided to explain how relative deprivation translates into physiological deregulation and higher mortality. In the second part of the chapter, the authors focus on the oldest-old. The analyses and the comparison of two population-based samples of very old people, the Tampere Longitudinal Study on Ageing (TamELSA) and the Vitality 90+ Study, indicate that basically the same social factors predict the length of future life both at young and at very old ages. According to the authors, in order to better understand the influence of social factors, we need to have a better comprehension of the processes of the social life course and a better knowledge of how the consequences of relative positions in society are translated into physiological processes.

In the following chapter (Chapter 14), John Wilmoth and Mike Dennis examine mortality differentials related to social or environmental origin, according to a number of social categories: marital status, education, income, occupation, place of birth, race and ethnicity, and place of residence. These categories represent the most important dimensions of social stratification. In this chapter, the authors summarize the key results and the main controversies from studies of differential mortality in the United States. This includes explanations of differentials by marital status, trends in differentials by education and income, effects of specific occupation on mortality risks, differentials by place of birth, existence of differentials by race or ethnicity, the Black-White mortality crossover, the role of socioeconomic status in racial or ethnic differential and even the effects of place of residence.

Jacques Vallin explores the mortality differentials related to gender in the next chapter (Chapter 15). Women live on average longer than men. Excess male mortality is observed at all ages in developed countries but its intensity varies greatly. The typical age pattern of the male/female mortality ratio observed in many countries has two peaks. The first, around age 20, is very high and almost entirely due to violent deaths (in particular road traffic accidents involving two-wheeled vehicles) but has only a slight influence on the differential in life expectancy. The second peak, observed between ages 55 and 75, is responsible for most of the differential in life expectancy at birth. It is probably mainly due to behavioural factors. Relative excess male mortality is known to be much lower among the oldest-old. But what is the precise situation after age 80? At first, the

author shows a sharp increase in excess male mortality at advanced ages, over recent decades, in low mortality countries. The chapter, then, examines the possible reasons, behavioural or biological factors, explaining such excess male mortality and its increase in recent decades. The analysis of the causes of death does not confirm the hypothesis of the predominance of biological factors in the excess of male mortality among the oldest-old.

CHAPTER 13. SOCIAL DETERMINANTS OF MORTALITY IN THE OLDEST-OLD: SOCIAL CLASS AND INDIVIDUAL WAY-OF-LIFE

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Introduction

This paper discusses the role of social factors as determinants of longevity, with special focus on the oldest-old population. In ageing research, genetic and environmental—including social environment—factors are often presented as two separate, mutually independent sets of determinants. There is, however, constant interplay between genes and environment, between biological and social factors; and basically it is often impossible to distinguish between their specific impacts as determinants of longevity. Besides their "own" impact, environments, then, can be understood as contexts, or settings, for genetic influences. As far as humans are concerned, social and cultural characteristics of environments are of fundamental importance.

Social development and improving living conditions have led to a steady increase in life expectancies in all countries where this development is not severely disturbed. Today, country differences in life expectancies are largely explained by social factors; negative trends are seen in countries undergoing major social changes, such as Russia.[1] There is also abundant empirical evidence that social factors such as position in the social hierarchy, and individual choices and activities during the life course, have a major impact on differences in the likelihood of disease and illness, and in life expectancies. The focus of this paper is on individual mortality differences within one society.

Given the multidisciplinary nature of the problem and the often complicated designs employed, research on the social determinants of longevity involves many theoretical, conceptual and analytical problems. This paper begins with a brief discussion of the role of the major social determinants in research on longevity in normal human populations and in younger-old ages. We then move on to the status of research in the oldest-old and the

[1] In St. Petersburg, there was a marked increase in the total death rate between 1990 and 1993, and a decrease after that, resulting in an increase of 12.3% from 1990 to 1998. However, in the population aged 60 years or more, death rate increased only in the age group 60–64. In the age groups of 80–84 years and 85+ death rates decreased by 3.4% and 4.5%, respectively (Dorofeyev 2000).

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problems involved in importing the results concerning younger age groups to this group of the population. Two studies using representative samples of the oldest-old population in Tampere, Finland, will be described to illustrate the prospects and the problems of longitudinal population studies.

In real life, living conditions, resources, social ties, motives, choices, behavioural preferences, and activities are all tied together in the complex totality of personal history. Since the role of different characteristics depends upon the context in which they appear, research into specific social variables as determinants of longevity will often remain a crude abstraction of reality. The social characteristics that have been studied most frequently as correlates of longevity include demographic variables such as ethnicity, place of residence, or marital status; indicators of social class such as occupational class or education; individual life-styles such as health habits; measures of social integration and social ties; and adopted styles of relating to one's own life. The categories are very different from one another. Some of the possible social determinants are permanent, such as race, or father's social class, others are variable during the life course, and the effects may be either reversible or irreversible; some of them are characteristic of a specific individual trajectory that at once includes certain influential determinants and excludes others. Joining a religious group, for instance, is a choice that may be necessarily followed by specific choices in life-styles, social networks, and even in occupational life. So although determinants of mortality differences are discussed here as separate indicators, it is important to bear in mind that in real life they are not independent from one another.

Social Determinants of Mortality

INDIVIDUAL LIFE-STYLES

Smoking is a good example of a determinant of longevity that is at once social and biological. The major determinants of the world-wide smoking "epidemic" are economic and commercial, the determinants of smoking at an individual level are both social-psychological and pharmacological. The biological processes through which smoking causes chronic disease and increased mortality are well documented. Even though there is selective survival among smokers in middle age, smoking remains a risk factor of mortality even in persons aged 65 and over (La Croix *et al*. 1991; Ferrucci *et al*. 1999). The effects, however, are not totally irreversible: Peto *et al*. (2000) showed that cessation of smoking even at the age of 60 considerably reduces the life-time risk of lung cancer. Alcohol use is another behaviour with direct biological effects, but it shows a more complex relationship with disease and mortality than smoking. Several studies on middle-aged and elderly samples indicate a J-shaped, or even a U-shaped association between alcohol consumption and all-cause mortality, where moderate drinkers may have reduced mortality compared to non-users (Gaziano *et al*. 2000; Gronbaek *et al*. 1998; Liao *et al*. 2000).

There is a growing body of evidence on the beneficial effects of physical exercise on health and longevity (Paffenberger *et al*. 1986), even in populations aged 65 and over (Bijnen *et al*. 1998; Ferrucci *et al*. 1999). In the EPESE data (Ferrucci *et al*. 1999) physical activity was associated both with survival and with fewer years of disability before death, and this was true both for smokers and non-smokers.

SOCIAL NETWORKS

Since the 1970s there has been extensive research into the association between social relationships and mortality. To some extent the concepts used in this research, such as social contacts, social networks, social integration, and social support, are used interchangeably: to some extent they refer to different steps of the assumed causal pathway. The main message from this body of research is that social contacts, social ties to other people, are beneficial, and at least remarkable social isolation increases the risk of mortality. Why this is the case is not entirely clear. The main line of thinking maintains that social support provided by social ties is likely, first, to encourage people to better health habits; and, second, to influence the ways in which people respond to and cope with different stressors. Moreover, social isolation as such may lead to physiological changes that increase susceptibility to disease. These pathways were suggested by Berkman and Syme in their seminal paper in 1979. In 1986, Syme suggested that social support could, rather, be understood as merely one aspect of a more general concept, i.e. control over one's destiny—a suggestion that comes very close to Antonovski's (1979) theory of experienced sense of coherence as a determinant of salutogenesis (that is: genesis of health in contrast to pathogenesis). The main line of theoretical thinking has changed very little since these days, even though the empirical evidence has continued to accumulate. By contrast there have been major changes in our understanding of the psycho-physiological, neuroendocrine mechanisms mediating the influences between social ties and social support, and health, respectively (for reviews, see Berkman 1988; Seeman and McEwen 1996; McEwen and Seeman 1999; Taylor and Seeman 1999).

Social networks have been conceptualized and measured as the quantity and quality of social contacts, as social participation and activity, and as instrumental and perceived social support. Both the concepts and variables used and the results vary. In many studies the results vary according to site, gender, or ethnic group (Kaplan *et al*. 1988; Seeman *et al*. 1993; Schoenbach *et al*. 1986); usually men have been found to gain more from rich social networks (see Shye *et al*. 1995). In older populations, there are studies indicating that network size or contact frequency as such have a protective effect on mortality (Blazer 1982; Seeman *et al*. 1987; Shye *et al*. 1995); but other studies show no protective effect (Palmore 1982; Hanson *et al*. 1989, Jylhä and Aro 1989). Instrumental social support or support from many sources in old age may be associated with higher, not lower mortality (Kaplan *et al*. 1994, Penninx *et al*. 1997), probably mainly because people in need of much instrumental support are likely to be in poorer health. It also seems that in studies with many indicators of social ties, the authors sometimes tend to base their conclusions on the positive associations identified and at the same time to disregard the results that show no association with mortality (e.g. Hanson *et al*. 1989; Avlund *et al*. 1988). These findings cannot negate the overall evidence on the relationship of social integration with survival, but certainly more work is needed in order to understand what is healthy in social networks—what, if any, is their independent causative role, and how do they work in different social contexts.

Cerhan and Wallace (1997) recently showed in a population-based sample of rural older people that, adjusted for education and changes in health status, people with a consistently low level of social ties were at higher risk of mortality than those with a consistently high level of social ties; but those who had changed their position during the follow-up did not

differ from those who had maintained their high level. The results support the idea that it is the long-term patterns of social integration rather than current conditions that are related to health and survival.

The social network indicator that perhaps most consistently has shown an association with survival in different cultures is the extent of social participation (Steinbach 1992 in the US; Sugisawa *et al*. 1994 in Japan; Weilin, Tibblin, and Svardudd 1985 in Sweden; Jylhä and Aro 1989 in Finland; Walter-Ginzburg *et al*. in Israel). Recently Glass *et al*. (1999) found that three types of social participation, namely social (e.g. visits to cinema, restaurant, or sporting events; or participation in social groups), fitness (active sports or swimming, walking, or physical exercise), or productive activities (e.g. gardening, or paid community work) were all associated with survival among a random population sample aged 65 and over. (But see Discussion p. xxx.) In a 13-year follow-up, those who participated more actively in any of the three types of activities had lower mortality than those who participated less. The analyses were adjusted for sociodemographic factors, smoking, disability, and history of cancer, diabetes, stroke, and myocardial infarction.

STYLES OF RELATING TO LIFE

A number of studies have suggested optimistic vs. pessimistic styles and general outlook on life as potential independent predictors of survival. It has been found that an optimistic rather than pessimistic disposition and an optimistic style to interpretations and expectations predicts outcomes in different chronic diseases, but there are also contradictory findings (see Taylor and Seeman 1999). A few studies with random older populations indicate an association between variables such as positive affect and better survival (Ostir *et al*. 2000), or dissatisfaction with ageing and higher mortality (Maier and Smith 1999).

The association observed in numerous population studies between self-rated health and mortality could, at least in part, be explained by the protective function of optimistic disposition (for a review, see Idler and Benyamini 1997). However, on the basis of the present literature it seems fair to conclude that the more reliable and comprehensive data we have on clinical conditions and physical health status, the lesser is the role of self-rated health as a predictor of mortality. Self-rated health should therefore be regarded as a summary measure of health, in the broad sense of the word, more than anything else (Jylhä *et al*. 1998). Having said that, it is true that both direct and comparative self-ratings of health do have a marked subjective component: there are no formal rules on how to use the information obtained on different dimensions of health to construct global ratings, and the ratings seem to be "calibrated" for age (Jylhä *et al*. 2001). Therefore, even if the differences in self-ratings of health mainly reflected differences in physiological and clinical status, individual explanatory styles are likely to influence interpretations of such information and thus may possibly be partly responsible for the association between self-rated health and mortality.

SOCIAL CLASS

The most convincing evidence for the association of genuinely social factors with human longevity is the relationship between socioeconomic status and mortality. In virtually all

industrialized countries, and in the developing world as well (e.g. Liang *et al*. 2000 for China), there is a gradient for lower mortality and longer life expectancy with higher socioeconomic position (Mackenbach *et al*. 1997, Marmot *et al*. 1997), and since the 1970s, these differences seem to be widening rather than narrowing (Crimmins and Sato 2001; Martikainen, Valkonen, and Martelin 2001). The results are basically similar irrespective of whether the indicator of socioeconomic status is occupational class, years of education, or, for instance, car ownership. Among children, the social class of parents, usually father (Valkonen *et al*. 1993) is associated with mortality. In older people, the level of education completed decades ago, or previous occupational class (Marmot and Shipley 1996; Martelin *et al*.1988) determines future life expectancy. In a study on middle-aged men in Scotland (Smith *et al*. 1997), father's social class, the social class of one own first regular job, and social class at the time of screening had a cumulative effect on 21-year mortality. However, the cause-specific mortality differences may vary from one's country to another. Kunst *et al*. (1999) recently showed that while men in manual classes had higher mortality from ischemic heart disease than men in non-manual classes in England, Wales, Ireland, and Nordic countries, there were no difference between classes, or even a reversed relationship, in Mediterranean countries, France, and Switzerland. Compared with Northern Europe, mortality differences in the US were smaller or about the same.

In Finland, the direction of the socioeconomic gradient seems to be similar for almost all major groups of causes of death, the most noticeable exception being breast cancer that shows a graded, but reversed, association between social class and mortality (Valkonen *et al*. 1993). The essential feature of social class differences in mortality is that there is not only a difference between "poor" or particularly deprived groups and others, but a gradient throughout the scale. In other words, it is the relative position in the hierarchy rather than the occupational class as such that matters.

In populations, the social characteristics relevant to health and longevity are not independent from one another. People in lower social classes are usually more likely to smoke, consume large amounts of alcohol, eat unhealthy food and not practice physical exercise than people in higher social classes. This, however, may depend on the development of each society and the status of different sub-groups. Cavelaars *et al*. (2000) found that in contrast to Northern Europe and older age groups, in Southern Europe higher educated women aged 20 to 44 years smoked more than women with lower education in the same age group. However, after taking into account these life-style factors, the social gradient in mortality usually remains (Marmot *et al*. 1997). There is also increasing evidence that people in lower classes participate less in social networks, receive less social support (Stanfeld and Marmot 1992; Marmot 1999) and express pessimistic expectations more often (see Taylor and Seeman 1999) than people in higher classes. Indeed, it has been suggested that psychosocial factors are an important pathway between social class and health.

It seems there are two different ways to explore why social class determines length of life. In epidemiological research it is common to try and break down the concept of social class into numerous individual, easily measurable variables describing behaviour and life conditions. Another alternative is to understand social class as a genuine influential social fact in its own right, as something that in modern societies essentially determines our way-of-life, and something that is not reducible to its constituent parts. Jeddi Hasan (1988)

explains how social class differences are created, and takes social class itself as the ultimate determinant:

> .... objective conditions, subjective perceptions, cognitions and activities of the people in a social class constitute an entity of interrelated components with properties acquired from the whole, defined as their way-of-life. Differences in morbidity and mortality between social classes depend on the differences in their ways-of-life, which are not reducible to the properties of their individual components.
>
> In economically developed societies mortality has been reduced as a result of advancing development and ever higher levels of need-satisfaction. The activity of people within the interactive systems of needs and ways-of-life produce means for the satisfaction of needs, extend and enrich the system of needs, and transform ways-of-life. Non-satisfied needs lead to physiological states, activities, and behaviours which increase the probability of disease and death.
>
> Socially determined needs are first formed and satisfied in the way-of-life of the highest social class(.....) The gradient of increasing deprivation from the highest to the lowest class is a cause of the gradients in morbidity and mortality. The gradient in health is an inevitable feature of societies with socioeconomic hierarchies, although its steepness may vary in time and place. (Hasan 1988, ii)

Along the same lines, Marmot (2003) emphasizes the differences in the means and abilities required for full participation in a given society as a major component in relative deprivation. Here, the concept of 'social participation' comes very close to the concept of 'need' used by Hasan.

Recent studies have tried to uncover the processes through which these genuinely social phenomena are translated into biological consequences. A new concept, the allostatic load, which describes the results of environmental and psychosocial exposures that require physiological (neural, endocrine, immune) mechanisms to maintain stability, has been put forward in an attempt to bring various pathways together (McEwen and Seeman 1999; McEwen and Stellar 1993, see also Ryff and Singer 1998). Basically, allostatic load refers to the cumulative impact of adaptive physiological responses, leading to dysfunctions across multiple regulatory systems (Seeman *et al*. 2004). Even though the empirical data to illustrate these suggested pathways are still scarce, the concept can help us understand the mechanisms through which relative position in the social hierarchy transforms into differences in morbidity and mortality.

Social Predictors in the Oldest-Old

Although the interest in the oldest-old population has rapidly increased among epidemiologists, demographers, sociologists, and gerontologists, data on the social predictors of mortality of the oldest-old are still very scarce. This is true both for life-time characteristics as possible determinants of mortality in extremely old age, and for current social factors in the oldest-old as possible determinants of future life expectancy. Both census

data, official register data and data from specific population studies could be used for this purpose. The number of social indicators in official register data is usually limited, and they only describe social status and living conditions rather than individual life-style or social activities. Sometimes there are problems with data reliability. Longitudinal population studies in older people using postal surveys or personal interviews usually comprise fairly small numbers of people over 80, and it is only very rarely that the results are reported separately for this group. Because of the high prevalence of sensory deficiencies, cognitive problems, and institutionalization, it is difficult to collect reliable and representative data for an examination of social factors at age 80 or 90 to be used as predictors in mortality studies.

It is not clear, therefore, whether the factors that are found to be predictors of survival at younger ages are similar to those at very old age. It has been proposed that if groups of population exposed to many risk factors have high mortality rates at younger ages, this might lead to the "survival of the fittest", and differences in mortality between groups of population would be different or even reversed at very old age compared to younger age groups. An interesting example is the case of possible racial "crossover" in mortality in the USA (Manton and Stallard 1981). It remains unclear whether this is due to non-comparable groups or inaccurate data (Preston *et al*. 1996) rather than real age differences in the pattern of mortality between ethnic groups (see also Grundy 1997).

Reliable large data sets from individual countries (Marmot and Shipley 1996 for the UK; Martelin *et al*. 1998, 1999 for Finland) and from a study of 11 European populations (Huisman *et al*. 2004) show that socioeconomic differences in mortality persist among the oldest-old. Both the Finnish studies and the European study are based on data from mortality registries linked with population census data. In Finland, individual death records and population census records for the whole population were linked in order to analyse mortality differences. Among all persons aged 80 years and over in Finland for the period 1971–90 (Martelin *et al*. 1998), in an analysis that adjusted for age and five-year period, an excess mortality of about 20% was found for both men and women with a basic education, compared to those with a higher education—and also between former manual workers and former upper non-manual workers. From the period 1971–75 to 1986–90, there was an increase in life expectancy at age 80 in all occupational classes and at all levels of education, but there was no trend towards diminishing differences between the social groups (Martelin *et al*. 1998).

A recent European study using data from Finland, Norway, Denmark,England and Wales, Belgium, France, Austria, Switzerland, Barcelona, Madrid, and Turin (Huisman *et al*. 2004) found that significant relative differences in mortality between levels of education persisted until the ages of 90+ in each country. The relative differences decreased with increasing ageing in many countries, but the absolute educational mortality differences increased. These results speak against the cross-over hypothesis and provide evidence for the hypothesis that socioeconomic position is a powerful predictor of future life expectancy even in the oldest-old.

Analyses on the effect of individual life styles at very old age are scarce. Recently the HALE project, surveying approximately 2300 men and women aged 70 to 90 years in 11 European

countries, reported that adhering to a Mediterranean diet, moderate alcohol use, physical activity and nonsmoking were associated with a lower ten-year mortality from all causes (Knoops *et al*. 2004) . Earlier, Fraser and Shavlik (1997) found that measured at the age of 84 and over, exercise, and consumption of nuts and fruits were associated with mortality during a 12-year period in the Adventist Health Cohort study. Subjects with prevalent heart diseases or cancer were excluded from the analysis. In a cohort of Danish nonagenarians (Nybo *et al*. 2003), smoking was not a significant predictor of 15-months mortality, but there was a tendency towards lower mortality with more moderate alcohol intake.

Tampere Longitudinal Study on Ageing (TamELSA): Social Determinants of Mortality in Octogenarians (See Figures 1 and 2)

INTRODUCTION

TamELSA is a longitudinal study on living conditions, health and functioning, life-styles and use of services among older people in Tampere, Finland (Jylhä *et al*. 1992). It was launched in 1979 as part of the Eleven Countries Study, later known as the European Longitudinal Study on Ageing initiated by the WHO (Heikkinen, Waters, and Brzezinski 1983; Ferrucci *et al*. 1995). Since baseline, two ten-year follow-ups have been carried out—in 1989 and in 1999–2000. Our focus here is on the social characteristics measured in people aged 80–89 as predictors of mortality during a 10 year-period.

Tampere is by Finnish standards a relatively large city in the southern part of the country. Traditionally an industrial city with numerous paper and textile mills, sometimes known as "Finland's Manchester", the town has changed dramatically in recent years and is now mainly known for its modern information technology and education and other services. In 1979, the population was around 165 000, compared to approximately 180 000 in 2000. From 1979 to 1999, the proportion of people aged 65 and over increased from 12.4% to 14.7% , and that of people aged 80 and over from 1.7% to 3.4%. In the whole country the proportions grew from 11.9% to 14.7% and from 1.7% to 3.3%, respectively. In Finland, life expectancy at age 80 in males has increased from 5.6 years in 1979 to 6.5 years in 1998, and in females from 6.6 to 8.2 years during the same period.

DATA

At baseline in 1979, stratified samples by sex and five-year age group in the population aged 60–89 were drawn from the Tampere population register, over-sampling the oldest age groups (men born in 1890–94, 1895–99 . . . . 1915–19; women born in 1890–94, 1895–99 . . . . 1915–1919). Altogether, 1059 persons were interviewed at home or in the institution where they lived. The response rate was 81%. In 1989, the survivors were interviewed again using a questionnaire that for the most part was identical with that used in 1979. Additionally, new cohorts aged 60–64 and 65–69 (born in 1920–24 and 1925–29) were interviewed. The overall response rate was 80.0%. Both community-dwelling and institutionalized persons were included. If the participant was unable to answer the questions because of poor health or cognitive status, a proxy respondent was used to answer the questions where subjective evaluations or opinions were not required.

We examined the predictors of mortality during a ten-year period among people aged 80–89 at the time of the interview. To increase the sample size in this age group, we combined the samples aged 80–89 in 1979 and aged 80–89 in 1989. We calculated a follow-up time of 10 times 365 days for both samples. As predictors, we used interview questions at baseline that were asked in exactly the same way both in 1979 and 1989. In 1979, 163 men and 158 women aged 80–89—altogether 321 persons—were interviewed, with a response rate of 79.7%. In 1989, 48 men and 103 women aged 80–89 were interviewed, the response rate being 83.5%. The final number of persons included in the analyses was 472. Altogether 106 (22%) of them lived in an institution, either in a nursing home or a hospital. A proxy respondent was used for 59 (12%) persons.

Vital statistics and dates of death were provided by the national Population Register Centre on the basis of personal identity codes. Vital statistics could be confirmed for all the participants. Population registers in Finland are considered comprehensive and reliable with respect to dates of birth and death (Kannisto *et al*. 1999).

MEASURES

All the predictor variables come from the baseline interview, either in 1979 or in 1989. In the analyses reported here, marital status was dichotomized as married versus non-married. Occupational class was coded using 16 categories from the Occupational and Industrial Classification (Statistics Finland 1976), and these were combined into three classes: non-manual occupations, manual occupations, and others (including farmers, housewives, and self-employed not comparable to non-manual occupations). Education was coded as low, medium or high by dividing the number of years of full-time education into thirds—separately for each five-year age group. This was done because the years of full-time education strongly associated with age. The respondents were divided into three groups on the basis of whether they lived (a) alone or with spouse only (b) with other family members than only spouse, or (c) in an institution. There were no respondents living with non-family members. Self-rated health was categorized into three classes: very good or good, average, and fairly poor or poor. Self-rated health in comparison with age peers was dichotomized as better versus not better (the same, worse, or cannot say). Reported chronic diseases that according to the respondent had been diagnosed by a physician and affected daily activities were coded into cardiovascular, musculoskeletal, nervous system, endocrine, gastrointestinal, infectious, respiratory urinary, diseases of skin, cancers, and others. Functional ability was assessed with a set of twelve questions dealing with basic activities of daily living (ADL) and instrumental activities of daily living (IADL) (for details, see Jylhä *et al*. 1992).

Social participation was assessed with a set of eight questions. The respondents were asked how many times they had visited the following places or taken part in the following occasions during the past 12 months: (a) family occasions, such as weddings, funerals, birthdays, etc.; (b) theatre, movies; (c) meetings or occasions arranged by various organizations; (d) library; (e) sports competitions, either as a participant or as a spectator; (f) religious occasions; (g) domestic travel, at least 60 miles; and (h) foreign travel (Jylhä *et al.* 1992). The respondent was categorized as active in family occasions if he or she had participated at least twice, and active in other activities if he or she had participated at least

once. On the basis of different activities participated in, a sum total was calculated. Social participation was categorized as low (score 0–1), moderate (2–3), and high (score 4 or more). Smoking was categorized as never *versus* past or present. Respondents were asked whether they practised physical exercise, such as brisk walking, jogging, or swimming (yes *versus* no). They were asked whether they ever felt lonely or whether they felt unnecessary (often, sometimes, never, or cannot say).

ANALYSIS

We ran a series of cross-tabulations and survival analyses, only part of which are reported here. First, we cross-tabulated the dichotomous variable indicating 10-year survival with the predictors. We then ran a series of Cox proportional hazards models to examine associations with the predictors and time of survival. All models were adjusted for age and period, and the models combining men and women were also adjusted for sex. Finally, where health status was considered as a possible confounder, the number of disabling diseases and/or functional ability was also adjusted for. SPSS 9.0 for Windows was used for the analyses.

RESULTS

Because of the stratified sampling method, the proportion of males was larger in the sample than in the reference population at baseline (45% vs. 14%) (Table 1). Almost two-thirds were 80–84 years of age. Every second participant had worked in a manual occupation. Two-thirds of the women were widows; every second man was still married.

A small majority suffered from two or more chronic conditions. More than half of the men and four out of ten women had difficulty even with basic ADL tasks. Men assessed their health as very good or good somewhat more often than women. Among women, very good or good self-rated health was as frequent as fairly poor or poor. More than half thought their health was better than that of their peers.

Most of the respondents lived with a spouse or alone. A greater proportion of women than men lived in an institution. The number of current smokers was only 6% in men and 1% in women; but half of the men had smoked in the past. Every second man and more than every third woman said they practised physical exercise. Half of the respondents had participated either in none or in only one social activity during the past 12 months. Every fourth man and 15% of the women had participated in four or more different types of activities. A clear majority of both men and women said they had good friends; approximately half also said they never felt lonely or unnecessary.

Table 1 shows the unadjusted proportion of people alive after 10 years according to predictor variables. In men, the proportion of survivors was somewhat higher among males who had previously been in non-manual occupations than in other occupations, and it was also higher among those who had a wife in non-manual versus other occupations. All health indicators were associated with survival, with the exception of self-rated health compared with age peers in men. Living arrangements, physical exercise, and social participation were also associated with survival in cross-tabulations. The correlations of survival with

Table 1. Distribution of demographic characteristics at baseline and percent of survivors after 10 years. Differences are tested by the chi2 –test. TamELSA.

				Alive after 10 years		
	Men %	**Women %**	**All %**	**Men %**	**Women %**	**All %**
Age (n = 472)						
80–84	66	64	65	16	26	22
85+	34	36	35	8	12	10
p				0.13	0.006	0.02
Period (n = 472)						
1979	77	60	68	13	23	18
1989	23	40	32	15	18	17
p				0.76	0.25	0.69
Gender (n = 472)						
Men	100	—	44	13	—	13
Women	—	100	55	—	21	21
p						0.03
Education (n = 470)						
Low	21	34	28	9	18	15
Medium	16	23	20	18	22	20
High	63	43	52	14	23	18
p				0.48	0.67	0.57
Occupational class (n = 470)						
Non-manual	40	26	32	18	24	19
Manual	48	42	45	12	42	17
Other	12	32	23	4	34	18
				0.17	0.91	0.86
Occupational class of spouse (n = 444)						
Non-manual	21	23	22	26	22	24
Manual	26	43	35	9	29	22
Other	47	8	26	10	5	10
Never married	7	26	17	14	16	16
p				0.06	0.06	0.02
Marital status (n = 471)						
Married	51	9	28	15	32	18
Widowed	39	64	53	12	21	18
Other	10	27	19	10	18	17
p				0.77	0.40	0.95

(*Cont.*)

Table 1. (Continued)

				Alive after 10 years		
	Men %	**Women %**	**All %**	**Men %**	**Women %**	**All %**
Disabling diseases (n = 472)						
0–1	47	44	46	19	24	22
2 or more	53	56	54	8	19	14
p				0.02	0.25	0.03
Functional ability (n = 472)						
Good	29	15	19	21	41	32
Moderate	38	27	41	16	25	21
Poor	33	58	40	3	15	7
p				0.005	0.001	<0.001
Self-rated health (n = 409)						
Very good or good	44	34	38	21	34	27
Average	31	33	33	12	19	16
Fairly poor or poor	25	33	29	8	19	15
p				0.12	0.05	0.02
Self-rated health compared with age peers (n = 356)						
Better	58	50	54	18	35	26
The same or worse	42	50	46	16	16	16
p				0.73	0.003	0.02
Living with (n = 470)						
Alone or with spouse	67	53	59	19	28	23
With other family members	15	21	18	3	22	15
In institution	18	26	23	0	7	5
p				0.001	0.004	<0.001
Smoking (n = 460)						
Never	45	95	73	13	22	20
Past or present	55	5	27	14	17	14
p				0.81	0.66	0.20
Physical excercise (n = 417)						
Yes	50	39	44	19	33	25
No	50	61	56	10	20	16
p				0.10	0.03	0.02

Table 1. (Continued)

				Alive after 10 years		
	Men %	**Women %**	**All %**	**Men %**	**Women %**	**All %**
Social participation (n = 467)						
High	24	15	19	26	41	33
Moderate	30	27	28	16	25	21
Low	46	58	53	5	15	11
p				0.002	0.001	<0.001
Good friends (n = 440)						
Yes	76	72	74	15	25	21
No	24	28	26	11	16	14
p				0.44	0.14	0.13
Feeling lonely (n = 412)						
Never	64	50	56	16	29	22
Sometimes or often	36	50	44	12	20	17
p				0.38	0.10	0.15
Feeling not needed (n = 412)						
Never	56	46	51	18	29	23
Past or present	44	54	49	11	20	16
p				0.18	0.12	0.08

good friends, feelings of loneliness, and feeling unnecessary were not significant, and there was no difference in survival between never-smokers and those who had smoked earlier.

Next, we proceeded to examine the correlation of demographic indicators, socioeconomic status, and health with mortality by using the Cox proportional hazards models which included age, sex, and period. Age was overall the strongest and most stable predictor of mortality in all our analyses. For example, in a model where age (as a continuous variable), sex, period, occupational class, disabling diseases, functional ability, and social participation were included as predictors, RR for each year of age was 1.07 (95% CI 1.03–1.11) (analyses not shown). The well-known higher mortality in males compared to females was true in our sample as well: age-adjusted RR for men was 1.25 (95% CI 1.03–1.50). Sex maintained its effect in most models in which both health and social indicators were included. By contrast, although age-adjusted mortality was somewhat lower in the 1989 sub-sample than in 1979, the difference was not close to significance according to any of the models (analyses not shown).

The socioeconomic indicators in our study were not statistically significant independent predictors of mortality, but they showed a suggestive pattern that is well-known in many other studies: people in non-manual occupations live longer than people in manual occupations, and the difference is wider still in comparison with the group "others" (Figure 1).

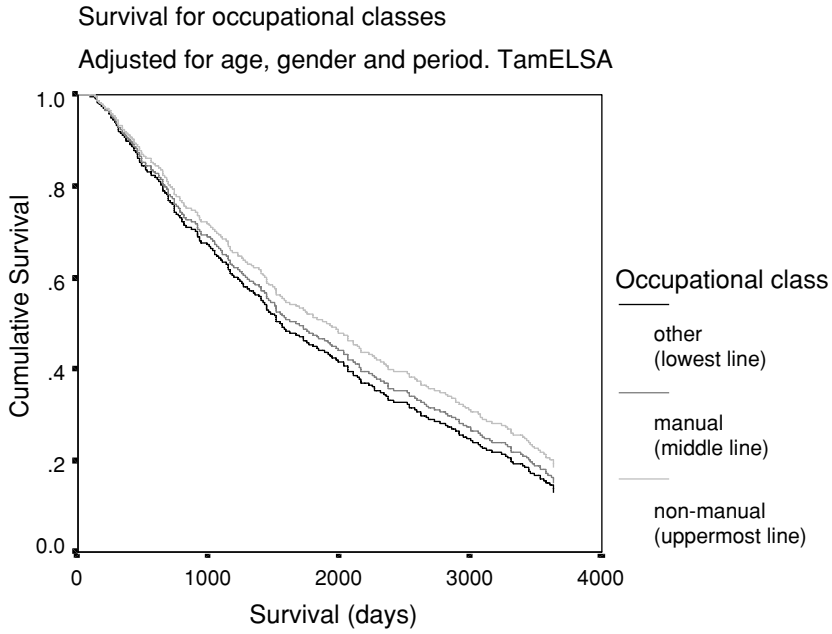

Figure 1. Survival curves for occupational classes. Adjusted for age, sex, and period. TamELSA Study.

Spouse's occupation was included in the analyses mainly because it has been shown that the family's way-of-life is often determined more by the husband's than by the wife's occupation. However, when the analyses were done separately for both sexes (not shown), men who were married to a woman who had had a non-manual occupation showed lower mortality than did the other groups, but no significant difference was found in women. Number of chronic diseases, functional ability, self-rated health, and self-rated health compared with that of age peers were all significant predictors of mortality (Table 2).

Analyses of life-styles and behaviour as predictors of mortality are often, and particularly in older populations, handicapped (statistically speaking) by selection by health status at baseline. People who are healthier are both more likely to show overall activity and less likely to die. To minimize this problem, we adjusted all our analyses on life-style indicators not only for age, sex, and period, but also for chronic diseases (Table 3).

People living in an institution and those living with family members other than only a spouse were more likely to die than those living alone or with a spouse. This, in spite of the adjustment for chronic diseases, may more than anything else reflect the inability of people in poor functional status to live without the help of younger people.

Smoking did not emerge as a significant predictor of death, probably partly because of the small percentage of current smokers, and because 55% of previous smokers had given

Table 2. Association of 10-year mortality with demographic characteristics and social position and health. Cox proportional hazards models, adjusted for age, gender and period. TamELSA.

	RR	95% CI
Level of education		
High	1.00	
Medium	0.95	0.72–1.27
Low	1.20	0.95–1.51
Occupational class		
Non-manual	1.00	
Manual	1.12	0.89–1.41
Other	1.20	0.90–1.60
Occupational class of the spouse		
Non-manual	1.00	
Manual	1.19	0.89–2.00
Other	1.37	0.99–1.89
Non-married	1.41	0.99–1.99
Marital status		
Married	1.00	
Widowed	0.96	0.74–1.25
Other	1.09	0.78–1.52
Number of chronic disabling diseases		
0–1	1.00	
2 or more	1.25	1.02–1.53
Functional ability		
Good	1.00	
Moderate	1.57	1.16–2.12
Poor	2.86	2.10–3.91
Self-rated health		
Very good or good	1.00	
Average	1.44	1.10–1.87
Fairly poor or poor	1.77	1.35–2.33
Self-rated health compared with age peers		
Better	1.00	
The same or worse	1.65	1.29–2.10

up smoking more than 20 years ago, and 40% more than 30 years ago. However, in a sub-sample including only those who at baseline were 60–79 years old, there was a graded increase in 10-year mortality from never-smokers to previous smokers and current smokers, respectively (analysis not shown).

Table 3. Association of 10-year mortality with health behaviour, social integration and evaluation of own life. Cox proportional hazards models, adjusted for age, gender, period and number of disabling chronic diseases. TamELSA.

	RR	95% CI
Living with		
Alone or with spouse only	1.00	
With other family members	1.30	0.99–1.71
In an institution	1.91	1.48–2.47
Smoking		
Never	1.00	
Past or present	1.04	0.79–1.36
Physical excercise		
Yes	1.00	
No	1.40	1.11–1.77
Social participation		
High	1.00	
Moderate	1.48	1.08–2.05
Low	2.17	1.60–2.93
Good friends		
Yes	1.00	
No	1.25	0.99–1.59
Feeling lonely		
Never	1.00	
Sometimes or often	1.01	0.81–1.27
Feeling not needed		
Never	1.00	
Past or present	1.16	0.93–1.45

Among the indicators of life-style and activity, two variables showed a stronger correlation with mortality than others: physical exercise and social participation. Adjusted for age, sex, period, and chronic diseases, people who said that they exercise were less likely to die (RR 1.40, 95% CI 1.11–1.77). Physical exercise was more common among people who had previously been in non-manual occupations than others, and it was also dependent on functional status at baseline. The association between physical exercise and mortality did not weaken very much when occupational class was introduced in the model, but it did weaken when functional status was also included (RR 1.13, 95% CI .88–1.46).

Social participation showed a graded association with mortality, mortality being lowest among those with the highest level of social participation and highest among those who participated less (Figure 2).

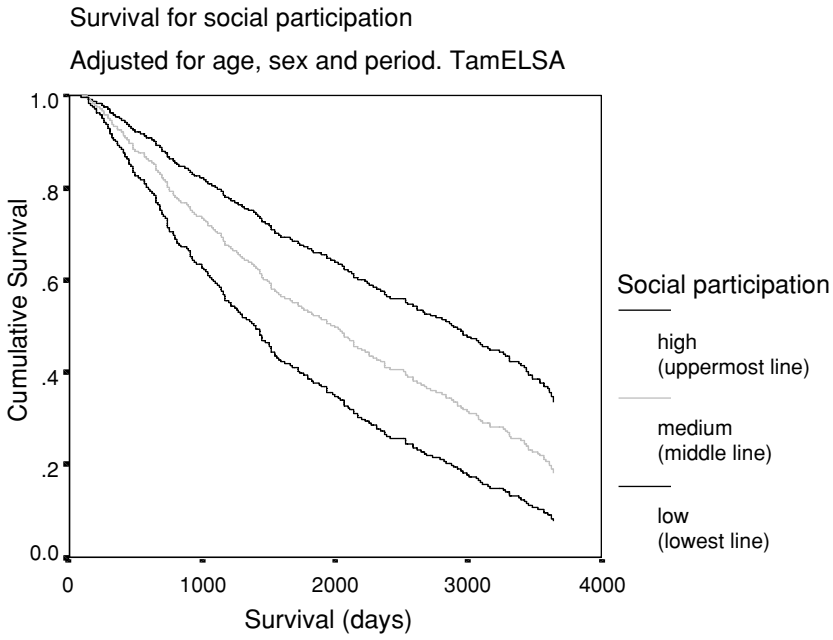

Figure 2. Survival curves for three categories of social activity. Adjusted for age, sex, and period. TamELSA Study.

The pattern of relationship found in both sexes in the cross-tabulations was maintained when age, sex, period, and chronic diseases were taken into account (Table 3). As in the case of physical exercise, the level of social participation differed between different occupational classes and different levels of functional ability. However, when these predictors were included in the model, RR for average level of social participation was 1.36 (95% CI .98–1.90), and RR for low social participation 1.62 (95% CI 1.16–2.28). To minimize the confounding effect of baseline health and functional status, we also carried out analyses in which deaths occurring within 18 months of the baseline interview were excluded. Those showing the lowest level of social participation were significantly more likely to die than those at the highest level.

Vitality 90+ Study: Social Determinants of Mortality in Nonagenarians (Figure 3)

MATERIAL AND ANALYSIS

The Vitality 90+ Study is a multidisciplinary project including epidemiological, autobiographical, psychological, and genetic analyses in the total population aged 90 years and over in Tampere (Jylhä and Hervonen 1999; Goebeler, Jylhä, and Hervonen 2003; Niemi *et al*. 2003). One part of the project is a repeated postal survey covering all home-dwelling

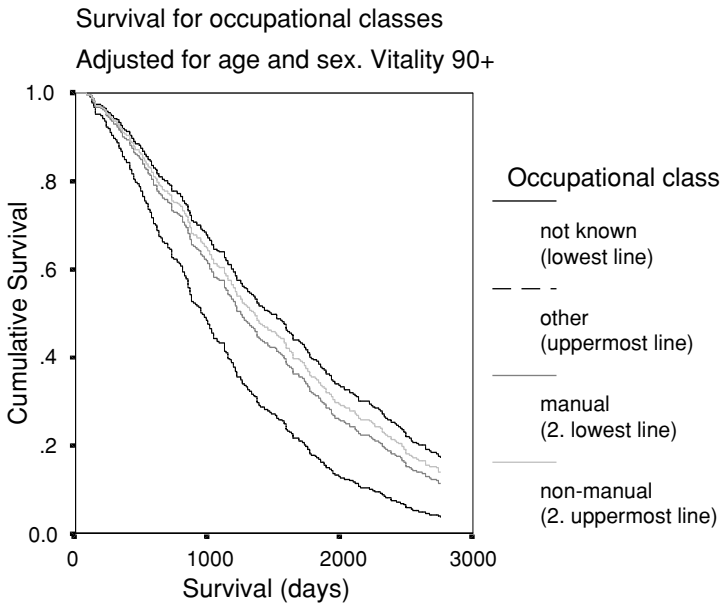

Figure 3. Survival curves for four occupational categories. Adjusted for age and sex. Vitality 90+ Study.

people in this age group. Under favourable circumstances, the postal survey proved a feasible method for collecting relatively basic and simple data among the oldest-old. In 1996, a short questionnaire was mailed to all 502 community-dwelling persons aged 90+ in Tampere. Of this group, 34% were 90-year-old, 20% 91 years, 28% 92–93 years, and 18% 94 years or older, the oldest being 102 years old. Altogether 81% were women. The response rate was 81.5%. (409 persons), and the respondents did not significantly differ from the basic population by age or sex. Vital statistics and dates of death were provided by the national Population Register Center on the basis of personal identity codes.

Occupational class was categorized as non-manuals (29% of the respondents), other occupations (manual workers, farmers, self-employed, and housewives) (63%), and pensioners for whom occupation was not known (8%). Outdoor mobility was used as a measure of functional status. The respondents were divided into three hierarchic categories: (a) can move outdoors without difficulty (37%); (b) can move outdoors without help but with difficulty (18%); (c) can move outdoors only with help (21%); and (d) cannot move outdoors at all (24%). Self-rated health was categorized as very good or good (32%), average (44%), and fairly poor or poor (22%).

Cox proportional hazards models were used to examine the association of the different indicators based on the 1996 survey with mortality during 7.5 years (90 months).

Table 4. Association of 7.5-year mortality with baseline characteristics. Cox proportional hazards models. Vitality 90+ Study. N = 395–409.

	Adjusted for age and gender		All variables simultaneously in the model	
	RR	**95%CI**	**RR**	**95%CI**
Age (per year)	—	—	1.06	1.01–1.12
Sex				
Women	—	—	1.00	—
Men	—	—	1.48	1.11–1.96
Occupational class				
Non-manual	1.00	—	1.00	—
Manual	1.10	0.87–1.41	1.05	0.82–1.36
Other	0.89	0.65–1.23	0.83	0.60–1.15
Not known	1.67	0.99–2.79	1.61	0.92–2.83
Self-rated health				
Very good or fairly good	1.00	—	1.00	—
Average	1.25	0.98–1.60	1.00	0.76–1.31
Fairly poor or poor	1.96	1.46–2.61	1.15	0.81–1.64
Outdoor mobility				
Without difficulty	1.00	—	1.00	—
Without help	1.38	1.01–1.87	1.33	0.96–1.86
Only with help	1.81	1.35–2.31	1.81	1.31–2.50
Not at all	2.46	1.83–3.30	2.34	1.65–3.33

RESULTS

During 7.5 years, 442 persons (88%) out of the total sample and 354 persons (87%) out of the respondents died. Age was a significant predictor of mortality (RR per year 1.10; 95% CI 1.06–1.15). Adjusted for age, mortality was higher for men than for women both in the basic population of 502 ((RR 1.25; 95% CI 0.99–1.59) and among the respondents, N = 409) (RR 1.22; 95% CI 0.93–1.59. Age and sex remained independent predictors of mortality even in the model where all the variables were included simultaneously (Table 4).

Adjusted for age and sex, the difference between manual and non-manual occupational categories was not significant. Risk of mortality was highest for those for whom the occupation was not known (Figure 3). Even though we have not yet been able to confirm this, there are good reasons to assume that this group includes more manual than non-manual workers. Both self-rated health and outdoor mobility were significant predictors of mortality. In the model where all variables were included simultaneously, outdoor mobility showed a strong graded association with mortality during a 7.5-year period. Compared to those who could move outdoors without difficulty, mortality was higher for those who

could move outdoors without help but with difficulty (RR 1.33, 95% CI 0.96–1.86), only with help (RR 1.80, 95% CI 1.31–2.50), or not at all (RR 2.34, 95% CI 1.65–3.33).

Discussion

The social determinants of life duration in very old age constitute a major challenge for research, for a number of reasons. First, it is very difficult to find reliable data sets with acceptable sample sizes—and even where such data sets are available, they are often confined to sociodemographic indicators while excluding data on individual choices or way of life. Second, the current life situation of octogenarians or centenarians is the outcome of decades of cumulative processes and diverging trajectories, the characteristics of which can hardly be described satisfactorily on the basis of one cross-sectional measurement. The present analyses should therefore be interpreted with caution.

In our TamELSA and Vitality 90+ studies we asked to what extent social factors measured at very old age determine future survival. We found that in octogenarians and nonagenarians, factors that were associated with mortality were the same indicators that have been found to predict mortality in younger adult age and in the younger-old. Age and sex were strong independent predictors of life duration. Sex, in our view, can be seen both as a biological (sex) and social variable (gender): old age as a stage of life is very different for men and women. Self-reported functional status and self-reported health were strong determinants of survival, and a favourable comparison of one's own health with that of age peers also predicted longer life. A higher level of social participation and physical exercise predicted better survival. Higher social class was not a significant predictor of longer survival, but the coefficients suggested a pattern well-known in several population studies. The associations of potential predictors were weaker than is often the case in younger populations, but the direction was the same. In these representative populations in Tampere, Finland, there were no signs of "crossover" in mortality, but those with better living resources were more likely to survive additional years even at a very old age. Our results, together with several other data sets, support the conclusion that even in very old age death is not a haphazard phenomenon: the social predictors of mortality are basically the same throughout the life course.

We used adjustments and analyses where deaths occurring during the first two follow-up years were excluded to ascertain that the correlation between social predictors and survival was not caused primarily by health differences at baseline. In spite of this, as our measures of health and functioning were not very sophisticated, we cannot exclude the possibility that the effects of physical exercise and social participation on survival partly reflected the better baseline health of people active in these fields. Moreover, it would certainly be overly simplistic to interpret these associated factors measured at age 80 or 90 as direct causes of future life duration. Physical exercise certainly has real beneficial health effects even at very old age, but taking physical exercise is also indicative of a life-style that has evolved during the whole life course and of maintaining an interest in life and one's own physical fitness. High social participation, then, can be interpreted as a sign of general integration in social life, or, a life that is experienced as meaningful. Individual factors associated with longer survival could perhaps best be understood not so much as direct or mediated causal

factors, but mainly as "markers" of a way-of-life that is characterized by a combination of health-protecting factors. In our societies, these factors are likely to be cumulative in many ways. In TamELSA, people in non-manual occupations and with a higher level of education were significantly more likely than others to take physical exercise and have a high level of social participation likely to result in a healthier and longer life. On the other hand, the life situation, life-styles and habits of the oldest-old have developed over several decades, not as separate, individual characteristics, but as "an entity of interrelated components" (Hasan 1988); and partly, being socially and culturally inherited, they can be traced back beyond the individual's birth. Further, the distinctive feature of human beings is that characteristics of social situation, social relations, or behavioural choices do not have a standard, mechanical effect on people and their health, but their effect is dependent on their personal meaning and their role in the total context of an individual life situation. This also means that concepts such as "predictor" or "determinant" may take on a meaning different from how it is used in the physical and biological world. To be successful, research on social determinants of longevity requires cooperation between demographers, biologists, and sociologists.

Conclusion

It is known that both individual lifestyles, social networks, social participation, and personal styles of relating to life are associated with mortality and survival. The most convincing evidence of the importance of social factors is the gradient for higher mortality with lower socioeconomic position. Recently, the concept of "allostatic load" has been provided to explain how relative deprivation translates into physiological dysregulation and higher mortality. In this paper, our focus was on the oldest-old. The analyses in two population-based samples of very old people, octogenarians in the TamELSA Study and nonagenarians in the Vitality 90+ Study, indicate that social factors do determine duration of life also at very old age. At all ages, the influence of social factors is partly explained by direct increased risks of specific diseases; but a large part of it is not. To understand this association at the social level, we need to have a better comprehension of the processes of life course where people are (actively and passively) selected into different positions in respect to control over one's life, and availability of social, cultural, and health-protecting resources. To understand this association at the biological level, we need a better knowledge of how the consequences of these relative positions in society are translated into neural, immune, and endocrinological regulative processes.

References

Antonovsky, A. (1979) *Health, Stress and Coping*. San Francisco, California: Jossey-Bass.

Avlund, K., Damsgaard, M. T., and Holstein, B. E. (1998) "Social relations and mortality: An eleven-year follow-up of 70-year-old men and women in Denmark", *Social Science and Medicine*, 47:635–643.

Berkman, L. F. (1988) "The changing and heterogeneous nature of ageing and longevity: A social and biomedical perspective", *Annual Review of Gerontology and Geriatrics*, 8:37–68.

Berkman L. F., and Syme, S. L. (1979) "Social networks, host resistance, and mortality: A nine-year follow-up study of Alameda County Residents", *American Journal of Epidemiology*, 109(2):186–204.

Bijnen, F. C., Caspersen, C. J., Feskens, E. J., Saris, W. H., Mosterd, W. L., and Kromhout, D. (1998) "Physical activity and 10-year mortality from cardiovascular diseases and all causes: The Zutphen elderly study", *Archives of Internal Medicine*, 158(14):1499–1505.

Blazer, D. G. (1982) "Social support and mortality in an elderly community population", *American Journal of Epidemiology*, 115:684–694.

Cavelaars, A. E., Kunst, A. E., Geurts, J. J., Crialesi, R., Grotvedt, L., Helmert, U., Lahelma, E., Lundberg, O., Matheson, J., Mielck, A., Rasmussen, N. K., Regidor, E., do Rosario-Giraldes, M., Spuhler, T., and Mackenbach, J. P. (2000) "Educational differences in smoking: International comparison", *BMJ*, 320(7242):1102–1107.

Cerhan, J. R., and Wallace, R. B. (1997) "Change in social ties and subsequent mortality in rural elders", *Epidemiology*, 8(5):475–481.

Crimmins, E., and Sato, Y. (2001) "Trends in healthy life expectancy in the United States 1970–1990: Gender, racial, and educational differences", *Social Science and Medicine*, 52:1629–1641

Dorofeyev, V. (2000) "Demographic situation in St. Petersburg. Background materials", *Improving the Planning of Medical and Social services within Elderly care*. St. Petersburg: Tacis.

Ferrucci, L., Heikkinen, E., Waters, E., and Baroni, A. (1995) *Pendulum: Health and Quality of Life in Older Europeans*. Florence and Copenhagen: INRCA and WHO.

Ferrucci, L., Izmirlian, G., Leveille, S., Phillips, C. L., Corti, M-C., Brock, D.B., and Guralnik, J. M. (1999) "Smoking, physical activity, and active life expectancy", *American Journal of Epidemiology*, 149(7):645–653.

Fraser, G. E., and Shavlik, D. D. (1997) "Risk factors for all-cause and coronary heart disease mortality in the oldest-old. The Adventist health study", *Archives of Internal Medicine*, 157(1)9:2249–2258.

Gaziano, J. M., Gaziano, T. A., Glynn, R. J., Sesso, H. D., Ajani, U. A., Stampfer, M. J., Manson, J. E., Hennekens, C. H., and Buring, J. E. (2000) "Light-to-moderate alcohol consumption and mortality in the physicians' health study Enrollment Cohort", *Journal of the American College of Cardiology*, 35(1):96–105.

Glass, T. A., de Leon, C. M., Marottoli, R. A., and Berkman, L. F. (1999) "Population based study of social and productive activities as predictors of survival among elderly Americans", *BMJ*, 319:478–483.

Goebeler, S., Jylhä, M., and Hervonen, A. (2003) "Medical history, cognitive status and mobility at the age of 90. A population-based study in Tampere, Finland", *Aging Clinical and Experimental Research*, 15(2):154–161

Groenbaek, M., Deis, A., Becker, U., Hein, H. O., Schnohr, P., Jensen, G., Borch-Johnsen, K., and Sorensen, T. I. (1998) "Alcohol and mortality: Is there a U-shaped relation in elderly people", *Age and Ageing* 27(6):739–744.

Grundy, E. (1997) "Demography and gerontology: Mortality trends among the oldest old", *Aging and Society*, 17:713–725.

Hanson, B. S., Isacsson, S-O., Janzon, L., and Lindell, S. E. (1989) "Social network and social support influence mortality in elderly men. The prospective study of 'Men Born in 1914' Malmö, Sweden", *American Journal of Epidemiology*, 13(1):100–111.

Hasan, J. (1988) "Social Class, Disease and Death. An Essay in Social Medicine". *Proceedings of the Society for Hornphysiology*, p. 6. Tampere.

Heikkinen, E., Waters, W. E., and Bzezinski, Z. J. (1983) *The Elderly in Eleven Countries. A Sociomedical Survey.* Copenhagen: WHO Regional Office for Europe (Public Health in Europe 21).

Huisman, M., Kunst, A. E., Andersen, O., Bopp, M., Borgan, J-K., Borrell, C., Costa, G., Deboosere, P., Desplanques, G., Donkin, A., Ganeyne, S., Minder, C., Regidor, E., Spadea, T., Valkonen, T., and Mackenbach, J. P. (2004) "Socioeconomic inequalities in mortality among elderly people in 11 European populations", *Journal of Epidemiology and Community Health*, 58:468–475.

Idler, E. L., and Benyamini, Y. (1997) "Self-rated health and mortality: A review of twenty-seven community studies", *Journal of Health and Social Behavior*, 38:21–37.

Jylhä, M., and Aro, S. (1989) "Social ties and survival among the elderly in Tampere, Finland", *International Journal of Epidemiology*, 18(1):158–164.

Jylhä, M., and Hervonen, A. (1999) "Functional status and need of help among people aged 90 or over: A mailed survey with a total home-dwelling population", *Scandinavian Journal of Public Health*, 2:106–111.

Jylhä, M., Jokela, J., Tolvanen, E., Heikkinen, E., Heikkinen, R-L., Koskinen, S., Leskinen, E., Lyyra, A-L., and Pohjolainen, P. (1992) "The tampere longitudinal study on ageing. Description of the study. Basic results on health and functional ability", *Scandinavian Journal of Social Medicine Supplement*, 47:1–58.

Jylhä, M., Guralnik, J. M., Ferrucci, L., Jokela, J., and Heikkinen, E. (1998) "Is self-rated health comparable across cultures and genders?", *The Journals of Gerontology: Social Sciences*, 53B(3):S144–S152.

Jylhä, M., Guralnik, J. M., Balfour, J., and Fried, L. P. (2000) "Walking difficulty, walking speed, and age as predictors of self-rated health: The women's health and aging study", *The Journals of Gerontology: Medical Sciences*, 56A(10):M609–617.

Kannisto, V., Turpeinen, O., and Nieminen, M. (1999) *Finnish Life Tables since 1751. Demographic Research* 1/1: Max-Planck-Gesellschaft.

Kaplan. G. A., Salonen, J. T., Cohen, R. D., Brandt, R. J., Syme, S. L., and Puska, P. (1988) "Social connections and mortality from all causes and cardiovasular disease: Prospective evidence from Eastern Finland", *American Journal of Epidemiology*, 128:370–380.

Kaplan, G. A., Wilson, T. W., Cohen, R.D., Kauhanen, J., Wu, M., and Salonen, J. T. (1994) "Social functioning and overall mortality: Prospective evidence from the kuopio ischemic heart disease risk factor study", *Epidemiology*, 5:495–500.

Knoops, K.T., de Groot, L. C., Kromhout, D., Perrin, A. E., Moreira-Varela, O., Menotti, A., and van Staveren, W. A. (2001) "Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: The HALE project", *JAMA*, 292(12):1433–1439.

Kunst, A. E., Groenhof, F., Andersen, O., Borgan, J-K., Costa, G., Desplanques, G., Filakti, H., do, M., Giraldes, R., Faggiano, F., Harding, S., Junker, C., Martikainen, P., Minder, C., Nolan, B., Pagnanelli, F., Regidor, E., Vagero, D., Valkonen, T., and Mackenbach, J. P. (1999) "Occupational class and ischemic heart disease mortality in the United States and 11 European countries", *American Journal of Public Health*, 89(1):47–53.

LaCroix, A. Z., Lang, J., Scherr, P., Wallace, R. B., Cornoni-Huntley, J., Berkman, L., Curb, J. D., Evans, D., and Hennekens, C. H. (1991) "Smoking and mortality among older men and women in three communities", *New England Journal of Medicine*, 324(23):1619–1625.

Liang, J., McCarthy, J., Jain, A., Krause, N., Bennett, J. M., and Gu, S. (2000) "Socioeconomic gradient in old age mortality in Wuhan, China", *The Journals of Gerontology: Social Sciences*, 55(4):S222–S233.

Liao, Y., McGee, D. L., Cao, G., and Cooper, R. S. (2000) "Alcohol intake and mortality: Findings from the national health interview surveys (1988 and 1990)", *American Journal Epidemiology*, 151(7):651–659.

McEwen, B. S., and Stellar, E. (1993) "Stress and the individual. Mechanisms leading to disease", *Archives of Internal Medicine*, 153(18):2093–2101.

McEwen, B. S., and Seeman, T. (1999) "Protective and damaging effects of mediators of stress: Elaborating and testing the concepts of allostasis and allostatic load". In: Adler, N. D., Marmot, M., McEwen, B. S., Stewart, J. (eds.), *Socioeconomic Status and Health in Industrial Nations. Sociological, Psychological and Biological Pathways.* New York, NY: The New York Academy of Sciences, pp. 30–47.

Mackenbach, J. P., Kunst, A. E., Cavelaars, A., Groenhof, F., Geurts, J. J. M., and the EU Working group on socioeconomic inequalities in health (1997) "Socioeconomic inequalities in morbidity and mortality in Western Europe", *The Lancet*, 349:1655–1659.

Maier, H., and Smith, J. (1999) "Psychological predictors of mortality in old age", *Journal of Gerontology: Psychological Sciences*, 54B(1):P44–P54.

Manton, K. G., and Stallard, E. (1981). "Methods for evaluating the heterogeneity of aging processes in human populations using vital statistics data: Explaining the black/white mortality crossover by a model of mortality selection", *Human Biology*, 53/1: 47–67.

Marmot, M. (1999) "Epidemiology of socioeconomic status and health: Are determinants within countries the same as between countries?". In: Adler, N. D., Marmot, M., McEwen, B. S., Stewart, J. (eds.), *Socioeconomic Status and Health in Industrial Nations. Sociological, Psychological and Biological Pathways.* New York, NY: The New York Academy of Sciences, pp. 16–29.

Marmot, M. G., and Shipley, M. J. (1996) "Do socioeconomic differences in mortality persist after retirement? 25 year follow-up of civil servants from the First Whitehall study", *BMJ*, 313:1177–1180.

Marmot, M., Ryff, C. D., Bumpass, L. L., Shipley, M., and Marks, N. F. (1997) "Social inequalities in health: Next questions and converging evidence", *Social Science and Medicine*, 44(6):901–910.

Martelin, T., Koskinen, S., and Valkonen, T. (1998) "Sociodemographic mortality differences among the oldest old in Finland", *Journal of Gerontology*, 53B(2):S83–S90.

Martelin, T., Koskinen, S., and Notkola, V. (1999) "Socioeconomic Position and Mortality in 1971–95 among the Finnish Elderly. Register-Based Follow-up Study of a Large Sample from the 1950 Census". Paper presented at the *European Population Conference EPC99*, The Hague, The Netherlands, 30 August–3 September 1999.

Martikainen P., Valkonen, T., and Martelin, T. (2001) "Change in male and female life expectancy by social class: Decomposition by age and cause of death in Finland 1979–95", *Journal of Epidemiology and Community Health*, 55:494–499.

Marmot, M. G. (2003) "Understanding social inequalities in health", *Perspectives in Biology and Medicine*, 46(Suppl 3):S9–S23.

Niemi, A-K., Hervonen, A., Hurme, M., Karhunen, P. J., Jylhä, M., and Majamaa, K. (2003) "Mitochondrial DNA polymorphism associated with longevity in Finnish population", *Human Genetics*, 112(1):29–33.

Nybo, H., Chr. Petersen, H., Gaist, D., Jeune, B., Andersen, Kj, McGue, M., Vaupel, J. W., and Christensen, K. (2003) "Predictors of mortality in 2,249 nonagenarians—the Danish 1905-cohort survey", *JAGS*, 15:1365–1373.

Ostir, G. V., Markides, K. S., Black, S. A., and Goodwin, J. S. (2000) "Emotional well-being predicts subsequent functional independence and survival", *Journal of the American Geriatrics Society*, 48(5):473–478.

Paffenberger, R. S., Hyde, R. T., Wing, A. L., and Hsieh, C. (1986) "Physical activity, all-cause mortality, and longevity of college alumni", *New England Journal of Medicine*, 314:605–613.

Palmore, E. B. (1982) "Predictorts of the longevity difference: A 25-year follow-up", *The Gerontologist*, 22:513–518.

Penninx, B. W., van Tilburg, T., Kriegsman, D. M., Deeg, D. J., Boeke, A. J., and van Eijk, J. T. (1997) "Effects of social support and personal coping resources on mortality in older age: The Longitudinal Aging Study Amsterdam", *American Journal of Epidemiology*, 146:510–519.

Peto, R., Darby, S., Deo, H., Silcocks, P., Whitley, E., and Doll, R. (2000) "Smoking, smoking cessation, and lung cancer in the UK since 1950: Combination of national statistics with two case-control studies", *BMJ*, 321(7257):323–329.

Preston, S. H., Elo, I. T., Rosenwaike, I., and Hill, M. (1996) "African-American mortality at older ages: Results of a matching study", *Demography*, 33(2):193–209.

Ryff, C. D., and Singer, B. (1998) "The contours of positive human health", *Psychological Inquiry*, 9(1):1–28.

Schoenbach, V. J., Kaplan, B. H., Fredman, L., and Kleinbaum, D. (1986) "Social ties and mortality in evans county, Georgia", *American Journal of Epidemiology*, 123:577–591.

Seeman, T. E., and McEwen, S. (1996) "Impact of social environment characteristics on neuroendocrine regulation", *Psychosomatic Medicine*, 58:459–471.

Seeman, T. E., Kaplan, G. A., Knudsen, L., Cohen, R., and Guralnik, J. M. (1987) "Social network ties and mortality among the elderly in the Alameda county study", *American Journal of Epidemiology*, 126(4):714–723.

Seeman, T. E., Berkman, L. F., Kohout, F., Lacroix, A., Glynn, R., and Blazer, D. (1993) "Intercommunity variations in the association between social ties and mortality in the elderly. A comparative analysis of three communities", *Annals of Epidemiology*, 3(4):325–333.

Seeman, T. E., Crimmins, E., Huang, M-H., Singer, B., Bucur, A., Gruenewald, T., Berkman, L. F., and Reuben, D. R. (2004) "Cumulative biological risk and socio-economic differences in mortality: MacArthur studies of successful aging", *Social Science and Medicine*, 58:18985–18997.

Shye, D., Mullooly, J. P., Freeborn, D. K., and Pope, C. R. (1995) "Gender differences in the relationship between social network support and mortality: A longitudinal study of an elderly cohort", *Social Science and Medicine*, 41(7):935–947.

Smith, G. D., Hart, C., Blane, D., Gillis, C., and Hawthorne, V. (1997) "Lifetime socioeconomic position and mortality: Prospective observational study", *BMJ*, 314:547–552.

Stansfeld, S. A., and Marmot, M. G. (1992) "Deriving a survey measure of social support: The reliability and validity of the close persons questionnaire", *Social Science and Medicine*, 35:1027–1035.

Steinbach, U. (1992) "Social networks, instutionalization, and mortality among elderly people in United States", *Journal of Gerontology*, 47(4):S183–S190.

Sugisawa, H., Liang, J., and Liu, X. (1994) "Social networks, social support, and mortality among older people in Japan", *Journal of Gerontology*, 49(1):S3–S13.

Syme, S. L. (1986) "Social networks in relation to morbidity and mortality". In: Isacsson, S-O., Janzon, L. (eds.), *Social Support–Health and Disease.* Stockholm: Almqvist and Wiksell International.

Taylor, S. E., and Seeman, T. E. (1999) "Psychosocial resources and the SES–health relationship". In: Adler, N. D., Marmot, M., McEwen, B. S., Stewart, J. (eds.), *Socioeconomic Status and Health in Industrial Nations. Sociological, Psychological and Biological Pathways.* New York, NY: The New York Academy of Sciences, pp. 210–225.

Statistics Finland. (1976). *Occupational and Industrial Classification* (In Finnish: Tilastokeskus (1976) *Asunto- ja elinkeinotutkimuksen ammattiluokitus*. Aakkosellinen hakemisto).

Valkonen, T., Martelin, T., Rimpelä, A., Notkola, V., and Savela, S. (1993) " Socio-Economic Mortality Differences in Finland 1981–1990", *Statistics Finland, Population*, 1, Helsinki, Finland.

Walter-Ginzburg, A., Blumstein, T., Chetrit, A., and Modan, B. (2002) "Social factors and mortality in the old-old in Israel: The CALAS study", *The Journals of gerontology: Social Sciences*, 57B:S308–S318.

Welin, L., Tibblin, G., Svardudd, K., Tibblin, B., Ander-Perciva, S., Larsson, B., and Wilhelmsen, L. (1985) "Prospective study on social influences on mortality", *Lancet*, 1:915–918.

CHAPTER 14. SOCIAL DIFFERENCES IN OLDER ADULT MORTALITY IN THE UNITED STATES: QUESTIONS, DATA, METHODS, AND RESULTS

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Introduction

Life expectancy at birth in the United States is among the lowest in the industrialized world (Population Reference Bureau 2000). In addition, variability in the timing of death seems to be much greater than in other wealthy nations (Wilmoth and Horiuchi 1999). One plausible hypothesis is that average longevity in the U.S. is relatively low because of greater inequality of health and mortality across the American population, so that the most disadvantaged groups pull down the average for the society as a whole. Thus, a thorough analysis of social differences in American mortality seems essential for a better understanding of the country's international ranking in terms of life expectancy.

Beyond the issue of international rankings, inequality in the face of death is an important topic in its own right. How large are the mortality differentials between social groups? What causes these differences, and how do they change over age and time? In this paper, we review the literature on mortality differentials across major social groups in the United States. We do not add new findings to an already vast literature. Rather, we attempt to organize the discussion about this topic and to review key results. Ours is not the first review of this complicated topic, and the interested reader should also consult the excellent articles by Feinstein (1993) and Hummer *et al.* (1998).

We focused our literature search on books and articles written since 1980, but we also reviewed earlier works if they have been cited frequently during the last two decades. We restricted the age range of our analysis to the older adult years, defined loosely as ages above 30 or 40 years, and gave preference to studies of mortality caused by major degenerative diseases, since those are the major killers in that age range. Therefore, we do not touch the vast literature on social differentials in infant and child mortality. We also do not review studies of differential mortality in young adulthood and associated causes of death, such as accidents, homicide, and maternal mortality. Although such causes contribute to mortality differentials at older ages as well, they play a relatively minor role compared to heart disease, cancer, stroke, and the other "diseases of old age."

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Finally, we chose to examine mortality differentials whose origin seems to be mostly social or environmental, rather than biological. For example, although sex differences in mortality clearly have an important social and environmental component, biology also plays a key role. Therefore, we found it convenient to exclude sex differences in mortality from this review and to concentrate on mortality differentials according to a number of social categories: 1) marital status, 2) education, 3) income, 4) occupation, 5) nativity, or place of birth, 6) race and ethnicity, and 7) place of residence. These groupings represent some of the most important dimensions of social stratification in the United States. They are also associated with significant differences in levels and patterns of mortality. In order to limit the scope of our review, we do not discuss differences in mortality by an individual's functional status, perceived health, or known risk factors, although studies of such differentials are well represented in the literature (e.g., Rogers 1995).

Questions and Hypotheses

The literature on social differences in mortality addresses a number of key issues. In this section, we review the major questions and hypotheses that give structure to this discussion. Some research has been concerned mainly with documenting and describing the mortality differentials that characterize the American population. Other inquiries have examined the causes of such differentials. Here, we offer an outline of the key topics that emerge from both of these styles of research.

MAGNITUDE OF DIFFERENTIALS

Mortality differentials are not easy to measure, and thus the first priority of research in this area has been to document the differences that exist. The methodological challenges are reviewed below. At the crudest level, the purpose of this careful measurement is merely to document the existence and measure the size of mortality differences among social categories. The description becomes much more interesting when it includes an analysis of changes in mortality differentials over age or time. A general finding has been that mortality differentials tend to diminish with increasing age, at least in relative terms (Kitagawa and Hauser 1973; Sorlie, Backlund, and Keller 1995; Elo and Preston 1996). This pattern raises important theoretical questions about the interrelated effects of selective attrition and biological ageing (see discussion below).

A key question driving descriptive analyses of mortality differentials is whether these differences have grown or diminished over time (Feldman *et al*. 1989; Pappas *et al.* 1993; Queen *et al.* 1994; Preston and Elo 1995; Duleep 1998; Schalick *et al.* 2000). The accurate measurement of temporal trends in mortality differentials is especially problematic (Duleep 1989). However, there is perhaps no more important question in this discussion than whether social groups are moving farther apart in terms of a life experience so fundamental as mortality, or whether some convergence has been achieved. It seems to be the clear ideological preference of most researchers of this topic that such differentials should diminish over time, and these sentiments echo statements issued by the American federal government (NCHS 1993, cited in Hoyert, Singh, and Rosenberg 1995). In addition, as suggested earlier, trends in mortality differentials over time may influence international rankings of life expectancy at birth.

For various reasons, then, descriptive analyses of mortality differentials are among the most important works on this topic. However, as we emphasize later in our discussion of methods, the instruments currently used to measure mortality differentials in the United States are less precise than would be desirable for a complete and accurate description of levels, patterns, and especially trends. Thus, work in this area will continue to be important.

CAUSAL EXPLANATION

It is imperative to remember that causal analyses of American mortality differentials are built on a descriptive base that is still both imprecise and incomplete. Nevertheless, even if empirical findings must be interpreted with caution, it is still useful to move beyond mere description and to ask deeper questions about the causes and meaning of these differentials. Causal analyses of mortality differentials in the United States have taken several forms. Here, we attempt to organize that discussion under several key headings.

Causes of Death Accounting for Differentials

At the most basic level of causal analysis, we may attempt to understand which causes of death account for observed differences in total mortality. Among young adults, for example, we might ask what proportion of a differential is due to external or violent deaths (accidents, homicide, and suicide), and what proportion is due to disease. Among older adults, the topic of this review, we may ask the same question, but the answer is likely to be less revealing since most deaths at older ages are the result of disease. Instead of focusing on the distinction between external mortality and disease, we must ask which major diseases account for the largest part of total mortality differentials at older ages.

A plausible hypothesis is that mortality differentials at older ages result mostly from two sorts of diseases: those for which individual behaviours like smoking and diet play a crucial role, and those for which there exist effective but expensive treatments. Thus, we might expect to find large differences across social groups in mortality from lung cancer due to differences in smoking habits. We might also find differences in various forms of cardiovascular disease (CVD) due not only to differences in smoking and diet but also to differences in access to medical intervention. If therapies for CVD become more effective over time but access is limited to certain groups, mortality differentials could widen; if access becomes more egalitarian, differentials could narrow. On the other hand, for ailments that are not obviously linked to personal behaviours and for which no effective treatment is currently available (such as some forms of cancer and most neurological disorders), mortality differentials should be small and relatively stable over time.

Correlation Among Different Mortality Differentials

One question that has been widely discussed in the literature is the correlation among the various dimensions of mortality differentials. The purpose of such analyses is to discover one or more primary dimensions of social differentiation and to interpret other forms of mortality variation as the product of differentiation along these primary dimensions. For the United States, the most common version of this question involves mortality differentials by race. Are these differentials due to different behavioural practices (and possibly genetic differences), or do they merely reflect the socioeconomic disadvantage of certain racial

groups, especially Blacks, in American society? Or are both sets of factors important, perhaps because they are interrelated?

Statistical analyses are often used to show that race becomes less important as an explanatory variable once socioeconomic indicators (e.g., education, income, wealth) are included in a regression equation (Sorlie *et al.* 1992; Rogers 1992; Menchik 1993; Sorlie, Backlund, and Keller 1995; Lantz *et al.* 1998; Hummer *et al.* 1999; Rogers, Hummer, and Nam 2000). But how should such a result be interpreted? It does not mean that race is unimportant, because race may itself be a cause of the socioeconomic disadvantage of certain groups. Likewise, it does not mean that socioeconomic status is more important than the personal behaviours that are characteristic of different racial groups, since such variables are usually missing from the same regression equation.

Rather, such analyses should be interpreted as mere comparisons of the predictive power of different variables. A plausible hypothesis is that income and other indicators of an individual's socioeconomic status are better predictors of subsequent mortality than is his or her race. An equally plausible hypothesis is that personal behaviours are even better predictors of mortality than is socioeconomic status. However, neither statement, even if true, implies that race or socioeconomic status is unimportant in the causal sequence that culminates in higher mortality among certain racial groups in the United States.

In short, the results of any regression analysis of mortality differentials must be interpreted in light of a broader causal model. In the case of racial differentials, a reasonable model is that race affects both an individual's socioeconomic status (because of opportunity structures and racial prejudice) and his or her personal behaviours (because of cultural differences). In turn, socioeconomic status affects access to medical care and has further effects on personal behaviours (for example, excess smoking and drinking may be a response to the stress associated with a disadvantaged social status). Personal behaviours and access to care in times of need are the immediate causes of mortality differentials by race, but both race and socioeconomic status contribute, directly or indirectly, to the final outcome. Questions for research concern the relative strengths of the different causal relationships in the model.

Socioeconomic status is related in complex ways to other mortality differentials as well. For example, mortality differentials by nativity, or place of birth or origin, may reflect partly the socioeconomic conditions of migrants. Relatively high or low mortality among migrants may be unsurprising once we account for the social position of the groups involved. On the other hand, mortality differentials by nativity may be contrary to what would be predicted based on socioeconomic status, emphasizing the need to look for other sorts of explanations. Indeed, sex differentials in mortality are quite the opposite of what would be expected based on the relative economic position of men and women.

Education, income, and wealth tend to be highly correlated, and thus mortality differentials in terms of these three variables are interrelated as well. Again, the paths of causation are complex, and it is difficult to assert that one or another dimension of social variation predominates. Family income and wealth during childhood influence educational levels, and educational attainment in turn affects adult earnings and accumulated assets. Income

and wealth may have direct positive effects on health, since they can be used to purchase medical care and healthy leisure activities. However, they may have negative effects as well because they make more affordable some unhealthy habits like excessive meat consumption, smoking, and drinking.

Educational attainment influences a person's income and wealth during adulthood and thus has an indirect impact on mortality. Education may have direct impacts on mortality as well, because it brings knowledge about health risks and may help open the doors to a complex and sometimes intimidating medical care system. Although income and wealth make health care more affordable, education may give people the vocabulary and the confidence needed to communicate effectively with doctors and other medical personnel. For people faced with multiple choices about how to spend their money, education may also encourage more healthy choices (for example, fish instead of red meat, exercise instead of television, red wine instead of hard liquor) and thus may mitigate some of the negative health effects associated with high levels of income and wealth.

Personal Behaviours and Cultural Practices

From a public health perspective, perhaps the most important issue is whether differences in mortality between social groups are due to personal behaviours and cultural practices that could be modified through education and outreach. Interventions to alter smoking, drinking, or dietary habits may be important means of reducing mortality differentials. Medical care utilization is another aspect of personal behaviour that may account for mortality differentials and that could possibly be altered through public programs.

However, it is unclear whether interventions to alter the health habits of certain groups can reduce mortality differentials significantly. If group differences in mortality are highly correlated with socioeconomic differences, then targeted interventions seem less likely to be successful. In that case, improving the health of certain groups may require a broader strategy of social reform that reduces socioeconomic inequality in general. But if it can be shown that a significant part of mortality differentials is attributable to individual behaviours tied to cultural traditions rather than to socioeconomic deprivation, successful interventions may be possible without disrupting the existing social order. Furthermore, even if such behaviours are predicted (in a statistical sense) by the disadvantaged social status of certain groups, it may still be possible to intervene using education and outreach to mitigate self-destructive habits.

When faced with specific examples, it may be difficult to distinguish between behaviours that result from socioeconomic disadvantage and those clearly tied to cultural traditions. For example, sub-optimal dietary habits may be a cultural adaptation to a history of socioeconomic deprivation. Even if the historical pattern of social inequality is corrected over time, the group may retain its culinary traditions as an important part of its identity. Likewise, alcoholism in certain groups may not be a longstanding cultural tradition, but rather a recent response to social marginalization in a changing world. In this framework, however, it does not matter whether a cultural practice is new or old, only that it can be identified as a cause of excess mortality and modified through a targeted intervention.

Temporal Ordering of Differentiation

A recurrent issue in the analysis of some mortality differentials is whether individuals are more likely to die because they belong to certain groups, or whether they belong to certain groups because they are less healthy and thus more likely to die. In other words, does differentiation by social affiliation precede or follow differentiation by health status and mortality risk? Both causal pathways are interesting and worthy of study, although they imply different emphases. If individuals with poor health (or with family histories of health problems) are less likely to marry, then health status becomes an important factor in the analysis of marriage patterns.[1] On the other hand, if the health of individuals is unrelated to their probability of marriage, then mortality differentials by marital status provide important evidence about the pros and cons of married life.

The problem of making such distinctions using available data is quite difficult, and few analysts have dared to tackle this problem directly (Goldman 1993). Nevertheless, it is sufficiently general and must be considered as a possible explanation for many commonly observed mortality differentials. Aside from marital status, other examples that may result from selection into social categories on the basis of health status include mortality differentials by income, employment status, nativity, and even religious affiliation. Low income or unemployment may be either the result or the cause of poor health status and elevated mortality risks (Menchik 1993; Chapman and Hariharan 1994; Smith 1999). Migrants may have lower mortality because healthy people are more likely to immigrate, and perhaps also because some foreign residents return to their homelands when they become ill. Religious groups that eschew modern medical care may be selected for individuals with a lower propensity for ill health.

In each of these cases, it is possible and even likely that causation operates in both directions. For example, marriage markets may select for good health at the outset, but marriage itself may also lower mortality risks because of the protective effects of a stable and supportive family life. However, these two processes can also have opposite effects on mortality. For example, migration may select for good health prior to departure, but the challenges and prejudices that immigrants face in a new land may have adverse health impacts.

Concern about reverse causation has led many analysts to favour the use of educational attainment as the primary dimension of social variation used in the study of differential mortality. Unlike income and wealth, educational attainment is relatively fixed throughout life, and an individual's maximum level of education is usually obtained years before the adverse health events that cause the vast majority of deaths in modern society (Kitagawa and Hauser 1973; Preston and Taubman 1994).

Nevertheless, it is also possible that some individuals may simply be inclined to favour long-term over immediate gratification of desires. This sort of predisposition might encourage some people both to pursue educational goals successfully and to avoid risky health

[1] Lee and Panis (1996) suggest that there could also be *adverse* selection into marriage on the basis of health, if less healthy individual recognize the benefits of marriage and choose to marry (or to remarry more quickly) as a result.

behaviours, whereas those who favour the present over the future might be less successful as students and more prone to risk-taking in general (Fuchs 1986:214–42). On the other hand, since education is only partly an individual choice and is heavily constrained by family pressures and social norms, personality factors may have a limited influence on the level achieved. In that case, educational attainment would indeed offer an excellent opportunity for causal analysis of mortality differentials, relatively free from the effects of reverse or mutual causation.

Age Patterns of Mortality Differentials

As noted earlier, a common finding is that mortality differentials tend to diminish with age, at least in relative terms. The cause of this recurrent pattern is uncertain, however. One possibility is that selective attrition removes individuals who have the greatest mortality risks from all groups, but the cumulative force of selection is greatest for the most disadvantaged groups. Therefore, at older ages only the most robust members of disadvantaged groups remain, and these individuals compete more successfully with the remaining members of advantaged groups. In extreme cases, a "crossover" of the two mortality patterns may occur, whereby a disadvantaged group displays higher mortality at younger ages and lower mortality at the end of life (Manton and Stallard 1981). However, apparent mortality crossovers may also be the result of imperfect data, so caution is required in evaluating such empirical patterns (Coale and Kisker 1986; Elo and Preston 1994).

Selective attrition is not the only plausible explanation for the convergence of (relative) mortality differentials over age. Alternatively, the social factors that contribute to such differentials at younger ages may diminish at older ages. Elderly persons may reduce risky behaviours, like excess smoking and drinking, and retirement may bring a reduction in work-related stress (House, Kessler, and Herzog 1990). Such lifestyle changes may bring greater benefits to the groups most adversely affected at younger ages, leading to a narrowing of mortality differentials. In addition, government programs providing income support and medical care for the elderly may "level the playing field."

Thus, some important differences between social groups may be left behind as individuals grow older. Furthermore, due to the shared challenges of biological ageing, individuals may grow more alike as they age. Whereas the causes of mortality at younger ages are amenable to considerable social and environmental manipulation, it is possible that the problem of physiological ageing, which is the dominant cause of mortality at older ages, is much less tractable. The imprint of social disadvantage at younger ages probably remains and continues to exercise some influence at older ages, but these differences may eventually be overwhelmed by the biological forces of deterioration that affect all humans, regardless of social class.

Another force that may promote convergence, and even cross-over, of mortality rates at older ages might be called "social hormesis." In biology, "hormesis" refers to the positive aftereffects of exposure to mild levels of stress, which appears to increase average longevity in several non-human organisms (for a review, see Minois 2000). The most common example is exposure to low levels of radiation; but heat shock is another stressor that is known to raise the life expectancy of survivors in some laboratory settings. It seems at least plausible that a similar mechanism could operate in human populations among individuals

who are faced with relatively high levels of social stress during early and adult life. Survival at older ages may be enhanced by coping skills developed at younger ages in response to social adversity, in keeping with the familiar saying, "if it doesn't kill you, it makes you stronger."[2]

Community Effects

Mortality differentials by place of residence are commonplace. These differences may be due in part to differences in the socioeconomic status of individuals residing in these locations. However, community of residence may have direct effects as well for a variety of reasons. In general, the social and economic conditions of a community are related to the quality of housing stock, the availability of local medical resources, the presence of environmental contaminants, and the acceptability of certain behaviours (Anderson *et al.* 1996). All of these factors could have health effects on individuals in the community independent of their own socioeconomic status.

The health effects of community of residence may be especially pronounced in cases of residential segregation of economically disadvantaged and/or minority populations. Social isolation in these situations may lower self-esteem and promote feelings of alienation, thus encouraging personally and socially destructive behaviours. Daily contact with similarly disadvantaged individuals may promote feelings of hopelessness and discourage a positive outlook on the future (Sanders-Phillips 1996; Williams 1999; Polednak 1996). The geographic concentration of disadvantaged persons may also favour the development of social pathologies like crime, violence, and excess drinking and smoking. Indeed, one outcome of residential segregation in the U.S. is that low-status Blacks seem to experience qualitatively inferior residential environments compared to low-status Whites (Massey and Fong 1990). For these reasons, residential segregation may contribute to mortality differentials by race in the United States.

Another possible connection between community of residence and mortality differences is the potential psychological effect of relative deprivation. As discussed already, absolute deprivation, or poverty, is often thought to contribute to mortality differentials. However, it has also been suggested that individuals may suffer stress-related health problems due to a sense of inferiority created by relative deprivation (Wilkinson 1992, 1996). If correct, the hypothesis suggests that mortality differentials will never disappear so long as economic inequality exists in a society. Conversely, if economic inequality diminishes, mortality differentials should decrease as well.[3]

If relative deprivation is a cause of mortality differences in a population, it may seem that residential segregation of disadvantaged groups could help to ease the stresses of

[2] Friedrich Nietzsche apparently wrote, "That which does not kill me makes me stronger" (in *Beyond Good and Evil*). We thank Steve Austad for pointing this out.

[3] However, it is worth noting that even in the absence of economic differences, individuals would still be ranked (formally or informally) according to a variety of criteria (beauty, intellect, athletic ability, political power, holiness, etc.). Thus, some degree of psychological stress due to feelings of inferiority could remain.

perceived inferiority by minimizing contact with advantaged groups. However, given the ubiquitous images of wealth and glamour provided by television and other mass media, it seems unlikely that disadvantaged groups, even if geographically isolated in their place of residence, could be unaware of their relative position in society.

Summary of Data Sources

There are at least three types of data for use in computing mortality rates by social category (Valkonen 1993). The first draws information from two independent sources, typically death records and census data, each containing breakdowns for a given social category (e.g., sex, race, educational attainment). The second source of data on mortality differentials is longitudinal follow-up studies. These are studies where information is collected on individuals at multiple time points (e.g., some health and nutrition surveys) not merely for the purpose of mortality follow-up. The third format consists of cross-sectional survey or census data linked to subsequent death records, but with no other follow-up except to ascertain mortality status. This third type can be based on a single baseline data set with mortality follow-up over some period, or there can be several baselines at different times (e.g., annual health surveys) with mortality follow-up until a common endpoint.

In this section, we provide an overview of data sources for studying differential mortality in the United States and discuss general strengths and weaknesses associated with each type of data. We draw heavily on a review of this topic by Hoyert *et al.*(1995).

DATA FROM TWO INDEPENDENT SOURCES

Vital statistics and census data for any national population are typically classified according to some key social categories. Minimally, such data are broken down by age and sex. In the United States, racial categories are also a common feature of aggregate data. Using such information, it is possible to construct age-specific death rates by sex or race merely by dividing deaths for some group by population counts for the same group.

The advantages of such an approach are that it is simple to apply and that the results usually pertain to the entire population (not a sample). The major disadvantage is that the classification schemes used in the two sources may not be fully comparable, resulting in "numerator-denominator bias." In the case of sex, we can safely assume that the two classification systems will be almost identical. However, an individual's race may be recorded differently in the two data sources, especially for individuals belonging to less numerous racial groups (Rogers, Carrigan, and Kovars 1997).

In the United States, it appears to be more likely that an individual's race or ethnicity will be recorded as Asian and Hispanic in a census than on a death certificate. Census data are derived from self-reported information and thus tend to reflect a great diversity of race and ethnicity, whereas death certificates completed by doctors or medical examiners are more likely to classify individuals as either Black or White. Such errors probably have only minor

effects on mortality estimates for larger groups, like Whites and Blacks,[4] but are known to produce an important downward bias in death rates for smaller race/ethnic categories, like Asians and Hispanics (Rosenwaike, Hempstead, and Rogers 1991; Rosenberg *et al.* 1999). Caution in the interpretation of calculated mortality rates is especially appropriate in the case of Hispanics, since some detailed studies of death certificates have found that a substantial fraction of decedents with Spanish surnames were not recorded as being of Hispanic origin (Polednak 1995; Sorenson 1998).

Mortality rates along dimensions other than sex and race are even less reliable. In some cases, the two classification schemes are clearly not compatible. For example, the census asks individuals about current occupation, whereas the death certificate contains information on "usual occupation" (Hoyert *et al.* 1995). Even if the two data sources appear to contain a breakdown by the same variable, it is important to be skeptical about whether the meaning and interpretation of the variable were in fact the same. In other cases, one of the data sources (typically the death certificate) may simply lack the desired categories.

"Followback surveys" are an attempt to address some of these difficulties. Such surveys collect census-type information from next-of-kin for a sample of decedents in the population of interest. For example, the National Mortality Followback Survey (NMFS) of 1986 was based on a 10% sample of death certificates. Next-of-kin were contacted about six months after a death and were asked to complete a questionnaire about the decedent (Hoyert *et al.* 1995). A more recent NMFS was conducted in 1993. One advantage of such surveys is that they can be designed to provide more information about the characteristics of decedents than is typically available on a death certificate. The other advantage is that the information is collected through reports by next-of-kin, which should be closer in meaning to the self-reports of individuals than are death certificates completed by medical personnel. In theory, at least, followback surveys should minimize numerator–denominator bias, but since the data for numerator and denominator are drawn from two different sources, it is still possible that they are not fully comparable.

LONGITUDINAL STUDIES (COMPLETE FOLLOW-UP)

A number of studies follow groups of individuals over a period of several years and collect information at several time points. In these cases, mortality follow-up is not the primary intention of the longitudinal study design. Nevertheless, mortality information is often available either indirectly (when it is known merely that an individual died during some given interval) or directly (when exact information on date, and possibly cause, of death is obtained for decedents). Routine follow-up of study participants may be supplemented by searches in the National Death Index (NDI) or Medicare beneficiary records. Using multiple sources for mortality follow-up helps to ensure the completeness and accuracy of information about the timing and circumstances of death.

[4] The measurement of Black–White mortality differences is probably affected more by differential accuracy in age reporting (see Elo and Preston 1994; Hill, Preston, and Rosenwaike 2000) than by inconsistent racial classification.

Another advantage is that longitudinal data of this sort are well suited to the analysis of the causal processes that influence mortality differentials by social group. It is possible in some cases to study whether social differentiation precedes or follows divergence in mortality risks. For example, does lower income result in increased mortality, or does poor health lead simultaneously to increased mortality risks and lower income? With data on all three variables (health, income, and death) over several years of a person's lifetime, it is possible to address such questions directly (Menchik 1993; Chapman and Hariharan 1994). Without such information, it is impossible to do more than just speculate about reverse and mutual causation.

A potential disadvantage of data in this format is their limited scope. If the data refer to a single cohort, they do not permit an analysis of temporal change in the variables of interest. Even if multiple cohorts are followed, studies of mortality change over age and time may be awkward, since cohorts are observed over different age ranges. But perhaps the most significant difficulty with data in this format is that sample sizes may be too small to measure mortality differences between relatively small social groups.

MATCHED DATA (FOLLOW-UP FOR MORTALITY STATUS ONLY)

A third source of information on mortality differentials consists of cross-sectional survey or census data that have been linked to subsequent death records. In these studies, there is no follow-up of participants other than to ascertain the date and, possibly, the cause of death.

The first data set of this type was the classic Matched Records Study, which linked a national sample of death records during four months, May–August 1960, to Census records from April of the same year (Kitagawa and Hauser 1973:184). Given the limited computer technology of the time, records had to be matched manually by searching through files of Census records organized by block. The restriction of the sample of deaths to a short time period soon after the Census enumeration was intended to facilitate the matching procedure, on the theory that the address on the death certificate should usually fall within the block where the person was residing a few weeks or months earlier. Nevertheless, only about 77 percent of the deaths in the sample were successfully matched to a corresponding Census record (Kitagawa and Hauser 1973:187). Then, as now, data analysis had to rely on an assumption that the probability of a successful match was unrelated to the covariates of interest.

Today, computers are used to perform a similar form of record linkage. Now, however, instead of linking backward from a sample of deaths to an earlier census (like Kitagawa and Hauser), the usual strategy is to link forward from a sample survey to a complete list of deaths. The National Death Index (NDI) was created for this purpose and covers all deaths occurring in the United States from 1979 onward. A researcher can submit a list of names and other identifying information to the National Center for Health Statistics (NCHS), which searches for possible deaths among individuals on the list over a specified range of years. The search returns only a list of potential matches (zero, one, or more) for each individual on this list. For each potential match, the NDI provides information about the closeness of each match, as well as the date of death, the state where the death occurred, and the death certificate number (NCHS 1990). The researcher has the responsibility of

cleaning this list to eliminate "false positives" and of contacting the various states to obtain copies of death certificates, if needed.

For the United States, the most widely used data set based on this type of match procedure is the National Longitudinal Mortality Study (NLMS). There are two versions of the NLMS: one that can be analysed only within the U.S. Census Bureau and another that has been released to the public. The public-use sample in its current form consists of five rounds of the Current Population Survey (CPS) during 1979, 1980, and 1981, linked to death records during 1981–1989 using the NDI. The version that is not available to the public contains linked records from more rounds of the CPS over a broader range of years, plus an "enumeration sample" from the 1980 Census (Rogot *et al.* 1992b).

A disadvantage of the public-use NLMS is that users cannot know when an individual entered the study, because the date of survey has been suppressed by the Census Bureau in order to minimize the possibility that participating households could be identified (in conformity with Title XIII regulations, which apply to all data produced by the Census Bureau, including the CPS). For this reason, the public-use NLMS refers to a fuzzy nine-year time period beginning around mid-1980 and ending in mid-1989. The NLMS was the data source for numerous studies during the past decade (e.g., Rogot *et al.* 1992b; Sorlie, Backlund and Keller 1995; Elo and Preston 1996; Anderson *et al.* 1996; Backlund, Sorlie, and Johnson 1996; Johnson, Sorlie, and Backlund 1999). These data have been used to assess the magnitude of mortality differences in the U.S. during the 1980s and to describe their age pattern. However, the NLMS design is not well suited to an analysis of temporal trends in mortality differentials unless combined with results from other studies that may not be fully comparable (Preston and Elo 1995).

In addition to the NLMS, the annual National Health Interview Survey (NHIS) for years 1986–1994 has been linked to death records through the end of 1995 using the NDI to create the NHIS-NDI. These data have been used in a comprehensive analysis of mortality differentials made by Rogers *et al.* (2000). Unlike the NLMS, the NHIS-NDI provides complete information about when an individual enters and exits the study population. Because the NHIS is conducted by NCHS and not by the Census Bureau, the same measures to safeguard the identity of participants are not required (nevertheless, a breach of confidentiality seems highly unlikely). For this reason, the NHIS-NDI may ultimately prove to be more useful than the NLMS, especially for the study of trends in mortality differentials.

The major advantages of data in this form are their size and their potential temporal breadth. The baseline surveys used (such as the CPS or the NHIS) are relatively large and provide detailed information about the national population. The NDI is a relatively inexpensive means of follow-up and can theoretically be used to follow survey participants until all of them have died. When annual surveys (like the NHIS) are combined into a single data set, with mortality follow-up through the NDI, researchers have the opportunity to track the evolution of mortality differentials over time and across a broad age range.

There are, however, some unresolved problems with this kind of data for the United States. It has been reported in the literature that approximately 93% of deaths can be identified successfully using the NDI. Our unpublished results, based on both the NLMS and the

NHIS-NDI, suggest that this figure may be significantly lower in some population subgroups. Obviously, differential success in linkage would bias estimates of mortality differences. Another problem is that most of the baseline surveys used in these studies (e.g., CPS, NHIS) exclude the institutionalized population. At older ages, residents of nursing homes (part of the institutionalized population by definition) are among the most likely to die (McConnel and Deljavan 1982). In addition, the frequency of institutionalization differs across population groups and over age, further complicating an analysis of mortality differentials using such data.

Some of these problems with the data source may eventually be resolved. It should be possible to improve the linkage procedure and to expand coverage to include the institutionalized population. However, a more fundamental disadvantage of this sort of data is that they offer little opportunity to address issues of causation at an individual level. When faced with possible reverse or mutual causation, researchers can do little to resolve the issue using such information. However, other data sources may also be used for mortality follow-up, such as Social Security administrative records (Olson 1999). Such data offer richer analytic possibilities, because they contain information on individuals over the life course (e.g., earnings histories) in addition to vital status.

Methods of Analysis

Many methods can be used for the quantitative analysis of mortality differentials. We will not attempt a complete review of this topic but only offer some highlights of important techniques and issues.

MEASURES USED FOR COMPARISON

In any comparative study, the first task is to choose an appropriate measure. Three common choices for a comparative analysis of mortality are death rates, probabilities of dying, and life expectancies.

Death Rates

By definition, death rates are the number of deaths over some interval of age and time divided by the person-years of exposure over the same interval. Such values can be computed for the population as a whole or for sub-groups, if deaths and exposures are classified according to the same categories. When the characteristics of deaths are found through a matching procedure, the matched sample of deaths can be used to classify all decedents in the population according to the characteristics of interest by assuming that the matched decedents are representative of the population as a whole. If this assumption is correct, the procedure yields unbiased estimates of mortality rates by social group.

Probabilities of Death or Survival

Demographers often consider death rates to be the fundamental unit of analysis, but two alternative measures are probabilities of death or survival. Although these measures are easier to understand for non-specialists, they also present some conceptual difficulties in comparative studies of mortality. A fundamental problem is that all mortality differences

expressed in terms of probabilities of death or survival disappear if the time interval is sufficiently short or long, since these probabilities then approach zero or one by definition. On the other hand, death rates measure the intensity of dying at any moment, or over some interval of age and time, and do not in general converge toward zero or one as the interval shrinks or expands.

Furthermore, according the standard mathematical model, discrete probabilities of death or survival are functions of the continuous hazard curve over some age interval, not the other way around. Therefore, an analysis of differences in death rates, which are discrete approximations to the underlying continuous hazard function, brings us closer to the causal processes producing mortality differentials than does a study of differences in probabilities of death or survival. We conclude that, at least from the specialist's point of view, there are sound reasons for viewing mortality differentials in terms of rates rather than probabilities. These same arguments apply to the odds of death or survival, which are merely functions of probabilities.

Life Expectancies

Yet a third alternative is to measure mortality differences in terms of life expectancy (at birth or at some later age). This approach also appeals to non-specialists, who can understand a concrete concept like the average duration of life in a population better than an abstract notion like a death rate.

METHODS OF COMPARISON

In addition to choosing the metric (rates, probabilities, life expectancies), it is also necessary to choose a method of comparison. Perhaps the simplest, and certainly the most common, technique is to compute the ratio of death rates (or probabilities or life expectancies) for the two groups being compared. Alternatively, one may merely compute the difference in these values for the two groups. This distinction in methods of comparison is sometimes referred to as "relative versus absolute" differences, or "proportional versus absolute" differences (see also Mackenbach and Kunst 1997).

As in the previous section, the distinctions outlined here are not merely academic. There are published examples where the magnitude of a mortality difference either increases or decreases over age or time depending on the measure and method of comparison (Martikainen and Valkonen 1998). There is probably no answer in general to the question of which method of comparison is the correct one.

MULTIVARIATE ANALYSIS

Multivariate statistical methods have been widely used in the study of mortality differentials, mostly as a means of understanding the interrelated effects of alternative explanatory variables. As mentioned earlier, a common approach has been to introduce socioeconomic variables (like income, wealth, education, and occupation) into a regression equation already containing the variable of primary interest, such as race, ethnicity, marital status, or nativity. If the coefficient of the primary variable diminishes after such controls are

introduced, it is said that socioeconomic status accounts for some part of the observed mortality differential (by race, etc.).

There are a number of familiar multivariate methods, and the choice amongst them depends mostly on the dependent variable used in the analysis. Logistic regression is used when the dependent variable is a probability (of death or survival), whereas Poisson regression is used to model death rates. Hazards models, or survival analysis, are especially useful when data are available in the form of survival times for individuals.

Notably, all three of these methods express mortality differentials in relative terms: the coefficients of a Poisson regression are an estimate of the relative death rate in a social category (compared to some reference group); logistic regression yields estimates of the relative odds of dying; finally, the most common form of hazards modelling (the proportional hazards model) assumes that the relative risk of dying is constant across the age range, and coefficients are estimates of the magnitude of that relative risk (for a particular social category compared to some reference group).[5] Alternative multivariate approaches that express and analyse mortality differentials in absolute terms may be worth exploring as well.

There are also important choices about the variables used in a multivariate analysis. Ideally, micro-data should be used to depict individual characteristics that may be correlated with mortality differences, but in many data sets only a limited number of variables are measured at an individual level. In such situations, one strategy is to link the micro-data to aggregate data from another source, and to use the aggregate information as a proxy for individual characteristics. For example, if a micro-data set contains a race variable for all individuals but no information about income, it may be possible to obtain an income proxy in the form of the mean or median income of the census tract where an individual resides. However, this approach often results in biased estimates of individual-level effects and must be applied with caution (Geronimus, Bound, and Neidert 1996).

ALL-CAUSE VS. CAUSE-SPECIFIC MORTALITY

Most studies of mortality differentials in the United States have focused on all-cause mortality. However, for testing various hypotheses, it is essential to analyse differences in cause-specific mortality as well. Since the total mortality rate at a given age is merely the sum of cause-specific rates, including information on cause of death does not usually require a fundamentally different method of analysis.

At younger adult ages in the United States, it is particularly important to consider the contribution of violent causes of death (accidents, homicide, suicide) to difference in mortality by social class. At older adult ages, these causes may be important as well, but their importance is eclipsed by the major causes of death at older ages. Since much of the

[5] As noted already, mortality differentials tend to converge at older ages. This fact makes the proportional hazards assumption questionable in general, although it may still be useful and appropriate for analyses over a limited age range.

mortality decline of recent decades is attributable to the reduction in cardiovascular disease mortality at older ages (CDC 1999), it is especially important to analyse the contribution of mortality from heart disease and stroke to trends in mortality differentials among the elderly.

Summary of Key Results

In this section we summarize key results from studies of differential mortality in the United States. We also highlight the main points of controversy and suggest directions for future research.

EXPLANATIONS OF DIFFERENTIALS BY MARITAL STATUS

Mortality is lower among married people than among their single, divorced, or widowed counterparts in many countries. In general, the mortality differential by marital status is larger for men than for women and, when expressed as a relative risk, tends to diminish with age. Divorced persons usually experience the highest levels of mortality compared to married, single, or widowed individuals (Hu and Goldman 1990). Unmarried persons who are poor experience higher mortality risks than would be predicted on the basis of their marital status and economic conditions alone (Smith and Waitzman 1994).

Mortality differentials by marital status have been attributed to the "protective" and the "selective" effects of marriage, or to a combination of these two factors. Married people may have lower death rates (1) because they enjoy greater social support in general and especially in times of need, (2) because the presence of family members may dissuade risky behaviours like excess smoking and drinking, and/or (3) because the social networks provided by marriage and family may improve access to information about health and to medical services (Gove 1973; House, Karl, and Umberson 1988; Smith and Waitzman 1994; Murray 2000). In addition, departures from the married state, through either widowhood or divorce, are often stressful and may have negative health impacts (Goldman, Korenman, and Weinstein 1995; Lillard and Waite 1995).

However, it is also possible that mortality differentials by marital status result from healthy people being more likely to get married. Some studies have examined the correlation between the proportion of the population that is single or divorced and the level of excess mortality for these groups (compared to married persons). It has been argued that a negative correlation provides evidence for selection, since a low proportion of single or divorced suggests that individuals in these states are highly selected (Livi-Bacci 1985; Kisker and Goldman 1987). Although this finding has been replicated in large international comparisons, this particular interpretation is dubious, since it is also possible that the rarity of single and divorced persons in a society contributes negatively to their health status by increasing their social isolation (Hu and Goldman 1990).

In the analysis of marital mortality differentials, the problem of making accurate causal inferences about the relative contribution of selection versus protection based on aggregate data is probably insurmountable (Goldman 1993). An alternative strategy is to examine

mortality differentials by marital category in longitudinal studies that include measures of health status. By controlling for an individual's health status at baseline, it is possible to determine the magnitude of mortality differentials by marital status corrected for the selective effects of marriage on health.

A longitudinal study of elderly persons in the United States during 1984–1990 based on the Longitudinal Study of Aging (LSOA, a nationally representative sample of the non-institutionalized population aged 70 and over in 1984) found that marital status usually had only modest effects on mortality. An exception was found among widowed males, who showed a measurably higher risk of death (Goldman, Korenman, and Weinstein 1995). Surprisingly, never-married elderly women were found in this study to have better health outcomes than their married counterparts. This finding says little about the selective effects of marriage, since most marriages in this population had occurred many years earlier. The authors note, however, that "elderly singles have a distinct advantage over their formerly married counterparts since they have not experienced the stress and changes in the social and economic environment associated with both divorce and widowhood" (Goldman, Korenman, and Weinstein 1995:1727). It is also possible that long-time single people are better prepared to cope with the loneliness and social isolation of old age compared to their counterparts who were married for most of their lives.[6]

Lillard and Panis (1996) employ the longitudinal Panel Study of Income Dynamics (PSID) to address a complicated set of questions about the relationships between marriage and health. They consider not only the possibility that marriage may select positively for good health, but also that there may be adverse selection if less healthy people seek out marriage because of its perceived benefits (social support, care giving, etc.). In an analysis using structural equations modelling, they conclude that both types of selection occur commonly in the male marriage market (they consider men only). Positive selection dominates overall and among never-married men in particular, and thus it usually accentuates the mortality advantage due to the direct effects of marriage. However, adverse selection dominates among divorced men over age 50 who remarry, and thus it counteracts to some extent the favourable effects of marriage on the observed mortality differential.

TRENDS IN DIFFERENTIALS BY EDUCATION

Ever since the study by Kitagawa and Hauser (1973), studies of mortality differentials in the United States have favoured the use of educational attainment as the primary indicator of social class. Some advantages of this choice have been mentioned already. Obviously, educational attainment influences other key socioeconomic variables, such as income and wealth. Furthermore, educational attainment is relatively stable after early adulthood and is influenced very little by later changes in health status. For these reasons, a key question has been whether mortality differentials by educational level have been increasing or decreasing in recent decades in the United States.

[6] Grundy (this volume) suggests that the apparent reversal of health status at older ages between never-married and married older women may be due in part to the exclusion from the analysis of the institutionalized population.

Feldman *et al.* (1989) address this question by comparing the NHEFS[7] data for years 1971–84 to Kitagawa and Hauser's results for 1960. There are some differences in the type and quality of the data underlying the two studies. Kitagawa and Hauser's data were characterized by relatively poor match rates (see above) but are based on a sample of the entire U.S. population. Although the NHEFS data have better match rates, they exclude the institutionalized population. Feldman *et al.* conclude that, in general, educational differences in mortality increased over this time period for White men but did not change for White women. However, the educational differentials derived from the NHEFS have fairly large standard errors (due to a small sample size), and these errors are nearly large enough to obscure the existence of an educational gradient in mortality altogether. This, combined with the fact Kitigawa and Hauser did not report standard errors, makes any trend analysis based on these two sources rather problematic.

Pappas *et al.* (1993) use the larger NMFS (numerator) and NHIS (denominator) data sets from 1986 to ask the same question, again in comparison to Kitigawa and Hauser's results. Similar to Feldman *et al.*, they find that an index of educational dissimilarity in mortality rates increased over time for all population subgroups. This uniform increase leads to the conclusion that educational differences in mortality have widened over time. However, no standard errors are reported, so again the statistical certainty of the finding is unclear.

Preston and Elo (1995) attempt to settle this question by using the much larger NLMS data set for 1979–1985 (i.e., version one of the public-use NLMS). They point out that the Pappas *et al.* data are subject to numerator–denominator bias. However, NLMS data are also subject to biases due to exclusion of the institutionalized population and, possibly, differences in rates of linkage (using the NDI) between social groups. Leaving aside these non-sampling errors, the much larger sample size allows for greater precision in the estimation of mortality rates.

The estimates of Preston and Elo generally lie within the confidence region of the Feldman *et al.* rates but have much lower standard errors. On the other hand, these estimates yield lower educational differences than the Pappas *et al.* estimates. Considering several measures of educational inequalities in death rates, Preston and Elo conclude that differences have probably narrowed over time for White women but widened for White men. The authors express doubts about the exact magnitude of these changes because of the imprecision of Kitagawa and Hauser's results (due to the relatively low match rate). However, they conclude that the direction of the trends would not change given plausible adjustments to the earlier data.

Whereas most studies express mortality differences in terms of the relative risk of death, some authors have computed educational differences in life expectancy at different ages. Rogot *et al.* (1992a), using the full NLMS for 1979–1985, compute life expectancy by

[7] NHEFS is part of the National Health and Nutrition Examination Study (NHANES) and stands for NHANES Epidemiologic Followup Study.

educational attainment for both men and women. Based on a graphical comparison to the findings of Kitagawa and Hauser, these authors concur with Preston and Elo that there was a slight widening of differentials for White men and a slight narrowing for White women. Curiously, the magnitude of life expectancy differences by education varies widely depending on the study. For instance, Rogot *et al.* (1992a) show differences in life expectancy at age 65 (from lowest to highest educational group) of 3.3 years for men and 2.4 years for women. However, comparable differences based on an analysis of the National Long-Term Care Study were 2 years for men but a remarkable 7.6 years for women (Manton, Stallard and Corder 1997).

Probably the most interesting finding that emerges from this body of literature is the differing trends in educational differences in mortality by sex. Why has the gradient increased for men but decreased for women? No satisfactory explanation seems to be available in the literature, so this topic remains an important area for future research.

TRENDS IN DIFFERENTIALS BY INCOME

The traditional focus on trends in mortality differentials by educational attainment may or may not be warranted. While education is undoubtedly a primary determinant of economic status through its impact on occupation and wages, it is debatable whether educational attainment is indeed the proximal cause of social differentiation affecting mortality risks. Why not examine income or wealth? Wealth measures are notoriously difficult to obtain and measure, so the majority of evidence about mortality differentials pertains to differences in income. Nevertheless, two studies seem to indicate that mortality differences by wealth may be at least as important as those by income, suggesting that further research would be warranted (Menchik 1993; Attanasio and Hoynes 2000).

Duleep (1989) uses CPS data linked to records from the Social Security Administration (CPS-SSA) to compare relative mortality differences by income during 1973–78 to those documented in Kitagawa and Hauser. Due to data limitations, results are limited to white males aged 25–64. Relative mortality differences by income appear to have widened over the period. Whether absolute differences and differences in life expectancy widened over the period cannot be determined from the article.

Pappas *et al.* (1993) and Schalick *et al.* (2000) use the NMFS (numerators) and NHIS (denominators) for various years to examine whether mortality differences by income have increased or decreased over time. As noted previously, data that draw deaths and exposures from different sources are subject to numerator–denominator bias, but if this bias is similar for the two periods, the trend should be unaffected. Using Kitagawa and Hauser's estimates for 1960 as a baseline, the Pappas *et al.* study concludes that relative mortality differences by income widened between 1960 and 1986 for all major population subgroups (by race, sex, etc.). Again, issues of statistical uncertainty are unresolved, if only because we do not know the reliability of the 1960 results of Kitagawa and Hauser. The study by Schalick *et al.* uses data from the 1967 and 1986 versions of the NMFS and the NHIS. Their findings are sensitive to the measure of inequality employed. Using an absolute measure it appears that mortality differences by

income have decreased, whereas using a relative measure such differences have increased.[8] Since mortality declined over the period, even a moderately large widening of relative differences can be consistent with a narrowing of absolute differences.[9]

EFFECTS OF SPECIFIC OCCUPATION ON MORTALITY RISKS

An early study of occupational differences in mortality showed substantially higher mortality levels among labourers than among non-labourers, but it found few differences between large (and heterogeneous) groups of non-labourers (Moriyama and Guralnick 1956). Kitagawa and Hauser (1973) also documented substantial mortality differences by occupation, but their data did not permit a multivariate analysis that would have separated the effects of income, education, and other factors from those due directly to a person's occupation.

More recent studies have investigated more thoroughly the relationship between occupational mortality differentials and other socioeconomic factors (Moore and Hayward 1990; Johnson, Sorlie, and Backlund 1999). A key finding is that most mortality differences by occupational category can be explained by accompanying levels of income and education. However, some specific occupations present elevated risks beyond those predicted by a person's socioeconomic position: taxi drivers, cooks, longshoremen, and transportation operatives. Other occupations present unusually low risks: lawyers, natural scientists, teachers, farmers, and a variety of engineers (Johnson, Sorlie, and Backlund 1999).

Moore and Hayward (1990) make an important substantive and methodological point about the need to study occupational careers rather than merely a person's current occupation. "For example, men in physically demanding and debilitating occupations may move to other less risky occupations before dying" (p. 32). Aside from this selection mechanism, there may be other factors at work as well. The authors find, for example, that a person's mortality is negatively related to the substantive complexity of his longest occupation and to the physical and environmental demands of his current or latest occupation.

Another study about the effects of specific occupations concluded that "writers die young" compared to comparable professions (Kaun 1991). The study, which was based on a random sample from an unnamed source, found that writers have a mean life span about ten years less than other creative artists (artists, cartoonists, composers, conductors, dancers, musicians, singers, painters, and photographers). However, this difference reduces to about seven years after adjustment for sex and date of birth, which is still quite remarkable. The author attributes the elevated mortality risk to the fundamental character of a writer's work, which "provides little, if any, short-term satisfaction, and to the contrary, some fair amount of pain" (p. 397).

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[8] Their absolute measure was the "slope index of inequality," while their relative measure was the "relative index of inequality" (see also Preston and Elo 1995).

[9] Preston and Taubman (1994) suggest that we should discuss mortality in terms of "goods," such as survivorship, rather than "bads," such as mortality. Given that the absolute difference in mortality rates narrowed, we can infer that the ratio of survival rates also narrowed.

DIFFERENTIALS BY NATIVITY, OR PLACE OF BIRTH

In the United States, mortality among the foreign-born tends to be lower than among native-born persons, but not in all cases. Because some race/ethnic groups are composed of a high fraction of foreign-born persons, observed race/ethnic mortality differentials are strongly influenced by nativity status. Hummer *et al.* (1999) provide an excellent overview of the relationship between nativity and race/ethnic mortality differentials.

Among non-Hispanics, foreign-born adults (above age 25) have been found to have a lower risk of death across the age range, especially among men. Using the full NLMS, Sorlie *et al.* (1993) show that non-Hispanic foreign-born adult men have death rates that are from 16 to 55 percent lower than their age-matched native-born counterparts. For women, this differential is smaller (from 7 to 28 percent) and is statistically significant only above age 45.

On the other hand, among Hispanic adult men a foreign-born mortality advantage exists only above age 45, and foreign-born Hispanic women show a statistically significant mortality advantage (compared to native-born Hispanics) only in the 45–64 year age range. However, adult Hispanics as a whole tend to have relatively low mortality compared to non-Hispanics, except perhaps among young adults (Sorlie *et al.* 1993). Thus, although there is less difference between native-born and foreign-born Hispanics in terms of their mortality profiles, both groups are advantaged compared to the general population at older adult ages.

Most Blacks in the U.S. are native-born and the mortality differential between them and most other population groups is relatively large (see below). However, the minority of foreign-born Blacks appears to be a highly advantaged group. In their study of Black and White residents of New York City, Fang *et al.* (1997) found that foreign-born Blacks had the lowest adult mortality of the four groups considered (foreign- and native-born Whites and Blacks). Along other indicators of social status, such as employment rates and educational attainment, foreign-born Blacks were again found to be the most favoured of these four group.

An important aspect of the relationship between nativity and mortality is that it tends to differ across the age range. Hummer *et al.* (1999) report that foreign-born Hispanics tend to have higher death rates at ages 15–44, even after controlling for socioeconomic factors, but that this relationship reverses itself at older ages. Rosenwaike (1983) found such a reversal among Puerto Rican immigrants living in New York City, and a similar pattern has been noted among the foreign-born in France as well (Brahimi 1980).

It seems likely that foreign-born individuals are selected for a relatively high health status at the time that they immigrate. Swallen (1997) finds that foreign-born residents in the U.S. have low mortality compared to persons in their homeland, even for sending countries like Japan or the United Kingdom where health conditions are favourable. Nevertheless, young immigrants face a variety of disadvantages as they attempt to establish themselves in the labour market and in other social arenas. Therefore, it is primarily at older ages, when the disadvantages of social and economic integration have been overcome, that the selective effects of immigration are reflected fully in the mortality profile of the foreign-born.

EXISTENCE OF DIFFERENTIALS BY RACE OR ETHNICITY

Mortality differentials by race have been known for a long time in the United States. The Black-White difference is especially large but has diminished in recent decades. National life tables (based on vital statistics and census data) show a difference in life expectancy at birth of 8.3 years between Blacks and Whites around 1950, which dropped to 6.9 years around 1990.[10] At age 30, the Black-White difference in life expectancy fell more modestly, from 5.9 years around 1950 to 5.6 years around 1990 (NOVS 1954; NCHS 1997). The existence and general magnitude of these differences are well confirmed, at least for recent decades, by studies using matched records (e.g., Kaufman *et al.* 1998; Elo and Preston 1997; Behrman *et al.* 1991; Sorlie *et al.* 1992; Rogers 1992). Furthermore, mortality differentials by race are accompanied by well-documented differences in health and morbidity (Manton and Stallard 1997).

The causes of mortality differences by race are only partially understood, and some empirical characteristics of these differences are still open to dispute. For example, the difference in mortality between Blacks and Whites diminishes with age and, arguably, may even reverse directions at older ages (see discussion of the mortality crossover below). Across the age range, this racial difference in mortality is accounted for at least in part by differences in socioeconomic status (SES) between Blacks and Whites, but the fraction of the entire differential that should be attributed to inequality in SES is uncertain (see below). There is no strong evidence that racial mortality differentials in adulthood are due to genetic differences between racial groups (Neel 1997).

It is difficult to measure mortality for racial or ethnic groups in the United States other than Blacks and Whites because of inconsistencies in the reporting of these designations in vital statistics and census data, resulting in the numerator–denominator bias mentioned earlier. For these groups, the only reliable means of estimating mortality is linked records, which ensure that race or ethnicity is classified by the same method in both numerator and denominator. Since such studies were rare before 1980, reliable information on mortality levels among Hispanics and Asians is available only for the most recent decades (Barringer, Gardner, and Levin 1993; Sorlie *et al.* 1993; Liao *et al.* 1998). Reliable mortality estimates for Native Americans are still difficult to obtain (Young 1997; Snipp 1997).

Much like Blacks, most Native Americans were born in the United States. Their cultures have a long history of economic marginalization and mixed success in assimilation. There are several notable features that emerge from the study of Native American mortality. First, the data problems are fairly severe (Snipp 1997; Young 1997). Native Americans are not easily identified in national health statistics, and mortality estimated from such sources is severely underestimated (Sorlie *et al.* 1992, as reported in Young 1997). For this reason, the most widely used source of information is data collected directly by the Indian Health Service (IHS), which only covers those Native Americans living on reservations and using the IHS. However, since many Native Americans do not live on reservations, the IHS data

[10] Technically, data for 1950 are for non-Whites.

are not representative of the entire population and thus mortality estimates from this source may well be biased.

The Native American mortality experience is in many ways similar to that of Blacks. Young adult mortality is much higher than the White population, principally due to more deaths due to external causes, especially accidents (Young 1997; Kunitz 1990). Pathologies associated with alcohol and diabetes are also well documented. At middle and older ages, where these causes of death are less important in relative terms, Native American mortality converges to that of Whites. At the highest ages (above 65 years), measured mortality is around 80% of White levels due to exceptionally low death rates from cancer and heart disease among Native Americans. However, the same issues of age misstatement that apply to the Black population are important here as well (see below).

Both the Hispanic and Asian populations contain a significant share of first- or second-generation immigrants from a variety of nations. Thus, they probably form more heterogeneous groups than Black Americans. As noted already, Hispanic and Asian mortality must be considered alongside differences in mortality by nativity (Hummer *et al.* 1999; Rogers, Hummer, and Nam 2000).

The mortality difference between Hispanics and non-Hispanics is especially intriguing because it seems to defy the conventional wisdom, which states that socially disadvantaged minority groups should have higher mortality than the majority population. However, mortality estimates based on matched records demonstrate that Hispanics in the United States enjoy low levels of mortality in spite of their socioeconomic disadvantage, a phenomenon that has been called "an epidemiological paradox" (Markides and Coreil 1986). For example, during 1979–1987 mortality above age 25 among Hispanic Whites was about 74 percent (men) or 82 percent (women) of the level for non-Hispanic Whites (Sorlie *et al.* 1993). In the same study, the Hispanic mortality advantage was observed for major causes of death like cancer and cardiovascular disease, although Hispanics were more likely to die from diabetes and homicide (men only).

The Hispanic mortality advantage is most pronounced at middle and older ages. At younger adult age (25–44 years), Hispanic status is associated with no apparent advantage (Sorlie *et al.* 1993) or higher mortality (Hummer *et al.* 1999; Rogers, Hummer, and Nam 2000). Some authors have proposed that Hispanic mortality at older ages is lower than for the rest of the U.S. population because sick immigrants may return to their home countries to die (Rosenwaike 1983). However, this hypothesis seems to be contradicted by the fact that U.S.-born Mexican Americans also display lower old-age mortality than other native-born non-Hispanic Whites (Hummer *et al*. 1999). Likewise, Cuban Americans, who are unlikely to return to Cuba, show lower mortality as well (Sorlie *et al.* 1993).

Mortality among Asian Americans is generally lower than among Whites (Barringer, Gardner, and Levin 1993; Hummer *et al.* 1999; Gardner 1980; Rogers, Hummer, and Nam 2000). This has been known at least since the study by Kitagawa and Hauser (1973), who documented the lower mortality of Japanese and Chinese Americans. This advantage has been observed over all adult ages and for all major categories of cause of death. Although there is considerable SES diversity among Asian sub-populations (e.g., recent

Hmong immigrants versus native-born Japanese Americans), Asians have on average similar levels of income and higher levels of education compared to Whites, which should yield at least a slight mortality advantage (other factors being equal). Furthermore, since mortality (at least at older ages) tends to be lower for the foreign-born, and since a substantial fraction of Asians living in the United States are immigrants, lower mortality among Asians is not surprising. Nevertheless, even after conditioning on socioeconomic factors and nativity, an Asian mortality advantage is still evident (see below).

THE BLACK–WHITE MORTALITY CROSSOVER

Even though Blacks are more likely to die at younger ages, their death rates at older ages appear to be lower than for Whites. Two explanations for this phenomenon, known as the Black–White mortality crossover, have competed for acceptance during the past few decades. One perspective holds that the crossover is merely an artifact of faulty age data. Indeed, it is well known among demographers that consistent age exaggeration (i.e., an upward bias in reported age) results in a downward bias in estimated death rates at older ages (Coale and Kisker 1990). It has also been shown, however, that even random age misreporting (with no consistent upward or downward bias) also results in underestimates of death rates at these ages. This occurs because misclassification of deaths from younger to older ages is numerically more significant than misclassification in the other direction, due to the rapidly diminishing tail in the age distribution of deaths (Preston *et al.* 1996). Because age data for elderly Blacks are known to be less accurate than for elderly Whites, this explanation of the origin of the mortality crossover is at least plausible.

Nevertheless, another plausible explanation suggests that the Black–White mortality crossover is real and not merely an artifact of poor measurement. According to well-specified mathematical models, it is possible that the elderly survivors of a high-mortality group can be more robust (and thus have lower mortality) than the survivors of a low-mortality group if three conditions hold true: (1) the two populations are internally heterogeneous in terms of mortality risks (i.e., members of each group have variable risks of dying across the age range); (2) the relative mortality risk for an individual (compared to some average mortality profile) is constant over age; and (3) mortality levels differ widely at younger ages. Under these conditions, the ordering of the two groups in terms of their mortality experience could reverse itself at older ages, yielding a crossover such as observed for Blacks and Whites in the United States (Manton and Stallard 1981).

An important criticism of this explanation is that such models do not usually account for the potential effects of scarring on the elderly survivors of the high-mortality group, even though some research points toward the impact of early life conditions on old-age mortality (e.g., Barker 1998; Costa 1998). Nonetheless, it seems at least possible that the effects of scarring could diminish with age or be dominated by the effects of mortality selection. Another possibility is that the survivors of a group that is disadvantaged in younger life could enjoy lower mortality at older ages because of better coping skills developed in the face of adversity—an example of social hormesis, as mentioned earlier. In short, the existence of mortality crossovers by race in the United States remains an intriguing though unproven hypothesis.

Indeed, it is difficult and perhaps impossible to find positive proof for the mortality selection hypothesis, since there is no simple means of measuring the differential risks of mortality among individuals within population sub-groups. For this purpose, it would be necessary to obtain *in vivo* physiological measurements that are complete and reliable predictors of subsequent mortality risks. With such measurements, it would be possible to compare the relative importance of mortality selection and physical scarring in the aftermath of adverse health conditions during early life. Unfortunately, studies of this sort are difficult to conduct, and a clear link between specific physiological parameters and individual mortality risks has been only partially established. Therefore, we lack a direct and convincing demonstration that the Black–White mortality is in fact due to mortality selection, even though mathematical models demonstrate that such an outcome is theoretically possible.

On the other hand, there have been important empirical studies addressing the hypothesis that the crossover may result from faulty data. A careful study of beneficiary records from the Social Security Administration suggested that the Black–White crossover was real at least above age 90 (Kestenbaum 1992). It is believed that age reporting in the Social Security records is more accurate than in vital statistics and census data, so the presence of a mortality crossover in these data is important evidence that the crossover phenomenon may be real.

Other researchers have studied the accuracy of age reporting on death certificates during the 1980s by matching these records to census information for the same individuals from the late nineteenth or early twentieth centuries (Preston *et al.* 1996; Hill, Preston, and Rosenwaike 2000). This technique suggests that inaccurate measurement is the cause of the Black–White mortality crossover at least below age 95. At the very highest ages, however, the crossover remains even after cleaning the data by this method. The authors suggest that this apparent difference may be real, or it may be due to random variation given the small number of cases above age 95 (Hill, Preston, and Rosenwaike 2000).

In conclusion, the issue of the Black–White mortality crossover remains an open question, although the extent of the phenomenon, if it exists at all, is surely much smaller than originally claimed. A narrowing of racial differentials in mortality at older ages is not implausible, since governmental support systems in the United States help alleviate social inequality in general among the elderly (much more so than at younger ages). However, a reversal of the differential requires that mortality selection and social hormesis dominate physical scarring in terms of their combined impacts on old-age mortality. Unfortunately, the mechanics of such a theory are difficult, if not impossible, to test empirically.

ROLE OF SOCIOECONOMIC STATUS IN RACIAL OR ETHNIC DIFFERENTIALS

As noted earlier, Blacks tend to have relatively high levels of mortality compared to Whites or to the American population in general. Conversely, Asians and Hispanics seem to have a more favourable mortality experience. The literature appears to indicate that these racial differences interact with socioeconomic status in different and somewhat unpredictable ways, so we treat these issues separately in this section.

A common finding is that the level of excess mortality among Blacks decreases after controlling statistically for socioeconomic status. In other words, when the level of income

or educational attainment is held constant, the mortality difference between Blacks and Whites is smaller than for the two groups as a whole. This reflects the fact that Blacks tend to have lower levels of income and education, which are associated with higher levels of mortality. In addition, it has been noted that mortality differences by income and education are generally larger than those by race (Navarro 1991).

Existing studies do not agree on the question of whether Black–White mortality differences can be explained by variation in socioeconomic status. Some authors (Menchik 1993; Lantz *et al.* 1998) find that excess mortality among Blacks disappears (i.e., becomes statistically insignificant) after taking account of differences in SES. On the other hand, some studies with larger samples (Sorlie *et al.* 1992; Rogers 1992; Sorlie, Backlund, and Keller 1995; Hummer *et al.* 1999) find that Blacks have a statistically significant mortality disadvantage even after controlling for SES. Nevertheless, the magnitude of this disadvantage is reduced by at least 40% when socioeconomic variables are taken into account.

This issue is even more complicated, however, if we consider the interaction between race and SES for different major causes of death. For example, the Black–White mortality differential for homicide and some forms of cancer can be explained largely by differences in SES (Onwuachi-Sanders and Hawkins 1993; Greenwald *et al.* 1996). On the other hand, cardiovascular mortality differences by race contain an important residual element that cannot easily be attributed to SES or observable risk factors (Escobedo, Giles, and Anda 1997). Even within a single cause of death, such as stroke, the size of the racial mortality difference may differ according to income level (Casper, Wing, and Strogatz 1991).

It is important to note that the Black–White mortality differential diminishes with age whether or not one controls for SES. Thus, studies that lump together broad age groups tend to underestimate the excess mortality of Blacks at younger ages and overestimate this quantity at older ages. Similarly, the income-mortality gradient appears to be less steep for Blacks than for Whites, so that the racial differential can vary depending on the income class being studied (Kaufman *et al.* 1998).

If the Black–White mortality gap cannot be explained by differences in socioeconomic status, a portion of this differential must be due to race-specific personal behaviours and characteristics, and another portion to social factors, such as racism and segregation. Relevant personal behaviours and characteristics may include diet, smoking, driving patterns, exercise, and weight, which vary across race/ethnic groups as shown in Table 1 (note that the values in this table are not adjusted for either age or SES).

Although Asians as a group have lower mortality than the White population, they also have a more favourable distribution of SES characteristics.[11] This suggests that the Asian mortality advantage will be reduced if SES is taken in account. However, even after accounting for

[11] If nativity is considered part of SES, then Asians have a profile that definitely favours lower mortality compared to Whites, since a higher proportion of Asians are foreign-born. On the other hand, if nativity is not included in SES, Asians have slightly lower incomes but much higher levels of education compared to Whites, so on balance Asians still have a slight advantage compared to Whites in terms of SES.

Table 1. Percent who report particular risky health behaviours, by race-ethnic group and nativity, United States, 1990.

	Asian Americans		Mexican Americans		Other Hispanics		Non-Hispanic blacks		Non-Hispanic whites	
	FB	NB	FB	NB	FB	NB	FB	NB	FB	NB
No breakfast	15.4	15.3	14.3	28.7	13.6	28.1	17.4	22.9	18.7	23.1
Overweight	6.2	11.7	31.2	32.4	27.2	24.0	29.4	36.9	22.0	24.5
No seat belt	6.3	5.5	15.3	16.4	16.8	16.7	12.8	17.3	12.4	17.1
Light smoker	13.2	3.8	13.4	18.2	15.8	16.3	9.6	17.4	9.6	9.2
Heavy smoker	4.0	7.2	3.8	6.0	6.6	8.9	1.2	9.0	11.6	16.4
Heavy drinker	4.0	5.8	12.1	14.5	8.4	11.4	6.2	7.2	7.7	9.8
No exercise	58.7	47.5	71.8	57.9	70.5	58.3	71.0	65.4	70.5	57.8

Note: FB = Foreign Born; NB = Native Born.
Source: NCHS, 1993 (reproduced from Hummer *et al.* 1999)

differences in SES and nativity, Asian mortality is still about 30% lower than among Whites (Hummer *et al.* 1999). Therefore, just as SES and other factors work together to create higher mortality in the Black population, the two sets of effects combine to produce lower mortality in the Asian population.

The Hispanic mortality advantage is more complex. Hispanics have lower mortality in general, in spite of less favourable socioeconomic characteristics. Therefore, the Hispanic mortality advantage after controlling for SES is in fact larger than the observed mortality differential (Sorlie *et al.* 1993; Hummer *et al.* 1999).

How important are personal behaviours and characteristics in accounting for the mortality differentials by race and ethnicity that remain after controlling statistically for differences in SES? On average, the health behaviours and characteristics of Blacks resemble those of Whites, with the notable exceptions of a higher prevalence of obesity and a lower frequency of exercise. Asians seem to have more favourable health behaviours than Whites (see Table 1). It is unclear whether smoking is more or less common among Hispanics compared with non-Hispanic Whites (as summarized by Sorlie *et al.* 1993). Mexican Americans are more likely to be overweight and heavy drinkers than non-Hispanic Whites (see Table 1).

Lantz *et al.* (1998) find that controlling for health practices has only a minor impact on that portion of the Black–White mortality difference not attributable to SES. For this reason, it would be somewhat surprising if health practices explain the Asian or Hispanic mortality advantage (net of SES). Feldman *et al.* (1989) include health behaviours in proportional hazard regressions where heart disease is the outcome variable and where education is a key explanatory variable. If these health behaviours were important channels through which education affected heart disease, their inclusion in the regression should reduce educational differences in the outcome variable. However, including health behaviours in the analysis has only a minor impact on measured educational effects. This finding seems to suggest that the risks and benefits linked to a person's educational level, and possibly to

other SES characteristics, race, and nativity as well, operate through channels other than the commonly observed health behaviours, as summarized in Table 1.

If personal characteristics do not explain the non-SES effects of race/ethnicity on mortality, then perhaps social factors operating at an aggregate level are at play. The most obvious social factor affecting all such minority groups in the United States is a shared experience of segregation and discrimination. Indeed, race-based residential segregation has often been cited as a contributing factor in the excess mortality of Blacks (Williams 1999; Polednak 1993; Polednak 1996; Potter 1991; Jackson *et al.* 2000), as discussed in the next section.

EFFECTS OF COMMUNITY, OR PLACE OF RESIDENCE

It is well established that the risk of death is related to the socioeconomic characteristics *of individuals*. However, it is also possible that the average socioeconomic status *of a community* has a direct impact on the health and mortality of individuals residing in that community. The average socioeconomic well-being of the community may affect the quality of the housing stock, the availability of medical care, the level of exposure to environmental toxins, and various risky behaviours (e.g., drinking, smoking, drugs, violence).

An analysis of data from the National Longitudinal Mortality Study suggests that, although the effects of individual socioeconomic position are clearly more important, the socioeconomic status of the community "makes a unique and substantial contribution to mortality" in the United States (Anderson *et al.* 1996). Similarly, in a study of mortality by census tracts, Guest *et al.* (1998) document a positive correlation between unemployment, non-completion of high school, and community mortality levels. Finally, Polednak (1993) finds that the Black–White mortality ratio is positively related to the Black–White poverty ratio and the degree of residential segregation across metropolitan areas.

On the other hand, Daly *et al.* (1998) find that the income distribution of a community has little effect on the mortality risks of individuals after controlling for personal SES. Likewise, Jackson *et al.* (2000) study the association between the degree of segregation[12] in a census tract and individual mortality risks controlling for family income. However, it is difficult to interpret their findings, which indicate that the relationship between segregation and mortality is positive for some groups and negative for others.

The relationship between community of residence and mortality is by no means a simple one. It was noted already that residential segregation and associated social pathology could be contributing factors in the relatively high mortality of Blacks in the United States. On the other hand, Hispanic communities in the U.S. are thought to provide a supportive social environment that contributes to good health. These two results may seem contradictory. Apparently, social isolation of groups can lead to either worse or better health outcomes depending

[12] Jackson *et al.* (2000) measure segregation as the proportion of the census tract that is Black. A high percentage of Blacks in a census tract is taken as evidence of higher segregation, suggesting that an all-White neighbourhood is perfectly integrated whereas an all-Black neighbourhood is wholly segregated. In spite of these objections, it is possible that the measure serves as a good proxy for segregation in general and for the potentially negative effects of segregation on health and longevity in particular.

on the circumstances. We speculate that the difference hinges on the causes of the social isolation experienced by the group in question. For African Americans, residential segregation is the result of a long history of social and economic marginalization by the mainstream society, whereas for Hispanics (and other recent immigrant groups) it reflects a social cohesiveness associated with trying to become part of a new land. There are many subtleties to be considered in both cases, and this contrast should be explored in greater depth.

Another example of the effect of community, or place of residence, is the urban-rural mortality difference. In their landmark study, Kitagawa and Hauser (1973) showed that age-adjusted total mortality rates in 1960 were 5 percent higher in urban counties compared to rural ones, with the highest risk of mortality being found in urban counties that contain a central city. This finding seems anomalous in view of the fact that residents of rural areas tend to be poorer and less well educated on average than city dwellers. In addition, medical services are more widely available in cities. Nevertheless, other factors may help to make city life less conducive to good health. For example, urban social relationships may be more formal and impersonal, leading to anomie, social isolation, and psychological stress; in addition, overcrowding may contribute to the spread of infectious disease (Miller, Voth, and Danforth 1982).

Data from the NLMS confirm that a rural mortality advantage was still present in the United States during the 1980s (Smith *et al.* 1995). After adjusting for age and sex, it was estimated that rural residents had death rates that were about 7–9 percent lower than residents of central cities. This relationship did not change substantially after further adjustment for race/ethnicity, income, education, and marital status. In contrast, residents of suburban districts or urban areas outside central cities also showed an age-sex-adjusted mortality advantage of about 4–7 percent compared to those in central cities, but these differences become smaller and lose statistical significance once controls are added for the same socioeconomic variables.

Thus, residents of central cities experience higher mortality risks compared to all other residential groups in the United States, but these differences with respect to other residents of non-rural areas (i.e., suburbs and outside the central city) appear to be mostly a function of socioeconomic status. The rural mortality advantage, on the other hand, does not disappear after adjusting for socioeconomic differences and thus requires another explanation. Possible protective effects of rural residence may include a more favourable social and physical environment and fewer risky behaviours. Another possibility is that people with serious health problems move from rural areas to cities in order to be closer to health facilities (Smith *et al.* 1995). To our knowledge there has been no adequate empirical confrontation of these two hypotheses (which can again be labeled "protection" versus "selection") in the published literature.

The interaction between poverty, race, and place of residence is well documented by Geronimus *et al.* (1999) in their study of mortality at ages 15–64 among poor Black and White communities in the urban North and the rural South.[13] At least two key findings

[13] The authors acknowledge that their study design cannot distinguish simultaneously between the effects of North vs. South and urban vs. poor because of population size requirements.

from their analysis are worth noting here. First, poor Blacks in the rural South display a much smaller mortality disadvantage compared to poor Blacks in the urban North at comparable levels of socioeconomic status (even after adjustment for differences in the cost of living). A similar but reduced finding is reported for poor Whites. As a result, the magnitude of the rural mortality advantage among the poor appears to be much larger than among the population as a whole. Whereas the latter is usually less than 10 percent, the study by Geronomius *et al.* suggests that the former is at least 20 percent and sometimes more than 100 percent. Second, perhaps contrary to expectations, the excess mortality of these poor communities (compared to Whites nationwide) is not due primarily to the widely publicized causes of homicide and AIDS. Rather, most of the excess mortality in these areas in the age range of 15–64 was due to higher levels of chronic disease, in particular cardiovascular disease.

References

Anderson, R., Sorlie, P., Backlund, E., Johnson, N., and Kaplan, G. (1996) "Mortality effects of community socioeconomic status", *Epidemiology*, 8:42–47.

Attanasio, O. P., and Hoynes, H. W. (2000) "Differential mortality and wealth accumulation", *Journal of Human Resources*, 35(1):1–29.

Backlund, E., Sorlie, P., and Johnson, N. (1996) "The shape of the relationship between income and mortality in the United States: Evidence from the National Longitudinal Mortality Study", *Annals of Epidemiology*, 6:12–20.

Barker, D. J. P. (1998) *Mothers, Babies and Health in Later Life.* Edinburgh, UK: Churchill Livingstone.

Barringer, H. R., Gardner, R. W., and Levin, M. J. (1993) *Asians and Pacific Islanders in the United States. The Population of the United States in the 1980s: A Census Monograph Series*. New York: Russell Sage Foundation.

Behrman, J. R., Sickles, R., Taubman, P., and Yazbeck, A. (1991) "Black-White mortality inequalities", *Journal of Econometrics*, 50(1–2):183–203.

Brahimi, M. (1980) "La mortalité des étrangers en France", *Population*, 35(3):603–622.

Casper, M., Wing, S., and Strogatz, D. (1991) "Variation in the magnitude of black-white differences in stroke mortality by community occupational structure", *Journal of Epidemiology and Community Health,* 45(4):302–306.

Centers for Disease Control (CDC). (1999) "Decline in deaths from heart disease and stroke—United States, 1900–1999", *Morbidity and Mortality Weekly Report*, 48:649–656.

Chapman, K. S., and Hariharan, G. (1994) "Controlling for causality in the link from income to mortality", *Journal of Risk and Uncertainty*, 8(1):85–93.

Coale, A. J., and Kisker, E. E. (1986) "Mortality crossovers: Reality or bad data?", *Population Studies*, 40:389–401.

Coale, A. J., and Kisker, E. E. (1990) "Defects in data on old-age mortality in the United States: New procedures for calculating mortality schedules and life tables at the highest ages", *Asian and Pacific Population Forum*, 4(1):1–31.

Costa, D. (1998) *The Evolution of Retirement: An American Economic History, 1880–1990*. Chicago: University of Chicago Press.

Daly, M. C., Duncan, G. J., Kaplan, G. A., and Lynch, J. W. (1998) "Macro-to-micro links in the relation between income inequality and mortality", *Milbank Quarterly*, 76(3):315–339, 303–304.

Duleep, H. O. (1989) "Measuring socioeconomic mortality differentials over time", *Demography*, 26(2):345–351.

Duleep, H. O. (1998) "Has the U.S. mortality differential by socioeconomic status increased over time?", *American Journal of Public Health*, 88(7):1125.

Elo, I. T., and Preston, S. H. (1994) "Estimating African-American mortality from inaccurate data", *Demography*, 31(3):427–458.

Elo, I. T., and Preston, S. H. (1996) "Educational differentials in mortality: United States, 1979–85", *Social Science and Medicine*, 42:47–57.

Elo, I. T., and Preston, S. H. (1997) "Racial and ethnic differences in mortality at older ages". In: Martin, L. G., Soldo, B. J. (eds.), *Racial and Ethnic Differences in the Health of Older Americans.* Washington, DC: National Academy Press, pp. 10–42.

Escobedo, L. G., Giles, W. H., and Anda, R. F. (1997) "Socioeconomic status, race, and death from coronary heart disease", *American Journal of Preventive Medicine*, 13(2):123–130.

Fang, J., Madhavan, S., and Alderman, M. H. (1997) "Nativity, race, and mortality: Favorable impact of birth outside the United States on mortality in New York city", *Human Biology*, 69(5):689–701.

Feinstein, J. S. (1993) "The relationship between socioeconomic status and health: A review of the literature", *Milbank Quarterly*, 71(2):279–322.

Feldman, J. J., Makuc, D., Kleinman, J., and Cornoni-Huntley, J. (1989) "National trends in the educational differentials in mortality", *American Journal of Epidemiology*, 129:919–933.

Fuchs, V. (1986) *The Health Economy*. Cambridge, MA: Harvard University Press.

Gardner, R. W. (1980) "Ethnic differentials in mortality in Hawaii", *Hawaii Medical Journal*, 39:221–226.

Geronimus, A. T., Bound, J., and Neidert, L. J. (1996) "On the validity of using census geocode characteristics to proxy individual socioeconomic characteristics", *Journal of the American Statistical Association*, 91(434):529–537.

Geronimus, A. T., Bound, J., and Waidmann, T. A. (1999) "Poverty, time, and place: Variation in excess mortality across selected U.S. populations, 1980–1990", *Journal of Epidemiology and Community Health*, 53(6):325–334.

Goldman, N. (1993) "Marriage selection and mortality patterns: Inferences and fallacies", *Demography*, 30(2):189–208.

Goldman, N., Korenman, S., and Weinstein, R. (1995) "Marital status and health among the elderly", *Social Science and Medicine*, 40(12):1717–1730.

Gove, W. R. (1973) "Sex, marital status, and mortality", *American Journal of Sociology*, 79(1):45–67.

Greenwald, H. P., Borgatta, E. F., McCorkle, R., and Polissar, N. (1996) "Explaining reduced cancer survival among the disadvantaged", *Milbank Quarterly*, 74(2):215–238.

Grundy, E. (2006) "Marital status and family support for the oldest-old in Great Britain". In: Robine, J.-M., Crimmins, E. M. (eds.), *Human Longevity Individual Life Duration, and the Growth of the Oldest-Old Population*. New York: Springer, pp. 415–436 (Chapter 18).

Guest, A. M., Almgren, G., and Hussey, J. M. (1998) "The ecology of race and socioeconomic distress: Infant and working-age mortality in Chicago", *Demography*, 35(1):23–34.

Hill, M., Preston, S. H., and Rosenwaike, I. (2000) "Age reporting among white Americans aged 85+: Results of a record linkage study", *Demography*, 37(2):175–186.

House, J. S., Karl, R. L., and Umberson, D. (1988) "Social relationships and health", *Science*, 241:540–545.

House, J. S., Kessler, R. C., and Herzog, A. R. (1990) "Age, socioeconomic status, and health", *The Milbank Quarterly*, 68(3):383–411.

Hoyert, D. L., Singh, G. K., and Rosenberg, H. M. (1995) "Sources of data on socio-economic differential mortality in the United States", *Journal of Official Statistics*, 11:233–260.

Hu, Y., and Goldman, N. (1990) "Mortality differentials by marital status: an international comparison", *Demography*, 27:233–250.

Hummer, R. A., Rogers, R. G., and Eberstein, I. W. (1998) "Sociodemographic differentials in adult mortality: A review of analytic approaches", *Population and Development Review*, 24(3):553–578.

Hummer, R. A., Rogers, R. G., Nam, C. B., and LeClere, F. B. (1999) "Race/ethnicity, nativity, and U.S. adult mortality", *Social Science Quarterly*, 80(1):136–153.

Jackson, S. A., Anderson, R. T., Johnson, N. J., and Sorlie, P. D. (2000) "The relation of residential segregation to all-cause mortality: A study in black and white", *American Journal of Public Health*, 90(4):615–617.

Johnson, N. J., Sorlie, P. D., and Backlund, E. (1999) "The impact of specific occupation on mortality in the U.S. national longitudinal mortality study", *Demography*, 36(3):355–367.

Kaufman, J. S., Long, A. E., Liao, Y., Cooper, R. S., and McGee, D. L. (1998) "The relation between income and mortality in U.S. blacks and whites", *Epidemiology*, 9(2):147–155.

Kaun, D. E. (1991) "Writers die young: The impact of work and leisure on longevity", *Journal of Economic Psychology*, 12(2):381–399.

Kestenbaum, B. (1992) "A description of the extreme aged population based on improved medicare enrollment data", *Demography*, 29(4):565–580.

Kisker, E. E., and Goldman, N. (1987) "Perils of single life and benefits of marriage", *Social Biology*, 34:135–152.

Kitagawa, E. M., and Hauser, P. M. (1973) *Differential Mortality in the United States: A Study in Socioeconomic Epidemiology.* Cambridge, MA: Harvard University Press.

Kunitz, S. J. (1990) "Public policy and mortality among indigenous populations of Northern America and Australasia", *Population-and-Development-Review*, 16(4):647–672.

Lantz, P. M., House, J. S., Lepkowski, J. M., Williams, D. R., Mero, R. P., and Chen, J. (1998) "Socioeconomic factors, health behaviors, and mortality: Results from a nationally representative prospective study of U.S. adults", *The Journal of the American Medical Association*, 279(21):1703–1708.

Liao, Y., Cooper, R. S., Cao, G., Durazo-Arvizu, R., Kaufman, J. S., Luke, A., and McGee, D. L. (1998) "Mortality patterns among adult hispanics: Findings from the NHIS, 1986 to 1990", *American Journal of Public Health*, 88(2):227–232.

Lillard, L. A., and Waite, L. J. (1995) "Till death do us part: Marital disruption and mortality", *American Journal of Sociology*, 100(5):1131–1156.

Lillard, L. A., and Panis, C. W. A. (1996) "Marital status and mortality: The role of health", *Demography*, 33(3):313–327.

Livi-Bacci, M. (1985) "Selectivity of marriage and mortality: Notes for future research". In: Keyfitz, N. (ed.), *Population and Biology*. Liege, Belgium: Ordina Editions, pp. 99–108.

Mackenbach, J. P., and Kunst, A. E. (1997) "Measuring the magnitude of socio-econmoic inequalities in health: An overview of available measures illustrated with two examples from Europe", *Social Science and Medicine*, 44(6):757–771.

Manton, K. G., Stallard, E., and Corder, L. (1997) "Education-specific estimates of life expectancy and age-specific disability in the U.S elderly population: 1982 to 1991", *Journal of Aging and Health*, 9(4):419–450.

Manton, K. G., and Stallard, E. (1997) "Health and disability differences among racial and ethnic groups". In: Martin, L. G., Soldo, B. J. (eds.), *Racial and Ethnic Differences in the Health of Older Americans.* Washington, DC: National Academy Press, pp. 43–105.

Manton, K. G., and Stallard, E. (1981) "Methods for evaluating the heterogeneity of aging processes in human populations using vital statistics data: Explaining the black/white mortality crossover by a model of mortality selection", *Human Biology*, 53:47–67.

Markides, K. S., and Coreil, J. (1986) "The health of Hispanics in the Southwestern United States: An epidemiological paradox", *Public Health Reports*, 101(3):253–265.

Martikainen, P., and Valkonen, T. (1998) "Do education and income buffer the effects of death of spouse on mortality", *Epidemiology*, 9(5):530–534.

Massey, D. S., and Fong, E. (1990) "Segregation and neighborhood quality: Blacks, Hispanics, and Asians in the San Francisco Metropolitan Area", *Social Forces*, 69:15–32.

McConnel, C. E., and Deljavan, F. (1982) "Aged deaths: The nursing home and community differential: 1976", *Gerontologist*, 22(3):318–323.

Menchik, P. L. (1993) "Economic status as a determinant of mortality among black and white older men: Does poverty kill?", *Population Studies*, 47(3):427–436.

Miller, M. K., Voth, D. E., and Danforth, D. M. (1982) "The medical care system and community malady: Rural, urban, and suburban variations in impact", *Rural Sociology*, 47(4):634–654.

Minois, N. (2000) "Longevity and aging: Beneficial effects of exposure to mild stress", *Biogerontology*, 1:15–29.

Moore, D. E., and Hayward, M. D. (1990) "Occupational careers and mortality of elderly men", *Demography*, 27(1):31–53.

Moriyama, I. M., and Guralnick, L. (1956) "Occupational and social class differences in mortality". In: 1955 Annual Conference of the Milbank Memorial Fund, *Trends and Differentials in Mortality*. New York: Milbank Memorial Fund, pp. 61–73.

Murray, J. E. (2000) "Marital protection and marital selection: Evidence from a historical-prospective sample of American men", *Demography*, 37(4):511–521.

National Center for Health Statistics (NCHS). (1990) *National Death Index User's Manual*. Hyattsville, MD: Public Health Service.

National Center for Health Statistics (NCHS). (1993) *National Health Interview Survey, 1990: Health Promotion and Disease Prevention (HPDP) Sample Person Supplement*. Hyattsville, MD: Public Health Service.

National Center for Health Statistics (NCHS). (1997) *U.S. Decennial Life Tables for 1989–91*. United States Life Tables, Vol. 1, No. 1. Washington, DC: NCHS. (DHHS Pub. No. (PHS) 98–1150–1).

National Office of Vital Statistics (NOVS). (1954) *United States Life Tables 1949–51*. Vital Statistics Special Reports, Vol. 41, No. 1. Washington, DC: U.S. Department of Health, Education, and Welfare, Public Health Service.

Navarro, V. (1991) "Race or class or race and class: Growing mortality differentials in the United States", *International Journal of Health Services*, 21(2):229–235.

Neel, J. V. (1997) "Are genetic factors involved in racial and ethnic differences in late-life health?" In: Martin, L. G., Soldo, B. J., (eds.), *Racial and Ethnic Differences in the Health of Older Americans.* Washington, DC: National Academy Press, pp. 210–232.

Olson, J. A. (1999) "Linkages with data from Social Security administrative records in the health and retirement study", *Social Security Bulletin*, 62(2):73–85.

Onwuachi-Saunders, C., and Hawkins, D. F. (1993) "Black-white differences in injury. Race or social class?", *Annals of Epidemiology*, 3(2):150–153.

Pappas, G., Queen, S., Hadden, W., and Fisher, G. (1993) "The increasing disparity in mortality between socioeconomic groups in the United States, 1960 and 1986", *New England Journal of Medicine*, 329(2):103–109.

Polednak, A. P. (1993) "Poverty, residential segregation, and black/white mortality ratios in urban areas", *Journal of Health Care for the Poor and Underserved*, 4(4):363–373.

Polednak, A. P. (1995) "Estimating mortality in the Hispanic population of connecticut, 1990 to 1991", *American Journal of Public Health*, 85(7):998–1001.

Polednak, A. P. (1996) "Segregation, discrimination and mortality in U.S. blacks", *Ethnicity and Disease*, 6(1–2):99–108.

Population Reference Bureau. (2000) *World Population Data Sheet*. Washington, DC: Population Reference Bureau.

Potter, L. B. (1991) "Socioeconomic determinants of white and black males' life expectancy differentials, 1980", *Demography*, 28(2):303–321.

Preston, S. H., and Taubman, P. (1994) "Socioeconomic differences in adult mortality and health status". In: Martin, L., Preston, S. H. (eds.), *Demography of Aging*. Washington, DC: National Academy Press, pp. 279–318.

Preston, S. H., and Elo, I. T. (1995) "Are educational differentials in mortality increasing in the United States?", *Journal of Aging and Health*, 74:476–496.

Preston, S. H., Elo, I. T., Rosenwaike, I., and Hill, M. (1996) "African-American mortality at older ages: Results of a matching study", *Demography*, 33(2):193–209.

Queen, S., Pappas, G., Hadden, W., and Fisher, G. (1994) "The widening gap between socioeconomic status and mortality", *Statistical Bulletin/Metropolitan Insurance Companies*, 75(2):31–35.

Rogers, R. G. (1992) "Living and dying in the U.S.A.: Sociodemographic determinants of death among blacks and whites", *Demography*, 29(2):287–303.

Rogers, R. G. (1995) "Sociodemographic characteristics of long-lived and healthy individuals", *Population and Development Review*, 21(1):33–58.

Rogers, R. G., Carrigan, J. A., and Kovars, M. G. (1997) "Comparing mortality estimates based on different administrative records", *Population Research and Policy Review*, 16(3):213–224.

Rogers, R., Hummer, R., and Nam, C. (2000) *Living and Dying in the U.S.A.: Behavioral, Health, and Social Differentials of Adult Mortality.* San Diego, CA: Academic Press.

Rogot, E., Sorlie, P. D., and Johnson, N. J. (1992a) "Life expectancy by employment status, income, and education in the national longitudinal mortality study", *Public Health Reports*, 107:457–461.

Rogot, E., Sorlie, P. D., Johnson, N. J., and Schmitt, C. (1992b) *A Mortality Study of 1.3 Million Persons by Demographic, Social, and Economic Factors: 1979–1985 Follow-up. U.S. National Longitudinal Mortality Study. Second Data Book.* Washington, DC: U.S. Department of Health and Human Services, National Institute of Health, National Heart, Lung, and Blood Institute. (NIH Pub. No. 92-3297).

Rosenberg, H. M., Maurer, J. D., Sorlie, P. D., Johnson, N. J., MacDorman, M. F., Hoyert, D. L., Spitler, J. F., and Scott, C. (1999) "Quality of death rates by race and hispanic origin: A summary of current research", *Vital and Health Statistics Series 2: Data Evaluation and Methods Research*, 128:1–13.

Rosenwaike, I. (1983) "Mortality among the Puerto Rican born in New York city", *Social Science Quarterly*, 64(2):375–385.

Rosenwaike, I., Hempstead, K., and Rogers, R.G. (1991) "Using surname data in U.S. Puerto Rican mortality analysis', *Demography*, 28(1):175–180.

Sanders-Phillips, K. (1996) "The ecology of urban violence: Its relationship to health promotion behaviors in low-income black and Latino communities", *American Journal of Health Promotion*, 10(4):308–317.

Schalick, L. M., Hadden, W. C., Pamuk, E., Navarro, V., and Pappas, G. (2000) "The widening gap in death rates among income groups in the United States from 1967 to 1986", *International Journal of Health Services*, 30(1):13–26.

Smith, K. R., and Waitzman, N. J. (1994) "Double Jeopardy: Interaction effects of marital and poverty status on the risk of mortality", *Demography*, 31(3):487–507.

Smith, M. H., Anderson, R. T., Bradham, D. D., and Longino, C. F. Jr. (1995) "Rural and urban differences in mortality among Americans 55 years and older: Analysis of the national longitudinal mortality study', *Journal of Rural Health*, 11(4):274–285.

Smith, J. P. (1999) "Healthy bodies and thick wallets: The dual relation between health and economic status", *Journal of Economic Perspectives*, 13(2):145–166.

Snipp, C. M. (1997) "The size and distribution of the american indian population: Fertility, mortality, migration, and residence", *Population Research and Policy Review*, 16(1–2):61–93.

Sorenson, S. B. (1998) "Identifying Hispanics in existing databases: Effect of three methods on mortality patterns of Hispanics and non-Hispanic whites", *Evaluation Review*, 22(4):520–534.

Sorlie, P. D., Rogot, E., Anderson, R., Johnson, N. J., and Backlund, E. (1992) "Black-white mortality differences by family income", *Lancet*, 340:346–350.

Sorlie, P. D., Backlund, E., Johnson, N. J., and Rogot, E. (1993) "Mortality by Hispanic status in the United States", *Journal of the American Medical Association*, 270:2464–2468.

Sorlie, P. D., Backlund, E., and Keller, J. B. (1995) "U.S. mortality by economic, demographic, and social characteristics: The national longitudinal mortality study", *American Journal of Public Health*, 85:949–956.

Swallen, K. C. (1997) "Cross-national comparisons of mortality differentials: Immigrants to the U.S. and stayers in common countries of origin". Presented at the Population Association of America Annual Meetings, Washington, DC.

Valkonen, T. (1993) "Problems in the measurement and international comparisons of socio-economic differences in mortality", *Social Science and Medicine*, 36:409–418.

Williams, D. R. (1999) "Race, socioeconomic status, and health. The added effects of racism and discrimination", *Annals of the New York Academy of Sciences*, 896:173–188.

Wilkinson, R. G. (1992) "Income distribution and life expectancy", *British Medical Journal*, 304:165–168.

Wilkinson, R. G. (1996) *Unhealthy Societies—The Afflictions of Inequality.* London: Routledge.

Wilmoth, J. R., and Horiuchi, S. (1999) "Rectangularization revisited: Variability of age at death within human populations", *Demography*, 36(4):475–495.

Young, T. K. (1997) "Recent health trends in the native American population", *Population Research and Policy Review*, 16(1–2):147–167.

CHAPTER 15. MORTALITY DIFFERENCES BY SEX AMONG THE OLDEST-OLD

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Introduction

Women live on average longer than men. Excess male mortality is observed at all ages in developed countries, even during the childbearing years, which until relatively recently were characterized by an excess female mortality. But while excess male mortality is now present at all ages, its intensity nonetheless varies greatly. The pattern observed in many countries comprises twin peaks. The first, at around age 20, is very high and is almost entirely due to violent deaths (in particular road traffic accidents involving two-wheeled vehicles). Yet because total mortality at this age is very low, this excess mortality, though very high, has only a slight influence on the difference in life-expectancy values. It is the second peak, observed between ages 55 and 75, also quite high, which is responsible for most of the difference, given that it occurs at the ages where mortality is already high while the number of survivors is still large.

Excess male mortality is known to be much lower among the oldest-old. Less well known is that it is increasing sharply. What is the precise situation after age 80? What are the factors operating in advanced old age? Can they be attributed to the same causes as those responsible more generally for the difference in life expectancy between the sexes? Before attempting to reply, in part at least, to these questions, it is useful to review briefly the issue of sex mortality differences

The Mortality Inequality between the Sexes

In present-day populations, women, in general, live longer than men. In France, for example, with a life expectancy of just over 82 years, women live nearly eight years longer than men, whose average lifespan is just under 75 years. In some countries this difference is smaller and in others it is even larger, but throughout the developed world it is substantial. Why should this be so?

Women differ genetically from men by having a pair of XX sex chromosomes, whereas their male partners have an XY pair. Given that the Y chromosome is much smaller and carries far fewer genes than the X, it could be argued that some genetic functions are

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accomplished less well in men than in women, including, perhaps, some of those that regulate the ageing process and determine age at death. For example, certain hormonal processes that govern the functions specific to the two sexes are known to have beneficial (or harmful) effects on longevity, which could be a factor in the difference.

But this purely biological perspective fails to account for all the facts. The clearest proof that the difference is not simply biological is provided by the populations of pre-industrial societies (though also, closer to the present, by those of developing countries) where women occupied an inferior societal position and had a shorter life expectancy than men. At this stage of development, society which in this context means man—in effect deprived woman of the benefit of her innate natural advantage.

A context of economic and social progress and of improvement in women's societal position was necessary for this biological advantage of the female to become fully apparent. But when this came about, the mortality gains that women achieved went well beyond recovery of their inborn advantage (Vallin 1993, 1999).

How much of the nearly eight-year mortality difference between the sexes currently observed in a country like France is biologically determined, is hard to establish. Nonetheless, observations made at ages where external causes nowadays have a negligible role in sex differentials (infant mortality or, better still, foetal mortality), suggest a natural excess male mortality of the order of 15–20%. With the same difference of risk at all ages, the difference in life expectancy would be two years (Pressat 1973), which is well short of the eight years difference observed for France. Biological factors are thus probably a minor element in the explanation.

This additional component of excess male mortality was long believed to be the consequence of the risks specific to the male sex. On the one hand, men were more deeply involved in manufacturing industry and thus more exposed to the associated hazards (in particular workplace accidents and occupational diseases); while on the other hand, a range of detrimental health behaviours, such as smoking, drinking, and driving, were much more common among men than women. It is a fact that the period from the 1940s to the 1960s, marked both by rapid industrial growth and the spectacular rise in drinking and smoking and in road traffic accidents, did coincide with an unprecedented increase in excess male mortality.

However, this explanation is in itself not sufficient. Since that period women have not only taken up paid employment in large numbers but have adopted forms of behaviour closely modelled on those of men, including smoking, drinking, and driving. In these conditions a reduction in the difference in life expectancy between the sexes could have been expected, in line with that predicted by the stable population models of Ansley Coale and Paul Demeny (1966, 1983). The opposite in fact occurred, with most countries experiencing a further widening of the sex-mortality difference. Too much attention had been focused on the 'vices' of men and too little on the 'virtues' of women (Vallin 1993). Generally speaking, women are far more attentive than men to personal health questions. Not only is a whole sector of medicine and health care services (gynaecology) devoted specifically to women a compensation for the heavy penalty imposed in the past by repeated childbearing

but there is a fundamental cultural difference in men and women's attitudes to their body. The female body is required to stay youthful and attractive for as long as possible, whereas the demonstration of virility means that the man's body is exposed to physical extremes and risk-taking from an early age. As a result women have a very different attitude to prevention and medicine. Now that further advances in life expectancy depend increasingly on combating cardiovascular illness and cancer, and are achieved not by spectacular remedies like vaccines and antibiotics but by changes in personal behaviour (dietary, for example) and in attitudes to the body and health, women possess a singular advantage: they are culturally predisposed to taking care of their health whereas men have first to effect a radical change in behaviour and attitude. In nearly all the industrialized countries, female life expectancy has risen faster than men's once reduction in cardiovascular disease has overtaken that in infectious diseases as the main source of further mortality decline.

However, this is not the end of the story. Although men have so far benefited less than women from medical and social progress, there are signs that this state of affairs is beginning to change. Increasingly they are modelling their behaviour on that of women and adopting what for them is a new health culture. In the English-speaking countries, in particular, the life expectancy difference between men and women began to decrease in the 1970s. Even a more 'Latin' country like France has seen the gap narrow in recent years.

What is the situation among the oldest-old?

1. The Recent Rise in Excess Male Mortality

Until very recently mortality differences among the oldest-old received little attention. The main reason is not the serious inaccuracies of much of the available data, but rather the widely accepted view that excess male mortality diminished rapidly with age after 65 or 70 years and thus tended to be negligible at very high ages; and, moreover, that this negligible phenomenon involved only a very small proportion of the population. But this situation has changed radically as a result of the health improvements since the 1950s and the rectangularization of the survival curve. In France, for example, whereas the 1950 life table has little more than a third of women (35.4%) and less than a quarter of men (21.4%) surviving to age 80, in the 1998 table these proportions stand at nearly half (45.3%) for men and over two-thirds for women (69.9%). At age 90 the change is even more striking, with the survival probability having risen from 2.4 to 13.1% for men and from 6.6 to 31.1% for women! Clearly what happens after age 80 can no longer be dismissed as negligible. The rise in the number of very old people, combined with improved data collection, has also facilitated the production of more precise calculations of mortality among the oldest-old.

The 1990s saw major efforts undertaken to assemble comprehensive international data on oldest-old mortality. One of the most remarkable results is the database created by Vaïno Kannisto with the research groups of Odense University and the Max Planck Institute for Demographic Research. I would like to thank the Institute for having supplied me with a copy of the database.

a) Strengths and limitations of the Kannisto database Kannisto's database covers thirty countries[1] in the form of annual series of deaths at over 80 years, classed by age and year of birth, up to the last age group for which a death is observed. Naturally these series vary in length depending on the country. For Finland, for example, they begin in 1878, compared with only 1990 for post-reunification Germany. The series for France does not begin until 1950 even though the data are available from 1899. The last complete[2] year is usually 1995, though some series stop much earlier (1988 for Chile, 1990 for Hungary). By applying the method of extinct generations to these data, it is possible to calculate the members of each generation who remain at each birthday (working on the assumption of course that migration is negligible at these ages). These figures are in fact already calculated and incorporated in Kannisto's database. Using these data, an accurate calculation can be made of the probabilities of death at each age above 80 years, in either a cohort (by generation) or a period perspective (by calendar year). Trends in excess male mortality are best studied with the period data, which provide a good description of health status changes, at the population level.

For the purposes of the present study six countries were selected for which Kannisto's database contains series covering practically the whole of the second half of the twentieth century: England and Wales, Spain, France, Italy, Japan, and Sweden. With the exception of Sweden, these are the most populated countries in the database. Sweden was included because of its historically early health improvements. This group of countries has the advantage of combining those with high life expectancy but in significantly contrasted contexts (Northern Europe, Western Europe, Southern Europe, Japan).

Figure 1 displays the age-specific mortality curves after 80 years for each of the six countries for the last year of observation (1993 for Spain and Italy; 1995 for the others).

The curves are very close together, especially for men, and proceed smoothly up to age 95 for men and to just over 100 for women. Although the extinct generations procedure overcomes the problems of inconsistency between numerators and denominators, two problems are encountered at the higher ages, whose cumulative effects increase with age. One is the random error introduced by working with small numbers; the other is inaccuracy in reported ages at death. The latter can result either from observation errors as such (age misreporting) or from the data processing carried out by the national statistical services (with grouping of deaths or even redistribution to other ages, beyond a certain age).

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[1] 25 European countries (Germany, England and Wales, Belgium, Denmark, Scotland, Spain, Estonia, Finland, France, Hungary, Ireland, Iceland, Italy, Latvia, Luxembourg, Netherlands, Norway, Poland, Portugal, Czech Republic, Slovakia, Slovenia, Sweden, Switzerland) plus Australia, New Zealand, Canada, Japan, Singapore, and Chile.

[2] Since the data are organized for a reconstitution by generation, only the second Lexis triangle is given for the last year of observation. Since this is usually 1996, the last usable year for a period analysis is most often 1995.

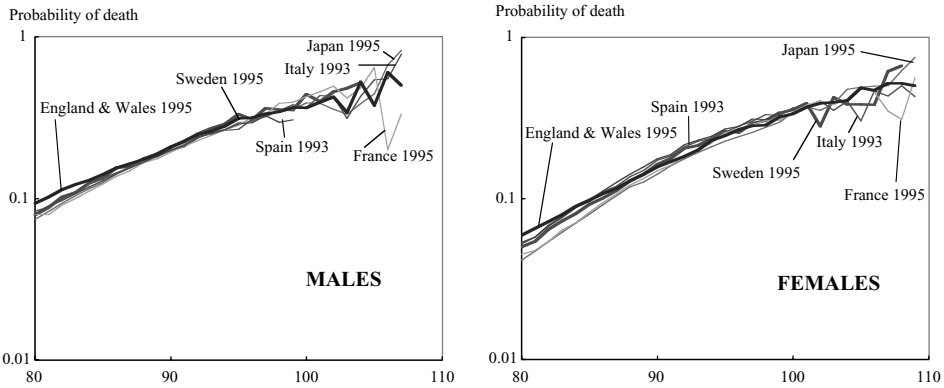

Figure 1. Age-specific mortality curves from 80 years for six countries from Kannisto's database at the most recent available date (1995; except Italy and Spain, 1993).

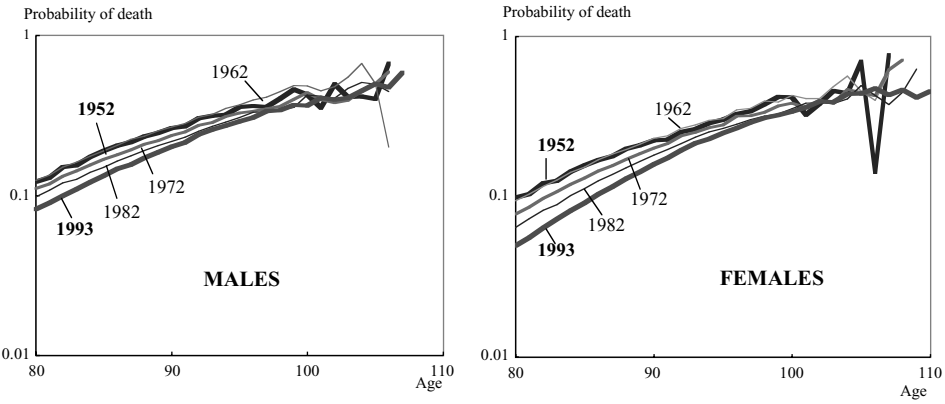

Figure 2. Age-specific mortality curves after 80 years for the cumulative total of six countries from Kannisto's database (1952–1993).

These shortcomings in the data on higher age mortality were more serious in the past and affected lower ages. Figure 2 gives a comparison, for all six countries, of the cumulated[3] mortality curves obtained at ten-year intervals since 1952 (the first available year for Italy). Aggregating the figures for the six countries greatly reduces the fluctuations at very high ages for the most recent year but they become increasingly large the further back in time we look. Here too the results appear entirely plausible up to around age 95 for men and to just over 100 for women but thereafter become steadily less reliable. It is therefore unlikely

[3] The life tables were calculated after cumulation of the deaths and populations of the six countries.

that the trend of sex differences in mortality can be observed correctly beyond age 100 or indeed even age 95, the reduction in the fluctuations having occurred at too recent a date.

b) A context of accelerating mortality decline Figure 3 shows the annual evolution of life expectancies at 80, 85 and 90 years in each of the six countries, calculated using the data available in Kannisto's database and completed for France up to the beginning of the

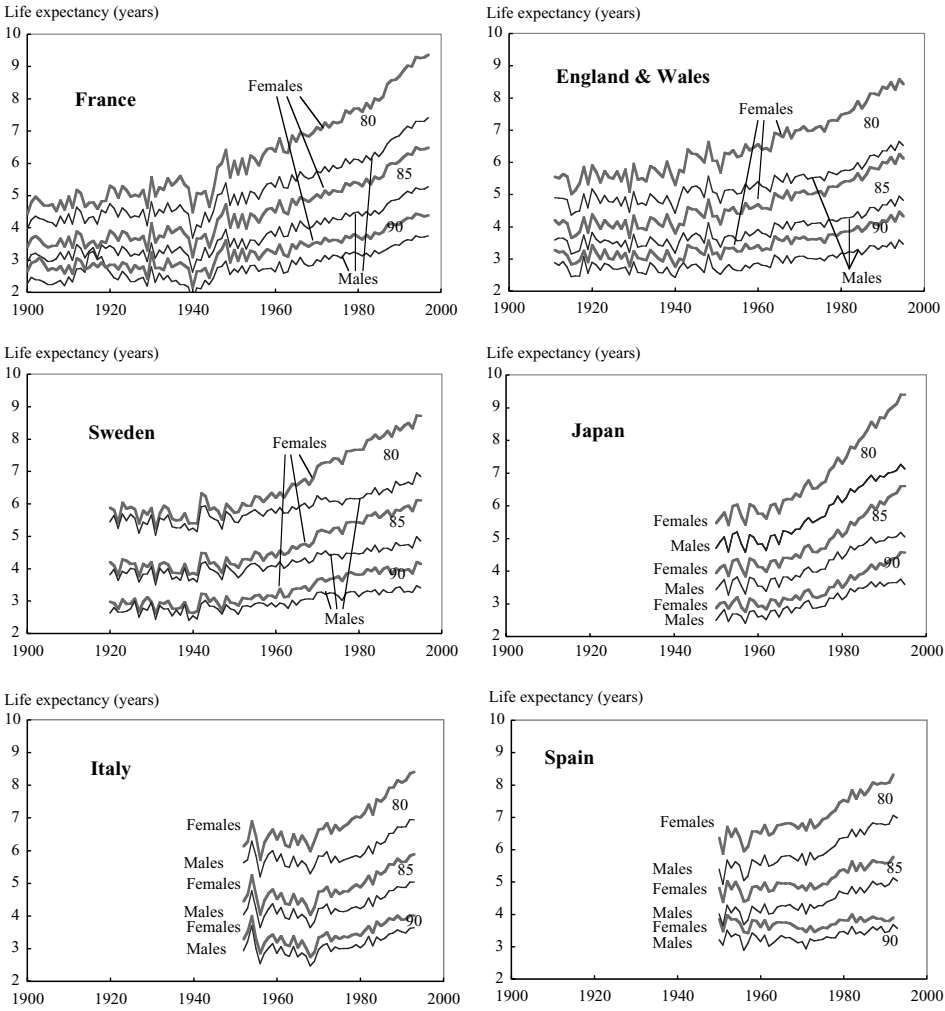

Figure 3. Life expectancy trends at 80, 85, and 90 years in France, England and Wales, Sweden, Japan, Italy, and Spain (the thick line is women and the thin line is men).

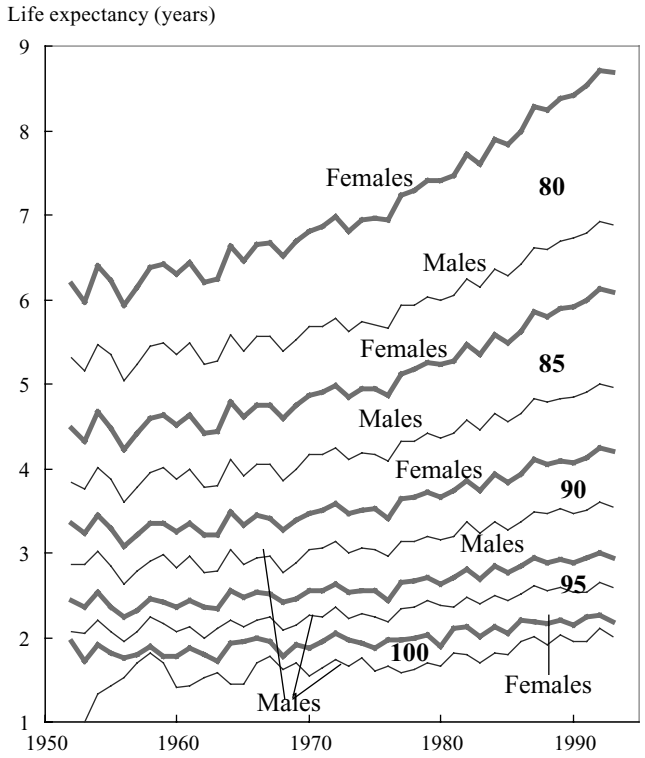

Figure 4. Life expectancy trends at 80, 85, 90, 95, and 100 years in the set of six countries selected.

century.[4] The long chronological perspective obtained for France, England, and Sweden reveals clearly the recent character of the fall in mortality at advanced ages. Until the 1950s the gains in these three countries were almost imperceptible if not actually non-existent. After the Second World War, however, a process of rising life expectancy got under way, subsequently accelerating, usually in the mid-1970s, and in some cases again around the late-1980s and early-1990s. The change varies between countries, and is much clearer at age 80 than at age 90, but is observed everywhere. This increase in life expectancy is usually much more marked for women than for men.

Figure 4, based on the cumulative data of the six countries for the period in which this is possible (1952–1993), illustrates very clearly the acceleration from the mid-1970s. This is indeed a major trend for this representative set of countries where life expectancies are at present the highest. By contrast, the acceleration observed in some countries at the end of the 1980s is hard to detect, thus confirming its more specific character.

[4] For France, the life expectancies have been taken from conventional life tables, but it will be seen later that at this level they differ little from the calculations made using Kannisto's database.

The cumulative data for the six countries can also be used to explore the changes occurring after age 90, at 95 and even 100 years. The acceleration of the 1970s is still clearly perceptible for life expectancy at 95 years, though is a good deal less marked at 100 years.

c) A sharp increase in excess male mortality, despite some contrasts Life expectancy at all ages is systematically higher for women than for men. This is already quite clear from Figures 3 and 4, and is confirmed explicitly in Figure 5. At every age and in every country, women's life expectancy is higher than men's. However, what is most clearly revealed by Figure 5 is a dramatic increase over recent decades in the difference in life expectancy between the sexes at these advanced ages. Exceptions to this pattern do exist but it is general at age 80. In France, for example, the difference in life expectancy between the sexes at this age doubled between 1950 and 1997, rising from 1.05 to 1.96 years (female life expectancy rose from 6.1 to 9.4 years, while that of men only went from 5.1 to 7.4 years). A near doubling of the difference in life expectancy at age 80 was also observed in England and Wales, where it grew from 1.0 to 1.9 years between 1950 and 1995. A threefold increase was registered in Japan, from 0.77 to 2.28, and in Italy, from 0.50 to 1.45. In Sweden, the difference increased almost tenfold, albeit starting from a very low level in 1950 (0.22 years) to finish close to that of England in 1995 (1.87 years). In Spain, however, the difference grew much less, increasing only from 0.97 in 1950 to 1.34 in 1993.

This widening of the mortality difference between the sexes has also varied considerably over time. Indeed, a number of contrasts are very clearly visible. In Sweden, for example, the deterioration was especially sharp in the early 1970s and subsequently much more gradual, whereas the exact opposite was observed in Japan. In the case of England and Wales, the sex differential in life expectancy at age 80 tended to narrow from the beginning of the 1990s, whereas it carried on widening almost everywhere else. It is also noteworthy that while in most countries (with the exception of Japan) the disparity has widened for life expectancy at age 80, the process is less marked at 85 years and altogether more muted at 95 years. Indeed, in Spain, where the growth in the disparity at 80 years is already much smaller than elsewhere, it is practically non-existent at 85 years and actually gives way to a reduction at 90 years. On the other hand, however, in England and Wales, where the difference starts to narrow for life expectancy at 80 years, its increase accelerates at 90 years.

A more precise illustration of these variations is provided by the changes in the ratios of excess male mortality in the various age groups (Figure 6). In France, the growth in excess male mortality is very strong at 80–84 years, with an acceleration at the end of the 1970s, and getting gradually weaker with age for the subsequent age groups. However, it is present at all ages. In England and Wales, a striking contrast is observed in recent years between the decline of excess male mortality at 80–84 years and more recently at 85–89 years, and its sharp increase at 90–94 years. This pattern is clearly suggestive of a cohort effect, probably related to a decline in smoking among men, dating from the 1960s and 1970s. Conversely, in Japan the increase in excess male mortality accelerated at the end of the 1970s at 80–84 years, at the start of the 1980s at 85–90 years, towards the end of the 1980s at 90–94 years, and had barely started at 95–99 years, as the phenomenon gradually

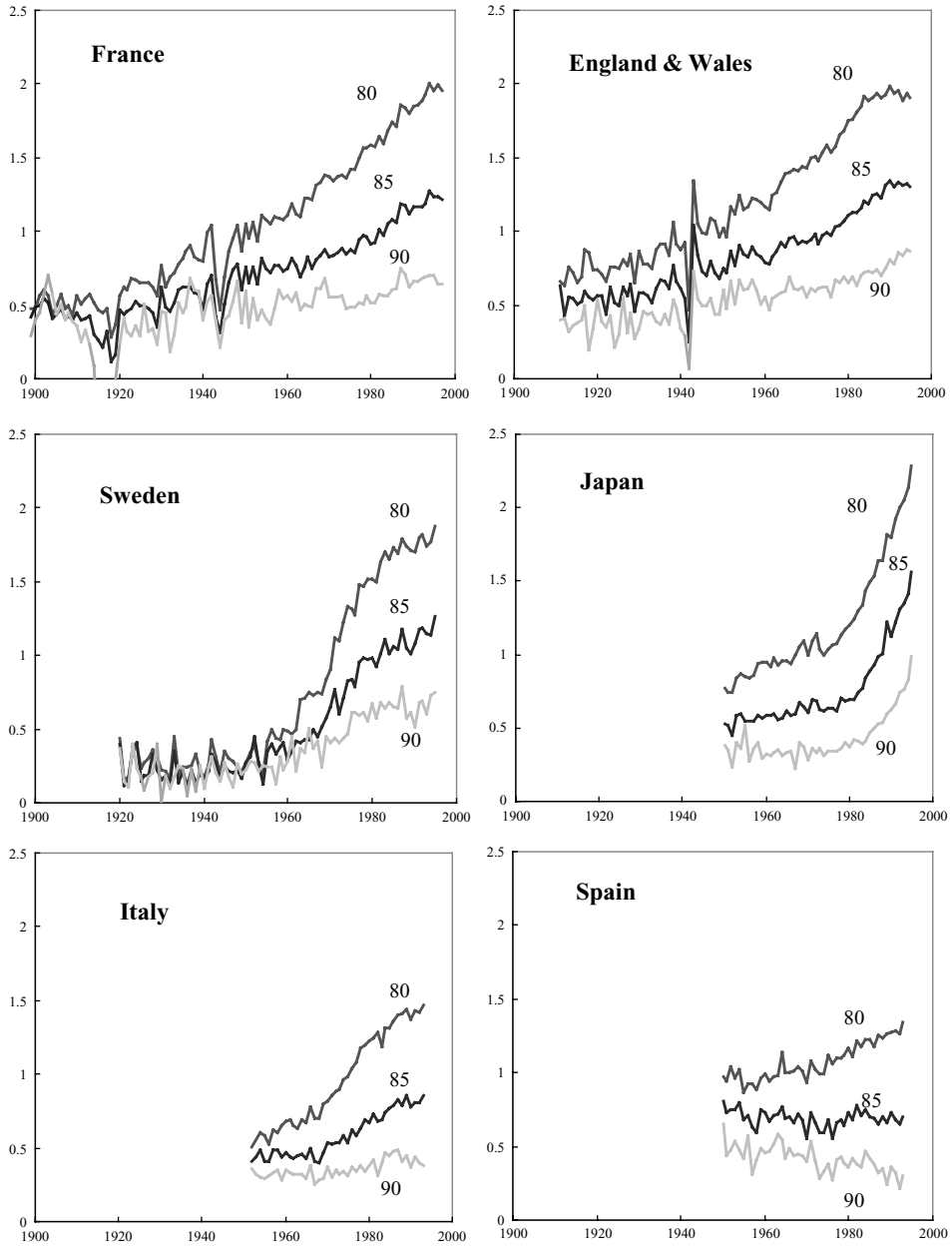

Figure 5. Difference in life expectancy between the sexes at 80, 85, and 90 years in six of the countries in Kannisto's database.

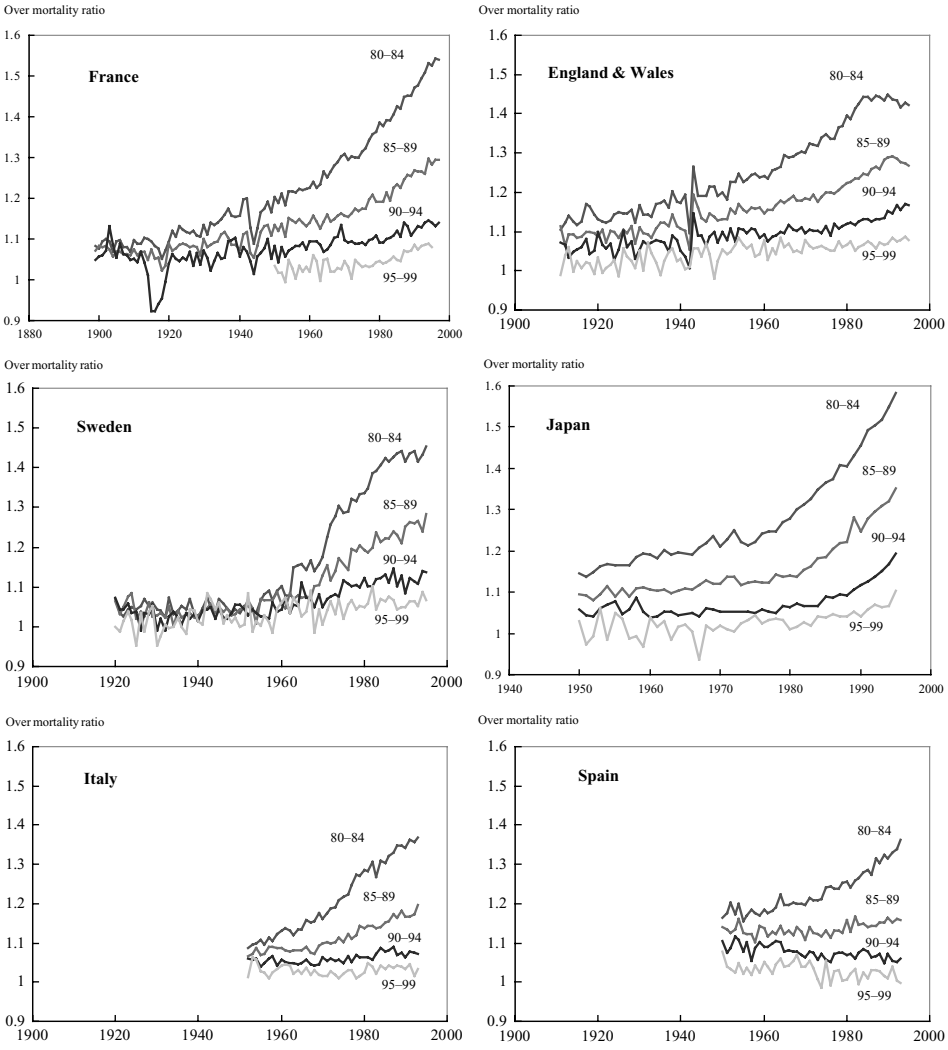

Figure 6. Change in excess male mortality ratios at 80–84, 85–89, 90–94, and 95–99 years in France, England and Wales, Sweden, Japan, Italy, and Spain.

spread to increasingly advanced ages. Lastly, in the two southern European countries, the increase in excess male mortality becomes really large only at 80–84 years. At 90–94 years and at 95–99 years, the increase is practically non-existent in Italy and actually gives way in Spain to a decrease. This reduction in Spanish excess male mortality at very high ages, running counter to the general pattern of change, is definitely the hardest aspect to explain. Arguably it can be attributed to observation errors specific to Spain (Kannisto 1994:15).

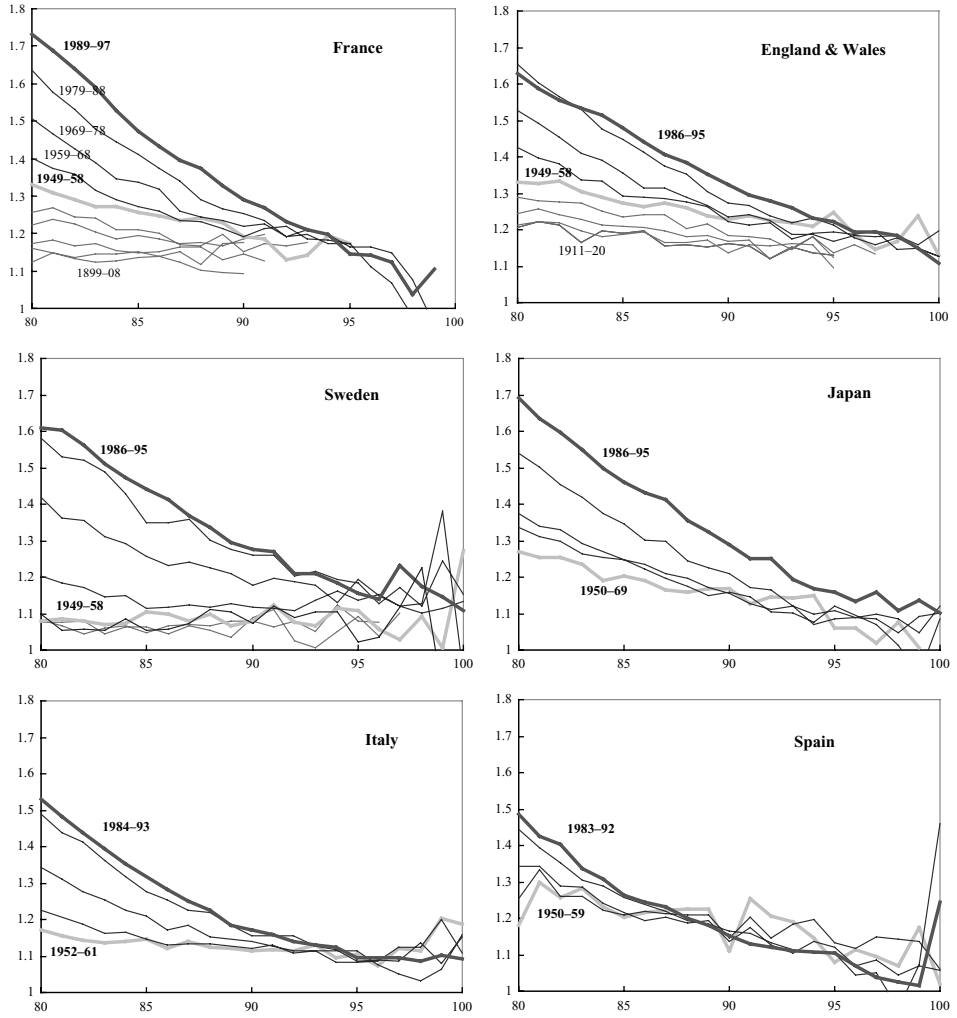

Figure 7. Age-specific excess male mortality ratios, at different times in six countries from Kannisto's database.

Lastly, Figure 7 represents the spectrum of excess male mortality at high ages in each country and its change over time, by displaying the ten-year averages of the age-specific excess male mortality ratios observed at different periods. The data for the 1950s and for the last available period are shown in thick lines. The intermediate data, and the pre-1950s data for France, England and Wales, and Sweden, are shown in thin lines.

In all the countries, of course, excess male mortality falls systematically with age (disregarding the fluctuations observed after 95 years). What can be seen, however, is the change over time in this curve of excess mortality by age. Spain is in fact the only country where

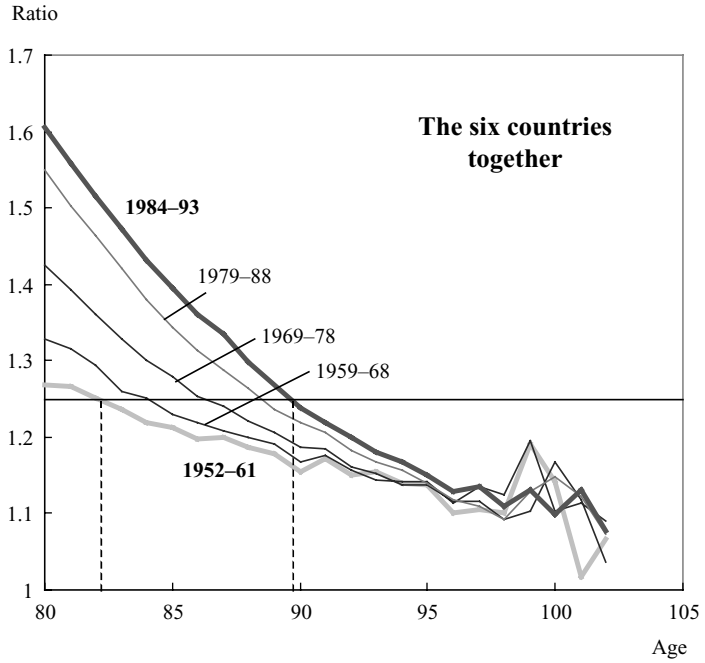

Figure 8. Excess male mortality ratio by age, at different times in the six countries combined.

it has barely changed. Everywhere else a substantial increase has occurred, though the chronology of this change varies between countries. In France, for example, it began very early, and the last half century simply reinforced the change that was already well under way in the first half of the twentieth century. In Sweden, on the other hand, the emergence of the phenomenon at the end of the 1950s was extremely abrupt, more so even than in Japan.

Furthermore, it is clear that in nearly every country it is the curve as a whole which rises and not merely for the earlier age groups. In other words, women do appear to have benefited the most, at least to date, from the mortality reduction at high ages, and excess male mortality is gradually and seemingly inexorably spreading to ever more advanced ages.

When the ratios of excess male mortality for the six countries combined (Figure 8) are calculated, we see, for example, that while in the 1950s the ratio of excess mortality fell below the 30% threshold shortly after age 80, in the 1990s this did not happen until close to age 90.

The rapid narrowing of this relative mortality difference with advancing age still occurs, but it does so at increasingly higher ages. It is also relevant to remember that because mortality increases exponentially with age, this sharp reduction in the relative difference at advanced ages in fact masks the continued existence of a very large absolute difference.

2. Is Excess Male Mortality among the Oldest-Old Related to That Observed at Younger Ages?

What are the reasons for this excess male mortality at very high ages? And why has it increased in recent decades? Providing answers to these questions is beyond the scope of the present study, but we can begin to explore some possible lines of inquiry. A first step is to establish whether or not excess male mortality among the oldest-old is closely linked to the excess male mortality observed at earlier ages and in particular during adulthood. This can be done by comparing the differences in life expectancy after 80 years with the general differences in life expectancy at birth or with the ratios of excess male mortality for the ages at which it is largest. Later we will examine which causes of death contribute most to excess male mortality at advanced ages.

The database compiled by Kannisto is insufficient for both of these tasks. Attention will therefore be confined to France for which far more complete and comprehensive information is available, though employing the more conventional forms of mortality analysis. The first step is to assess the comparability of the results obtained for the oldest-old using Kannisto's database with those from the conventional life tables which exist for France.

a) Comparability of conventional probabilities of dying at high ages with those obtained from Kannisto's database Figure 9 compares for France the change in the quinquennial probabilities of dying at high ages taken from the conventional French life tables,

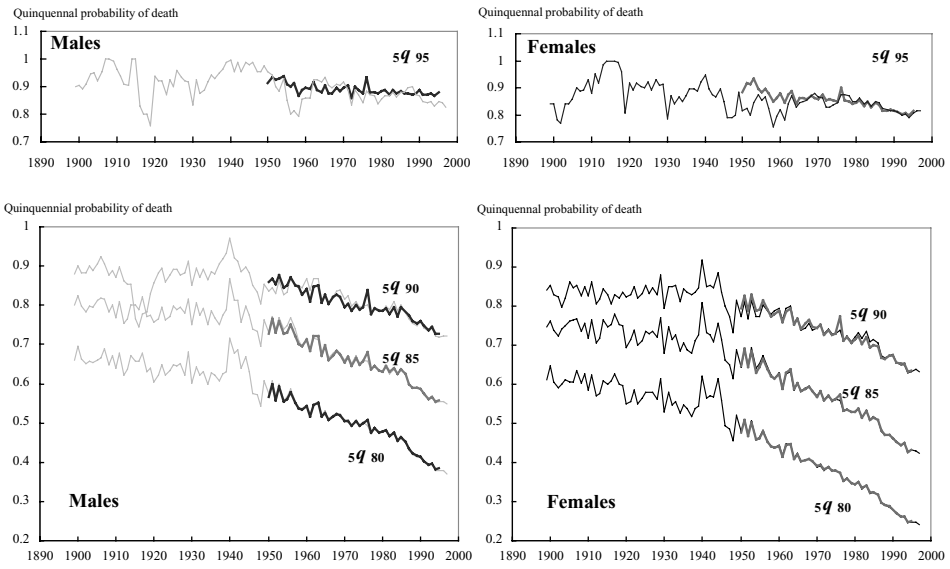

Figure 9. Comparison of conventional probabilities of dying (thin lines) with Kannisto's quotients (heavy lines) for France.

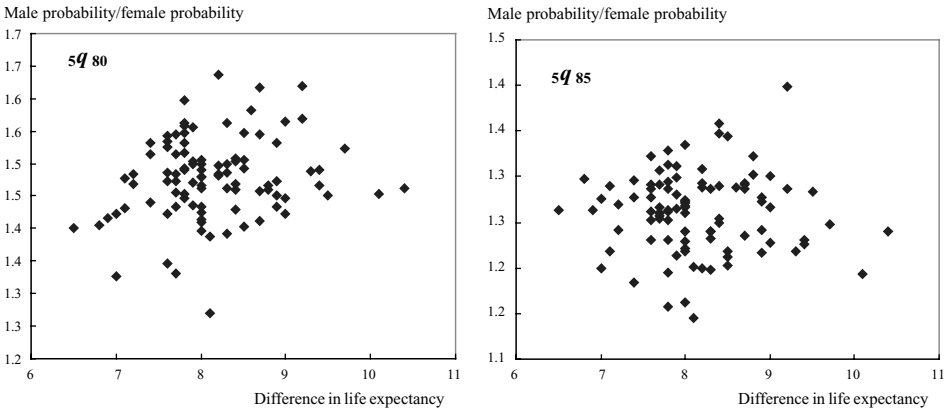

Figure 10. Correlation between excess male mortality ratios at 80–84 years or 85–89 years and life expectancy at birth. France 1989–1991.

with the probabilities of dying computed using the extinct generations method. The latter (shown in thick lines) concern only the period 1949–1995, while the former (thin lines) are available since 1899. The comparison of course concerns only the last half century.

While quite sizeable differences are sometimes observed for the oldest age group (95–99 years), they are negligible for the earlier age groups. Some differences do still exist, it is true, at 90–94 years, but they are altogether negligible, and the coincidence is complete at 80–84 years and nearly complete at 85–89 years. Analysis can thus be based on these last two age groups at least.

b) Relationship with the difference in life expectancy at birth Since life tables are available for all 95 French *départements*, the ratio of excess male mortality at 80–84 years or at 85–89 years can be compared with the difference in life expectancy at birth for each *département*. Correlating these two indicators for the period 1989–1991 using the life tables for the *départements* calculated from the 1990 Census (Isnard and Lavertu 1995) shows clearly that there is almost no statistical interdependence between them (Figure 10). The correlation coefficient between the two indicators is in fact only 0.207.

The same result is obtained when the operation is repeated for other periods for which life tables by *départements* are available. Figure 11 displays this for the periods 1952–1956 (INSEE 1964), 1961–1963 (Labat 1970), 1974–1976 (De Saboulin 1981) and 1981–1983 (Sautory 1986). No correlation is observed. The coefficients of correlation vary between 0.091 for the period 1974–1976 and 0.302 for the period 1952–1956 (with 0.094 for 1961–1963 and 0.141 for 1981–1983).

c) Relationship with excess male mortality in adulthood This does not necessarily mean that excess mortality at advanced ages is unrelated to the difference in overall life expectancy at birth. The former could be influenced by factors or events experienced earlier

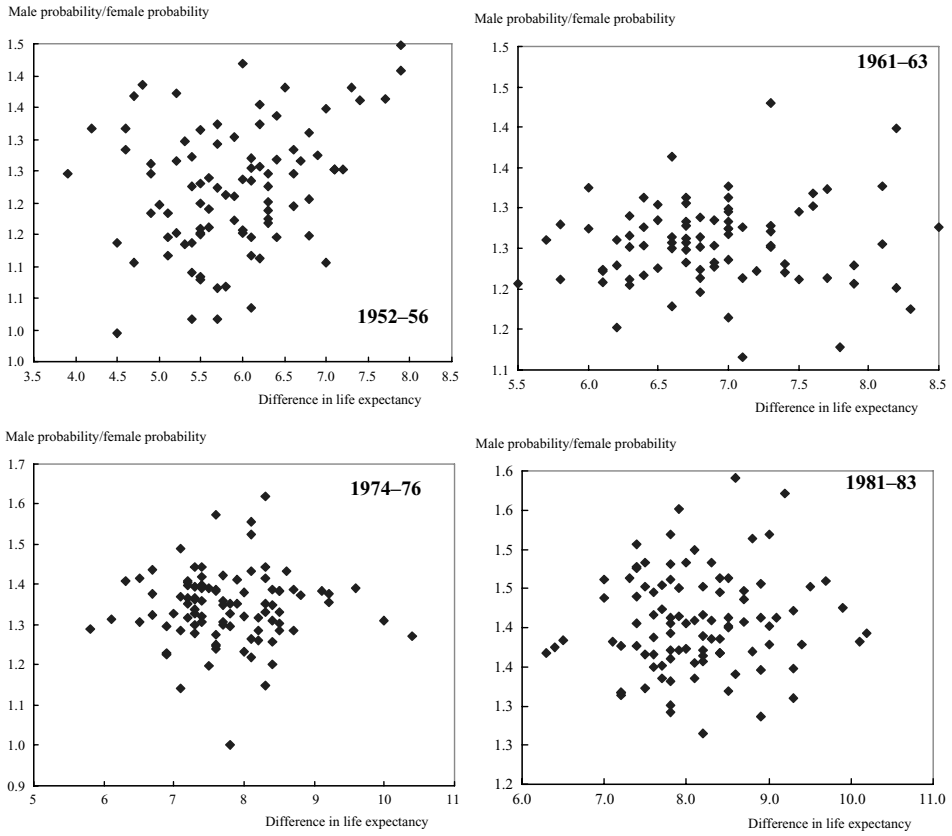

Figure 11. Correlation between excess male mortality ratios at 80–84 and life expectancy at birth at different periods. France.

in life. Analysis to establish this should ideally be based on departmental cohort life tables. Since such tables do not exist, an alternative approach to the question is to compare current excess mortality at 80–84 years with the excess mortality at a younger age for the time when the persons currently aged 80–84 were of that age. For example, the ratio of excess male mortality at 80–84 in 1989–1991 can be compared with the ratio of excess male mortality at 45–49 years in 1952–1956. The result is not significantly better (Figure 12), with a correlation coefficient of 0.318.

The results are no better if the analysis is performed using the data for 1961–1963, 1974–1975 or 1981–1993. In fact, the correlations are even weaker. The relationship between excess male mortality at advanced ages and excess male mortality in general or that observed at younger ages is thus fairly tenuous or even non-existent. Consequently, it is likely that excess male mortality at very high ages is governed by mechanisms quite different from those operating at earlier ages, in particular during adulthood, and which are responsible for most of the difference in life expectancy.

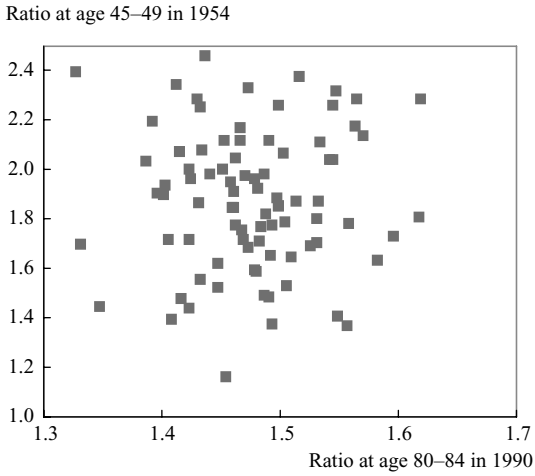

Figure 12. Correlation between excess male mortality ratio at 80–84 in 1989–1991 and excess male mortality ratio at 45–49 years in 1952–1956. France.

Behavioural factors, whether the health-harming behaviours especially common among men or, conversely, the health-enhancing attitudes more characteristic of women, are known to play a major role in overall excess male mortality, much more so than the purely biological and genetic factors. On the other hand, there are grounds for thinking that the latter play a dominant role in excess male mortality at the ages where the mortality risk itself is essentially biological in nature. This is already observed in the months following birth, when a slight excess mortality of boys (in the region of 20%) parallels a sex differential in late foetal mortality of the same scale and which is undoubtedly biological in origin. Given that as age increases, biological ageing becomes the main cause of death, it may be asked whether excess male mortality at advanced ages is not itself due primarily to the biological differences between men and women.

Can we answer this question by an examination of the causes of death?

3. Causes of Death

Thanks to the work carried out at INED to reconstruct coherent long-term series of causes of death, data on mortality by sex, age, and cause classified according to the Ninth ICD Revision, is available for France for the period 1925–1996 (Vallin and Meslé 1988, 1998; Meslé and Vallin 1996). This enables us to observe the change over time in the sex differential in the age-specific rates. Figure 13 depicts the changes in the difference between the standardized male and female rates for two main age groups: the '80 and over' group which is of interest here, and the '50–75 group' which is responsible for most of the difference in life expectancy between the sexes.

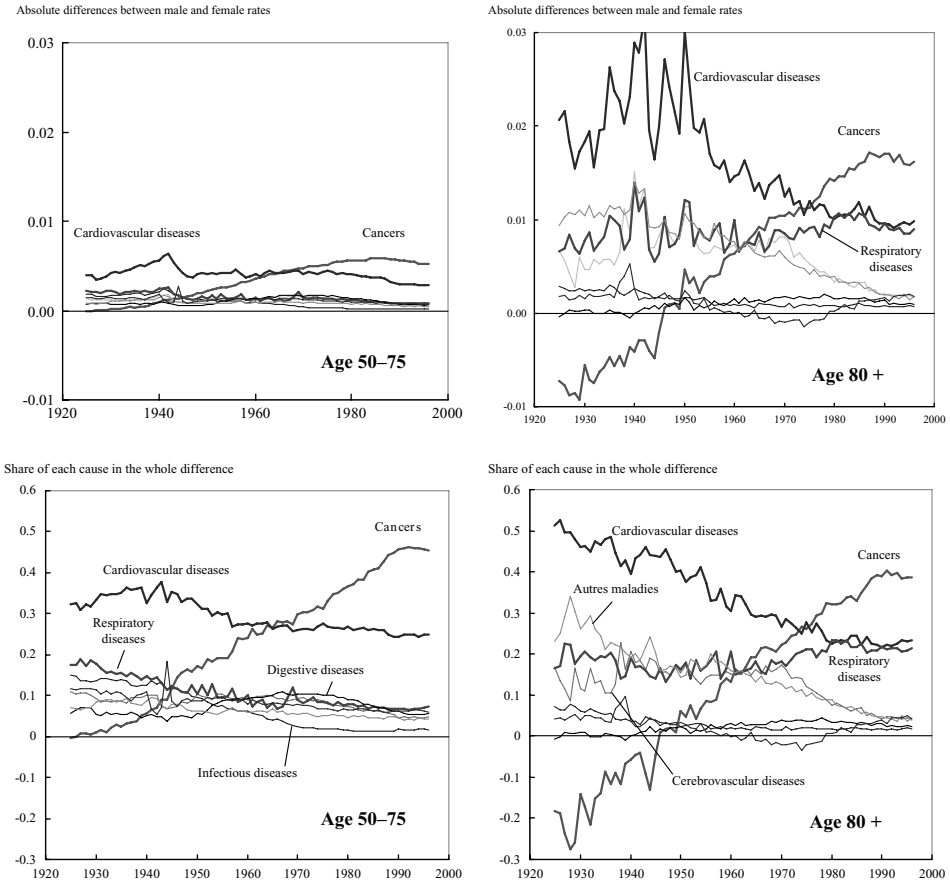

Figure 13. Difference between standardized male and female cause-specific mortality rates, and contribution of these differences to the difference for all causes, at ages 50–75 and 80 and over.

The differences in absolute values (upper panels of Figure 13) are of course much greater at age 80 and over, where the mortality rates are much higher, but comparison is easier in the two lower panels of Figure 13 which display the share of each cause in the total difference. At 50–75 years, cardiovascular diseases were for long the main source of the mortality difference between the sexes (slightly over 30%), followed by respiratory diseases and infectious diseases (between 15 and 20% each). Cancers are currently by far the largest single item, accounting for more than 40% of the total difference. Cardiovascular diseases are still responsible for nearly 30% but no other cause of death accounts for more than 10%.

At age 80 and over the pattern is substantially different. It is true that cancers have overtaken cardiovascular diseases as the main cause of excess male mortality, just as they did at

Table 1. Coefficients of correlation between the sex mortality difference* at 55–74 years and at 80 and over.

Cause	Coefficient of correlation
1. Infectious diseases	0.914
2. Tumours	0.989
3. Cardiovascular disease	0.659
4. Cerebrovascular disease	0.725
5. Disease of respiratory system	0.042
6. Disease of digestive system	0.657
7. Other diseases	0.782
8. Violent deaths	0.090
9. All causes	0.322

*Absolute difference between the standardized male and female rates.

50–75, now accounting for nearly 40% of the total difference. But the reduction in the role of cardiovascular diseases is much greater. In 1925 these diseases were responsible for over 50% of the mortality difference between the sexes, as against barely 25% at present. By contrast, the proportion of the difference imputable to respiratory diseases has remained stable at 20–25% over the entire period, whereas all the other causes now have virtually no effect on this difference.

This description can be expressed in summary form by analysing the correlations between the sex differences in mortality at 50–75 years and at 80 and over, based on the annual variations in these phenomena since 1925 (Table 1). It reveals a very similar pattern of change for infectious diseases and cancers, with correlation coefficients higher than 0.9 (and even close to 0.99 for cancers). Cancers have played a major role in the deterioration of excess male mortality both at very old ages and in adulthood. The correlation is slightly weaker for cardiovascular diseases, cerebrovascular diseases, and diseases of the digestive system (correlation coefficient around 0.7). Most striking of all, however, is the absence of almost any correlation for the diseases of the respiratory system and for violent deaths. Given their numerical importance, it is diseases of the respiratory system which are responsible for most of the fundamental contrast between excess male mortality at adult ages and at advanced ages.

We are a long way from confirming a biological explanation for the patterns and trends of excess male mortality observed among the oldest-old. First, the contrast with excess mortality at earlier ages is due primarily to diseases of the respiratory system, which can be assumed to reflect environmental factors rather than factors associated with the biological potential for survival. Second, and above all, the increase in excess male mortality at both advanced and adult ages is attributable to cancers. The relative importance of different cancer sites varies of course between the age groups. Among persons of adult age, most of the increase in excess male mortality is accounted for by cancers of the bronchus and lung, while in the older group the main reason is the contrasting levels and trends for prostate and uterus cancer (Figure 14). But is it plausible to say that prostate cancer is more closely

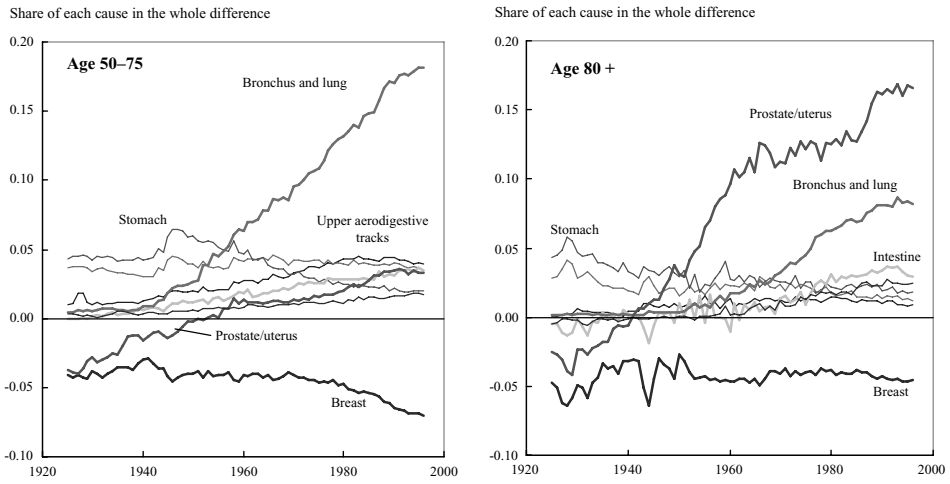

Figure 14. Contribution of different cancers to the mortality difference between the sexes at 50–75 years and at 80 and over.

linked than other cancers to the natural degeneration of the organism, and that the reduction in the incidence of cancer of the uterus in elderly women is indicative of the greater vital potential of the female sex? As elements on which to base a causal explanation, these arguments appear extremely weak.

References

Coale, A., and Demeny, P. (1966) *Regional Model Life Table and Stable Population*. Princeton: Princeton University Press, p. 871.

Coale, A., and Demeny, P. (1983) *Regional Model Life Table and Stable Population*. (*2nd edn*). New York: Academic Press, p. 496.

de Saboulin, M. (1981) *Données de Démographie Régionale 1975*. Paris: INSEE, p. 292. (Les Collections de l'INSEE no. D-82)

INSEE (1964) *Données de Démographie Régionale Déduites du Recensement de 1954 et des Statistiques d'état Civil des Années Voisines*. Paris: Imprimerie Nationale, p. 234. (INSEE-Résultats, no. 430–431, *Démographie-Société*, no. 45–46)

Isnard, M., and Lavertu, J. (1995) *Données de Démographie Régionale 1990*. Paris: INSEE, p. 233. (INSEE-Résultats, no. 430–431, Démographie-Société, no. 45–46)

Kannistö, V. (1996) *The Advancing Frontier of Survival*. Odense, Denmark: Odense University Press, p. 144. (Odense Monographs on Population Aging no. 3)

Kannisto, V. (1994) *Development of Oldest-Old Mortality, 1950–1990*: *Evidence from 28 Developed Countries*. Odense, Denmark: Odense University Press, p. 108. (Odense Monographs on Population Aging no. 1)

Labat, J.-C. (1970) *Données de Démographie Régionale 1962*. Paris: INSEE, p. 202. (Les Collections de l'INSEE, no. D 5)

Meslé, F., and Vallin, J. (1996). "Reconstructing long-term series of causes of death", *Historical Methods*, 29(2):72–87.

Pressat, R. (1973) "Surmortalité biologique et surmortalité sociale", *Revue Française de Sociologie*, 14(special issue):103–110.

Sautory, O., (1986) *Données de Démographie Régionale 1982*. Paris: INSEE, p. 273. (Les Collections de l'INSEE no. D 115)

Vallin, J. (1993) "Social change and mortality decline: Women's advantage regained or achieved?". In: Nora, F., Carol, M., Solvi, S. (eds.), *Women's Position and Demographic Change in the Course of Development*. Oxford: Clarendon Press, pp. 190–212, p. 368. (Coll. " International Studies in Demography").

Vallin, J. (1999) *Mortalité, Sexe et Genre*. Liège: UIESP, 8 + 42 pp. (Gender in population studies)

Vallin, J., and Meslé, F. (1988) *Les Causes de Décès en France de 1925 à 1978*. Paris: INED,PUF, 608 pp. (Coll. Travaux et Documents, Cahier 115)

Vallin, J., and Meslé, F. (1998) "Comment suivre l'évolution de la mortalité par cause malgré les discontinuités de la statistique. Le cas de la France de 1925 à 1993". In: Gérard, P. (ed.), *Enjeux des Classifications Internationales en Santé*. Paris: Éditions INSERM, pp. 113–156, 220 pp. (Coll. Questions en santé publique)

Section 5
Causes of the Trend in Mortality and Morbidity

SECTION 5. CAUSES OF THE TREND IN MORTALITY AND MORBIDITY

In the first chapter of this final section (Chapter 16), Bernard Jeune searches an explanation for the fall of mortality among the oldest-old and increased adult longevity from a medical point of view. He focuses on the cardio-vascular diseases (CVD) which is the only major group of diseases which has shown a remarkable decline in recent decades, in spite of the fact that it is still the major cause of hospitalization and death among the elderly. The author examines both aspects of this cardio-vascular revolution, the reduction in risk factors for CVD due to improvement of primary prevention (hypertension) and improvement of medical intervention reducing the case-fatality. Although other diseases such as cancer, dementia, diabetes and osteoporosis may have played some roles in increased longevity, their contributions are much more complex to assess and are much smaller (or even nil or negative) than those of CVD. For the future, new improvements in primary prevention (diet), treatments and secondary prevention, particularly among the oldest-old, should allow the CVD mortality to carry on its decline, leading to new improvements in longevity.

In the following chapter (Chapter 17), Graziella Caselli, James Vaupel, and Anatoli Yashin examine the same question from a demographic point of view. The chapter examines in detail the frontier of survival and searches an explanation for the mortality trajectories for the oldest-old. The authors investigate trends and age variations of old-age mortality, with focus on mechanisms of selective survival that underlie those observed patterns. They review some frailty models and present results of frailty model applications to the Danish Twin data and national mortality trends in Italy. These studies suggest that underlying trends and age variations on the individual level may be considerably different from the observed patterns at the aggregate level. An interesting implication is that the actual decline of old-age mortality, if adjusted for effects of mortality selection, may be considerably more pronounced than the observed reduction. The chapter also introduces the 'mortality surface' to understand better mortality for the oldest-old. But at the end the remarkable improvements in mortality and the deceleration of the age-trajectory of mortality remain puzzling phenomena. One promising direction for future longevity research is to incorporate in mortality analysis heterogeneity in frailty.

Lastly, in Chapter 18, Emily Grundy and Michael Murphy investigate changes in marital status, family support, and living arrangement for the oldest old in Great Britain. (i) Firstly they consider the current and future marital status distribution of the oldest-old population, including some trends in the availability of at least one child, under various mortality assumptions. (ii) Secondly, they describe the household characteristics of those aged 85 and over as well as the transitions between different types of household composition. (iii) Thirdly, they analyse the associations between marital status, living arrangement, and

social support. This final chapter discusses important social and familial implications for the future of the longevity revolution described and analysed in the chapters of this book.

In total, several new findings, hypotheses, approaches, and methods are presented and discussed in these eighteen chapters. They update our knowledge and provide new insights into human longevity. We believe that this highly interdisciplinary set of chapters will deepen our understanding of crucial issues in old-age survival.

CHAPTER 16. EXPLANATION OF THE DECLINE IN MORTALITY AMONG THE OLDEST-OLD: THE IMPACT OF CIRCULATORY DISEASES

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Introduction

Today's oldest-olds have benefited from the improved conditions in the first half of the 1900s which led to the dramatic decline in infant mortality and the most important causes of death, such as perinatal diseases, infectious diseases, tuberculosis, and respiratory diseases. These improved conditions were probably mainly socioeconomic, such as improvement of living and sanitary conditions, education, and personal hygiene, and much less related to medical improvements (McKeown 1965). However, better nutrition, including vitamins, and vaccinations probably also played a not negligible role in the first half of the 1900s. The improved nutrition at the beginning of the 1900s might even have contributed to the mortality decline several decades later, if reduced growth *in utero* and in early life really is related to adverse health outcome later in life, such as higher mortality from cardiovascular diseases (Barker 1998). But other studies do not support this fetal-origin hypothesis (Christensen *et al.* 1995; Kannisto *et al.* 1997; Stanner *et al.* 1997).

As a result of these improvements in the first half of the 1900s a much higher proportion of people survived to middle age. Of those who were born in Denmark in 1850 only about 50% survived to the age of 50 years. Of those who were born in 1900 about 90% survived to the age of 50; and almost 50% survived to the age of 80. Those who made it from 50 to 80 also had to survive the modern epidemics of cardiovascular diseases (CVD) and cancer. In the Western countries the epidemic of CVD seems to have peaked in the 1960s or 1970s, depending on the countries and the region. The epidemic of cancer has soared for most cancers until recently.

The growth in numbers of centenarians in recent decades is mainly due to the dramatic decline of mortality among the oldest-old (Kannisto 1994, 1996; Jeune and Kannisto 1997; Vaupel *et al.* 1998). About two-thirds of the growth in the number of centenarians in Scandinavia (Table 1), are due to the decline in mortality at the ages of 80–99 (Vaupel and Jeune 1995). Recently, based on data from Sweden, Wilmoth *et al.* (2000) have found that "for cohorts reaching extinction after 1969, about 95% of the rise in the maximum age at death is attributable to the decline in death rates above age 70". Kannisto (1994, 1996)

J.-M. Robine et al. (eds.), Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population, 357–394

Table 1. Average rate of growth from the 1970s to the1980s in the number of persons attaining age 100, and the proportion of this rate of growth due to improved survival from age 80 to 100 and other factors.

		Proportion (in %) of this rate of growth due to:				
		Improved survival from:				
Country	Annual average rate of growth (in%)	Age 80 to age 100	Age 50 to age 80	Birth to age 50	Decrease in net emigration	Increase in births from the 1870s to the 1880s
Denmark	77	66	13	5	0	16
Norway	51	65	10	8	3	14
Sweden	71	66	12	10	9	4

Source: Vaupel and Jeune 1995.

has suggested that period effects are more important for the decline in oldest-old mortality than cohort effects. However, it is not clear which periodical effects have been the most important in the decline of the mortality at the older ages.

A major contribution to an explanation may be found in the abundant epidemiological literature on the impact of risk factor reduction and improvement of medical interventions on CVD, as this is the only major group of diseases which has shown a remarkable decline in recent decades, and in spite of that still is the major cause of hospitalization and death among the elderly. Although contributions to an explanation might as well be searched for in the review of diseases such as cancer, dementia, diabetes, and osteoporosis, these contributions are much more complex to assess and are much smaller (or even nil or negative) than the contribution of the decline in the trends for CVD.

The main problem in the search for an explanation in the literature on the epidemiology of CVD is the fact that most epidemiological studies and clinical trials have examined middle-aged and younger-elderly men, but only a few have examined women and extremely few have examined the oldest-olds. Nevertheless, those who are oldest-old today were middle-aged and younger-elderly when these periodical changes occurred, at least in the beginning of the declining mortality from CVD.

From a medical point of view these periodical changes must be related to factors which have lowered the incidence of potential fatal diseases, and/or diminished the severity of such diseases, and/or reduced the case-fatality of such diseases, i.e. factors associated with improvement of life conditions and lifestyle causing a reduction in risk factors (primary prevention) and improvement of treatments, including risk reduction in patients (secondary prevention).

From a gerontological point of view a slowing down of the rate of physiological ageing which results in an improved resistance against age-related diseases and an improved long-term survival should be noted. An exhaustive explanation has to be found in a combination of such a slowing down of the rate of physiological ageing and a decline in these possible

trends of age-related diseases. An explanation should therefore be based on an understanding of the dynamics of multifactorial causes which have affected both the ageing process and the incidence, severity, and case-fatality of age-related diseases, perhaps with a different impact in subsequent periods. This understanding may be very complex and may never be evident until we know how age-related diseases are related to the fundamental mechanisms of ageing (Manton and Yashin 2000).

Causes of Death and Hospitalization among the Oldest-Old

The most important causes of death among the oldest-old are cardiovascular diseases, cancer and pneumonia. Due to increasing comorbidity with advancing age, less agressive medical care of the oldest-old, and a very low rate of autopsy among the oldest-old—not exceeding 10% in most countries—it is often difficult to assess the underlying cause of death. Furthermore, the concept of an underlying cause of death seems to be inappropriate for the oldest-olds as they may die of multiple competing causes. The opposite problem to competing causes "occurs when the evidence for *any* specific cause of death is inadequate but because death has occurred, some explanation has to be given" (Tunstall-Pedoe 1989). Therefore we have to be very cautious in interpreting trends in cause-specific mortality among the oldest-old based on official statistics.

A recent report from the USA (Desai, Zhang, and Hennesy 1999) has shown (Table 2) that deaths from heart diseases in 1996 accounted for 41% of all deaths among the oldest-old (aged 85 or more). Cancer ranked as the second cause of death among the oldest-old followed very closely by cerebrovascular diseases. Also pneumonia and influenza are important causes of death among the oldest-old.

These potentially fatal diseases were also the major cause of hospitalization in the USA in 1996. Hospitalization due to heart diseases accounted for a quarter of all discharges among older adults (65+years) and doubled among the oldest-old compared to 65–74-year-old adults. The hospitalization rates for pneumonia and cerebrovascular diseases among the oldest-old quadrupled compared to the rate of older adults aged 65–74. The hospitalization rate for fractures, mainly hip fractures, among the oldest-old was the third leading cause of hospitalization, almost the same as for pneumonia.

Table 2. Causes of death and hospitalization among the oldest-old 85 years+.

	Causes of death (proportion of all deaths)	Hospitalization rate (per 100,000)
Heart diseases	41 %	118
Malignant neoplasms	12 %	21
Cerebrovascular diseases	11 %	40
Pneumonia and influenza	7 %	54
Fractures		49

Source: Table constructed from tables in Desai, Zhang, and Hennesy 1999.

Cardiovascular disease, cancer, and osteoporosis share some common risk factors such as tobacco, poor nutrition, and lack of physical activity, which have changed during recent decades, in part as a result of preventive interventions. Furthermore, in developed countries high priority has been given to the innovation of treatment of these diseases. New diagnostic methods, based on high technology, and new treatments, often based on randomised controlled trials, have been implemented during recent decades. Improvement of survival to high ages is therefore to be expected as a result of changes in incidence, severity, and case-fatality of these very common age-related diseases. However, it seems that especially heart diseases "respond more rapidly to a change in lifestyle or environment than cancer" (Thom and Epstein 1994); and new research indicates that the lag time is shorter than previously assumed (Wilhelmsen 1997). Coronary heart disease is also "the first major noncommunicable disease for which community-wide prevention programs have been developed" (Beaglehole 1990).

Although international trends and variations in total mortality are not due to CVD-mortality alone, the trends and variations in total mortality are considered to reflect trends and variations in CVD-mortality: countries with the lowest overall mortality have the lowest CVD-mortality, e.g., in France and Japan (Thom *et al.* 1985, Beaglehole 1990). Around the mid-1900s CVD were reported as the cause of death in almost two-thirds of the overall number of deaths. In spite of the decline in CVD-mortality and due to the ageing of the populations CVD are still reported as the cause of death in more than half of the overall number of deaths. Recent analyses have shown that half up to three quarters of the decline in overall mortality can be ascribed to the decrease of death from CVD in most developed countries (Thom and Epstein 1994; Hunink *et al.* 1997; MMWR 1999a; Salomaa, Rosamund, and Mähönen 1999). Furthermore, the changes in the major risk factors for total mortality are considered to be strongly related to CVD. There is therefore very good reason to limit the search for an explanation in the literature on the epidemiology of cardiovascular diseases.

The Decline of Cardiovascular Mortality

Based on analyses of vital statistics there is no doubt that the mortality due to CVD has declined in most developed countries and in both sexes, although it began to decline at different periods with different rates of decline in different countries, regions, and socioeconomic groups. The decline apparently started in the USA in the early 1960s, and even in the 1950s in a few states (Borhani and Hechter 1964; Walker 1974; Gordon and Thom 1975; Cooper *et al.* 1978; Marmot *et al.* 1978; Stallones 1980; Levy 1981; Feinleib, Havlik, and Thom 1982; Kimm *et al.* 1983; Salonen *et al.* 1983; Goldman and Cook 1984; Whisnant 1984; Davis *et al.* 1985; Thom *et al.* 1985; Marmot and McDowell 1986; Wing *et al.* 1986, 1988; Dobson *et al.* 1988; Mackenbach *et al.* 1988; Ragland, Selvin, and Merrill 1988; Uemura and Pisa 1988; Epstein 1989; Stamler 1989; Thom 1989, 1993; Al-Roomi *et al.* 1989; Aase 1989; Beaglehole 1990; Bonita, Stewart, and Beaglehole 1990; Salomaa *et al.* 1992; Feinleib *et al.* 1993; Kodama 1993; Lanska 1993; Thom and Epstein 1994; Feinleib 1995; Bots and Grobbee 1996; Bonneux *et al.* 1997; Brophy 1997; Sans, Keesteloot, and Kromhout 1997; Beaglehole *et al.* 1997; Reitsma *et al.* 1999; Tunstall-Pedoe *et al.* 1999).

It seems that the mortality of CVD declined earlier among women than among men, earlier among middle-aged than among elderly, and earlier among the higher social classes than among the lower social classes. It also seems that the decline has been greater for higher rate than for lower rate countries, leading to a less intercountry variability; although Davis *et al.* (1985) did not find a correlation between the levels of rate and the percentage of changes among the more than five hundred 'state economic areas' in the USA in the period 1968–78. Several of the above-mentioned studies found a greater decline among the higher social classes than among the lower social classes, leading to a widening in social inequalities. Whether the decline among sexes has led to a narrowing of the sex differences is not evident (Davis *et al.* 1985); although there seems to have been a convergence for stroke mortality (Lanska 1993). The male-female ratio is still higher for CVD-mortality than for total mortality (about 3 versus 2).

In the USA, where the onset of decline of CVD-mortality occurred before 1970 in all the states (Ragland, Selvin, and Merrill 1988), the age-adjusted death rates for CVD already dropped over 35% in the period 1950–78, and two-thirds of this decline occurred in the period 1968–78 (Levy 1981; Feinleib *et al.* 1982). In this 10-year period the mortality from ischaemic heart disease (IHD) fell by about 30%, and from stroke by about 40%; while the non-cardiovascular death rate only fell by about 10%. Since 1950 the age-adjusted death rates for heart diseases have decreased by more than 50%, and for stroke about 70% (MMWR 1999a). In the period 1960–90 IHD mortality has declined between 2% and 4% per year in the USA (Hunink *et al.* 1997).

In Canada the age-adjusted mortality for IHD declined about 50% in both sexes in the period 1976–91 (Brophy 1997). The same magnitude of decline has been observed in Australia and New Zealand in the period 1970–85 (Dobson *et al.* 1988). In Japan both IHD and stroke mortality have declined by more than 50% since 1970 in spite of increasing fat intake (Shimamoto *et al.* 1989; Kodama 1993). In western European countries the decline in IHD mortality began later than in the USA—in most countries after 1970 (in several countries even after 1980 among men)—and with a smaller decline at least until the mid-1980s, but with approximately the same rate of decline in most countries. However there were slightly higher rates of decline in Belgium, France, Italy, and Spain (Sans, Keesteloot, and Kromhout 1997), and a much steeper decline in Finland, where the very high IHD mortality has declined by more than 50% since 1970 (Vartiainen *et al.* 1994; Salomaa *et al.* 1996). In most eastern European countries the IHD mortality rates are still increasing (Sans, Keesteloot, and Kromhout 1997; Tunstall-Pedoe *et al.* 1999); and in some newly developed countries a rapid increase in the 1970s and 1980s has been observed (Uemura and Pisa 1988; Beaglehole 1990).

Since 1950, and especially since 1970, the decline of stroke-mortality has been steeper than for IHD-mortality, and greater among women than among men in most countries (Shimamoto *et al.* 1989; Bonita, Stewart, and Beaglehole 1990; Kodama 1993; Feinleib *et al.* 1993; Lanska 1993; Thom 1993). In the USA in 1900, the proportion of stroke-mortality represented about 40% of the overall CVD-mortality, and this proportion declined gradually to about 20% until 1950. However, the reported decline in stroke-mortality is perhaps exaggerated as strokes may have been overdiagnosed in the first half of the 1900s (Whisnant 1984). In contrast to IHD-mortality the rate of decline was highest in countries

with the lowest rates, such as Australia, Canada, France, Switzerland, and the USA, with the exception of Japan, which had the highest rate in 1970 but experienced the highest rate of decline (7% per year). The eastern European countries which still have high stroke-mortality rates have experienced either an increase or no change since 1970. Except in these countries the stroke-mortality has declined by more than 50% in the period 1950–90. However, there seems to be a tendency to a levelling-off in stroke-mortality in some regions, while the decline in IHD-mortality has increased since the mid-1980s (McGovern *et al.* 1993; Sarti *et al.* 1994; Bonneux *et al.* 1997; Shahar *et al.* 1997; Reitsma *et al.* 1998).

Several authors have expressed concern about the validity of the causes of death reported on the death certificates that are the bases of vital statistics, especially for the comparisons of trends between countries and regions (Stehbens 1987, 1991; Burke, Edlavitch, and Crow 1989; Stamler 1989; Dobson *et al.* 1990; Madsen, Balling, and Eriksen 1990; Burnand and Feinstein 1992; Salomaa *et al.* 1997; Juel and Sjøl 1995; Osler *et al.* 1996; Rapola *et al.* 1997; Levy and Thom 1998; De Henauw *et al.* 1998; Tunstall-Pedoe 1998; Mähönen *et al.* 1999). Most of these authors have emphasized that classification errors in the official mortality statistics tend to progressively lower the IHD mortality rates. Comparing the ante-mortem with the post-mortem diagnoses of IHD in 986 necropsies at the Yale-New Haven hospital for 1965, 1975 and 1985, Burnand and Feinstein (1992) found "rising proportions in both true positive and false negative ante-mortem diagnoses". Improvements of diagnostic testing and criteria tend to increase the clinical accuracy and the identification of earlier unrecognized cases but may also increase the number of cases which with these strict criteria are not diagnosed. In a thorough review of diagnostic errors in certified causes of death—in particular for IHD—Stehbens (1987) has even concluded that vital statistics "are too unreliable for determining whether there has been an increase and a subsequent decline".

The main impression of this literature, which is supported by more valid epidemiological studies, seems to be that the decline is real, at least when trends on overall CVD mortality below the age of 65 years are compared, since a few CVD deaths below this age are misclassified as non-CVD deaths as the underlying cause. Inaccuracy of the death certificates seems to be a problem when trends for IHD-mortality are compared for ages above the age of 65 years. These problems are not only due to the revisions of WHO's ICD-classification, but also due to differences between countries and even between regions in each country in the manner heart diseases are classified as IHD, other heart diseases, or unknown causes, respectively. However, in several centres participating in the WHO MONICA Project the number of deaths from acute myocardial infarction (AMI) registered by strict criteria were not lower but higher than those reported in the vital statistics (Tunstall-Pedoe 1998). In Belgium about one third of the AMI registered by strict criteria as part of the participation in the WHO MONICA Project was coded as other heart diseases; and more than 10% were not coded as heart diseases at all (De Henauw *et al.* 1998). In Finland (Mähönen *et al.* 1999), where the proportion of autopsy is high (about 60% below the age of 65) and nearly all out-of-hospital deaths are autopsied, routine mortality statistics are quite accurate (validated by comparison with the FINMONICA register), with a very low proportion of false positive cases.

In Denmark more strict recommendations have contributed to a substantial increase in classification of deaths as from unknown causes, from about 1% in the 1960s to about 8%

in the 1990s (Juel and Sjøl 1995), including sudden unexpected death, which is often due to AMI. Another Danish study (Osler *et al.* 1996) has shown that the decline was of the same magnitude in both sexes whether AMI mortality was considered or IHD mortality narrowly defined (also including chronic ischaemic heart disease and angina pectoris)—but much less when IHD was broadly defined (also including asymptomatic heart disease and sudden deaths from unknown cause).

More reliable evidence of the decline in CVD mortality is found in population-based studies such as the two major multicentre colloborative studies—the WHO MONICA Project (MONItoring Trends and Determinants in CArdiovascular Disease) (Tunstall-Pedoe *et al.* 1999) and the Atherosclerosis Risk in Communities (ARIC) study (Rosamond *et al.* 1998) together with several other epidemiological studies (Puska *et al.* 1985; Goldberg *et al.* 1988; Kaplan *et al.* 1988; Shimamoto *et al.* 1989; Beaglehole 1990; Sytkowski, Kannel, and D'Agostino 1990; Sigfusson *et al.* 1991; Salomaa *et al.* 1992, 1996; Bots and Grobbee 1996; Curb *et al.* 1996; McGovern *et al.* 1996; Sakata *et al.* 1996; Wilhelmsen *et al.* 1997; Roger *et al.* 1999; Salomaa, Rosamund, and Mähönen 1999).

These studies have shown that the mortality from IHD decreased by 2–9% annually in the 1980s and 1990s (i.e. a greater decline than in the 1970s); and several of these studies have shown a decline in deaths from stroke of the same magnitude. Although the decline was less pronounced as age increased and less pronounced for women, in one of the few studies which included octogenarians (Roger *et al.* 1999), the percent decrease in the risk of heart death between 1979 and 1994 was substantial among the 80-year-olds (24% among women and 40% among men). Validation of the causes of death was not undertaken, but the Mayo Clinic in Rochester has good clinical and epidemiological registers. In addition, a Danish study (Osler *et al.* 1996) has shown that although the relative decline in IHD-mortality was highest below the age of 65 years, the reduction in the number of cases was 10-fold higher above this age.

Decline in the Incidence of Cardiovascular Diseases

Although there seems to be no doubt of the decline in the incidence of CVD in recent decades, differences between the results from different studies should be interpreted with some caution in view of differences in methodology and changes in diagnostic criteria. The two contrasting methods of identification of, e.g., AMI events or stroke—the 'hot pursuit' (follow-up of acute admissions) and the 'cold pursuit' (retrospective review of cases from hospital discharge lists)—result in "different sorts of case mixes, because 'hot pursuit' produces a large proportion of cases that finish up without their test results confirming the diagnosis, whereas 'cold pursuit' concentrates on confirmed cases" (Tunstall-Pedoe 1989). Although the agreement between these two methods in determining the history of AMI and stroke was high in the Minnesota Heart Survey (Rosamund, Shahar, and Luepker 1996), both methods gave 'true positive' and 'false negative' findings. Relying only on, e.g., definite AMI excluding non-fatal possible AMI, allows better comparisons; but it has the disadvantage of creating low event rates and high case-fatality rates (Thunstall-Pedoe 1998).

For assessment of trends in morbidity studies it is also important that incident cases can be clearly distinguished from prevalent cases (Whitney *et al.* 1992; Tunstall-Pedoe 1988, 1989; Rosamond, Shahar, and Luepker 1996; Salomaa *et al.* 1997). In most of the populations participating in the WHO MONICA Project, more than a half of non-fatal AMI events among men were definite AMIs, but non-fatal probable AMIs varied from 16% to 31%.

Including different categories of diagnoses has a substantial effect on both incident rates and case-fatality: using the MONICA 'definition 4', which includes fatal definite, fatal possible, non-fatal definite and non-fatal probable AMIs (and which corresponds closely to the clinical diagnosis of AMI), results in a very high decline of incidence and low decline of case-fatality (Salomaa *et al.* 1996). As almost one fourth of the included coronary events are sudden, out-of-hospital deaths, it is obvious that accurate assessment of these deaths could influence both incidence and case-fatality. Furthermore, several studies have shown that diagnoses of AMI have increased in recent decades due to improvements of diagnostical methods: especially the use of more sensitive enzyme markers has led to a higher detection of milder cases (Burke, Edlavitch, and Crow 1989; Dobson *et al.* 1990; Madsen, Balling, and Eriksen 1990; Levy and Thom 1998). These improvements of the diagnostic methods leading to a higher detection of milder AMI may have masked both the decline in incidence and in case-fatality (Chambless *et al.* 1997).

Nevertheless, according to a recent review by Salomaa, Rosamond, and Mähönen (1999), a consistent finding seems to be that the incidence of IHD has declined, but less so than mortality. In most studies the incidence of IHD has declined by a quarter to a third in recent decades, corresponding to a decline of 1–4% per year (Pell and Fayerweather 1985; Goldberg *et al.* 1988; Beaglehole 1990; The Nova Scotia-Saskatchewan Cardiovascular Disease Epidemiological Group 1992; Salomaa *et al.* 1992, 1995; Osler *et al.* 1996; Beaglehole *et al.* 1997; Hunink *et al.* 1997; Marques-Vidal *et al.* 1997; Wilhelmsen *et al.* 1997; Gregor *et al.* 1998; Kirchhoff *et al.* 1999; Lang *et al.* 1999; Osler *et al.* 1999; Tunstall-Pedoe *et al.* 1999, 2000; Bata *et al.* 2000; Goff *et al.* 2000; Kuuslasmaa *et al.* 2000; Madsen, Rasmussen, and Juel 2000).

The Framingham Heart Study (Sytkowski *et al.* 1990) showed a moderate (about 1% annually) but insignificant decline in the incidence of CVD among 50–59-year-old men already in the period 1950 to 1970, and estimated that it explained about a third of the decline in CVD mortality. Probably mainly due to the ageing of the population, the mean age of the first AMI in the Framingham Heart Study increased from about 60 years in the period 1950–69 to 65 years in the 1980s (Guidry 1999).

Until mid-1980 several studies found no decline in incidence in a variety of regions, including Minnesota in the USA (Burke, Edlavitch, and Crow 1989), Gothenburg in Sweden (Wilhelmsen *et al.* 1989), Auckland in New Zealand (Jackson *et al.* 1990), and eastern Finland (Salomaa *et al.* 1992). In the Minnesota Heart Survey the age-adjusted attack rate of definite AMI was similar in 1970 to that in 1980, and even increased when more sensitive enzymatic measures were used during the 1970s, enabling milder cases of AMI to be diagnosed. Nevertheless, in spite of these diagnostical improvements the incidence declined after 1985 in Finland (Salomaa *et al.* 1995, 1996), Sweden (Wilhelmsen *et al.* 1997) and New Zealand (Beaglehole *et al.* 1997).

In Denmark the incidence of AMI dropped by a third for men and a quarter for women in the period 1985–96—an average decrease of 3.5% per year for men and 2.5% per year for women—which is remarkable, especially for elderly people over 75 years (Madsen, Rasmussen, and Juel 2000). In the Danish MONICA study (Kirchhoff *et al.* 1999), the decline in the period 1982–1991 was a bit higher (4% in men and 2.5% in women aged 25–64 year) than the average of the centres which are part of the WHO MONICA Project—2.1% per year among the 28 populations which showed a decrease (Tunstall-Pedoe *et al.* 1999).

The trends in the incidence of stroke have been investigated much less than the incidence of IHD; and the results are more ambiguous, which is understandable as a higher survival rate for patients with heart diseases leads to a higher risk of stroke. Furthermore, until recent years the diagnostical improvements have been greater for stroke than for AMI, leading to a higher hospitalization rate for elderly stroke patients. A higher detection rate of stroke due to the introduction of CT-scanning in the 1970s may have contributed to an increasing incidence.

One of the first observations of a decline in incidence of stroke was reported in Rochester (Olmstead county, Minnesota) in the period 1950–80, both for women and for men, and with a steeper decline of the incidence rates since 1970 (Whisnant 1984). This decline in incidence corresponded approximately to the decline in stroke mortality in the same period (about 50%). Other studies have confirmed the decline in stroke incidence in a variety of areas in Minnesota until 1980. But there was a levelling off of the decline in the 1980s (Homer, Whisnant, and Schoenberg 1987; McGovern *et al.* 1992, 1993; Broderick 1993; Brown *et al.* 1996; Shahar *et al.* 1997). The decline has been confirmed in other countries, such as Finland (Sarti *et al.* 1994; Tuomilehto *et al.* 1996; Numminen *et al.* 1996) and Japan (Ueda *et al.* 1981; Shimamoto *et al.* 1989; Kodama 1993). However, in other studies from Australia, Denmark, New Zealand, Sweden, and the USA no changes or even increasing incidence were found either in men or women or both sexes (Terent 1988; Wolf *et al.* 1992; Harmsen, Tsipogianni, and Wilhelmsen 1992; Jørgensen *et al.* 1992; Lindenstrøm *et al.* 1992; Bonita 1993; Bonita, Broad, and Beaglehole 1993; Stegmayer, Asplund, and Wester 1994; Truelsen *et al.* 1997). Furthermore, divergent trends have been observed in the US with declining rates in most regions while the higher incidence of stroke in the southeastern region (the "stroke belt") is still increasing (Lanska and Peterson 1995; Perry and Rocella 1998; Lackland, Egan, and Jones 1999; Jones *et al.* 2000).

The best evidence that the decline is real is given by the WHO MONICA Project (Asplund *et al.* 1995; Thorvaldsen *et al.* 1995, 1997) and from regional studies from some of the participating centres (Sarti *et al.* 1994; Stegmayer *et al.* 1997; Tuomilehto *et al.* 1996; Thorvaldsen *et al.* 1999). In most populations participating in this multinational study the decline in incidence has been about 1–3% since the beginning of the 1980s. Based on the Danish MONICA data a recent study (Thorvaldsen *et al.* 1999) showed a substantial decrease in age-adjusted stroke incidence during the period 1982–1991—about 3% per year (Table 3). Interestingly this was also the case among the oldest-old, although the decrease occurred later (after 1985) than among younger age groups (before 1980). Due to a combination of prevention and the ageing of the population, the average age at the first stroke attack increased by 3 years.

Table 3. Annual changes in age-standardized stroke rates in different age groups, calculated by Poisson regression, controlling for 5-year age groups (The Danish MONICA Project).

Age	Stroke attacks % decrease	Incident stroke % decrease	Stroke mortality % decrease
Men			
25–54	51	43	44
55–74	40	26	0
75+	27	24	14
All	39	29	12
Women			
25–54	23	20	50
55–74	44	36	41
75+	44	31	29
All	41	31	34

Source: Thorvaldsen *et al*. 1999.

Decline of Case-Fatality, Severity, and Recurrent Events

The assessment of the case-fatality rate is very sensitive to diagnostic criteria as case-fatality depends on numbers of both fatal and non-fatal events (Tunstall-Pedoe 1998). If for example 'possible' or 'probable' non-fatal cases are included among the non-fatal events the case-fatality rate may be reduced substantially and the decline lowered, while the opposite, if 'unclassifiable' deaths are included, results in higher case-fatality and decline (Tunstall-Pedoe *et al.* 1994, 1999). The case-fatality is influenced by different proportions of autopsy and different diagnostic categorizations of out-of-hospital case-fatality, in particular the inclusion or exclusion of "unclassifiable deaths". In addition, a greater proportion of AMI-patients reaching the hospital due to a higher prehospital survival (either due to an earlier recognition of symptoms by patients, a decrease in severity, improvements of prehospital care, or secondary prevention and revascularization after previous heart diseases), may mask a decline in in-hospital case-fatality. That was already suggested by Goldman *et al.* (1982) as an explanation for a relatively constant in-hospital case-fatality in the Boston area in the 1970s, i.e. before thrombolytic treatment was used (the socalled prethrombolytic period), where about two-thirds of AMI-deaths occur out-of-hospital and the decline in case-fatality was mainly associated with a decline in these deaths.

Short-term mortality for AMI has been examined in several studies, often as one month and one year case-fatality divided into out-of-hospital and in-hospital case-fatality (Goldberg *et al.* 1988; Hopper *et al.* 1989; Beaglehole 1990; De Vreede *et al.* 1991; Salomaa *et al.* 1992; The Nova Scotia-Saskatchewan Cardiovascular Disease Epidemiological Group 1992; Pashos, Newhouse, and McNeil 1993; Stevenson *et al.* 1993; Tunnstal-Pedoe *et al.* 1994; Ferrières *et al.* 1995; McGovern *et al.* 1996; Salomaa *et al.* 1996; Beaglehole *et al.* 1997; Chamblers *et al.* 1997; Reitsma *et al.* 1999; Lang *et al.* 1999; Tu, Naylor, and Austin 1999; Bata *et al.* 2000; Tunstall-Pedoe *et al.* 1999, 2000).

In most studies the decline in the overall case-fatality in the thrombolytic period (since the mid-80s when thrombolytic treatment began to be used on a larger scale) seems to be about 1–3% per year, declining from a level of 40–50% in the mid-80s to about 30% or less in the mid-90s (although at a higher level if 'unclassifiable' sudden deaths are included). This was mainly among middle-aged men, and approximately equally divided between out-of-hospital and in-hospital case-fatality, but with a clear tendency to a higher decrease in in-hospital than in out-of-hospital case-fatality in recent years (while the opposite occurred before the mid-80s). The meta-analysis of thirty-six studies by De Vreede *et al.* (1991) showed that already in the prethrombolytic period, i.e. before the mid-1980s, the in-hospital case-fatality declined markedly (from about 30% to less than 20%). The decline of the age-adjusted in-hospital case-fatality in Denmark in the period 1978–1995 dropped from about 30% in the beginning of the period to about 20% in the mid-90s with a clear tendency to a steeper decline since 1985 (Videbæk and Madsen 1999).

This in-hospital decline in case-fatality may have been influenced by a decrease in severity (Burke, Edlavitch, and Crow 1989; Hopper *et al.* 1989; Dobson *et al.* 1990; Salomaa *et al.* 1995; Reitsma *et al.* 1999; Lang *et al.* 1999; Bata *et al.* 1997, 2000). Although the results of the few studies of the severity of hospitalized AMI are contradictory, the majority of studies found a consistent decrease in severity, especially in the thrombolytic period. One study showed already during the prethrombolytic period a clear decrease in median time from onset of symptoms to admission, and a consistent decline in severity of AMI. This, however, was smaller than the decline in in-hospital case-fatality (Hopper *et al.* 1989). In the FINMONICA study (Salomaa *et al.* 1995) a consistent decrease in both sexes was found in both definite ECG findings (declined almost by a half) and in the proportion of abnormal enzyme findings (declined by almost a third), indicating that the AMI of hospitalized patients becomes smaller. This was confirmed in the French MONICA study which found a clear consistent decline of case-fatality in the three participating centres in spite of an increasing proportion of milder AMI, and a consistent decrease of both overall and in-hospital case-fatality "whatever the definiton of event" (Lang *et al.* 1999). The Halifax MONICA study showed an increased severity, predicting 25% higher in-hospital case-fatality (Bata *et al.* 2000). The most thorough study of severity (the ARIC-study) provides mixed support for decrease in severity, showing stable hemodynamic and electrocardiographic indicators, but evidence of a decrease in enzymatic indicators and in the proportion of cardiogenic shock and definite AMI (Goff *et al.* 2000). This decrease in severity indexes may be due to an increasing number of admissions of milder cases and more sensitive diagnoses; but the decline in incidence and the decrease in case-fatality indicate some important factors, such as the declining levels of the major risk factors and the increase in thrombolytic treatments, which can produce less severe atherosclerosis and smaller infarcts.

The decline in case-fatality took place over a period when a number of important medical improvements began—the introduction of the heart-lung machine in 1951; artificial heart valves in 1953; and the introdution of antihypertensive medication (thiazide diuretics, methyldopa and reserpine) in the 1950s; followed by the introduction of prehospital resuscitation and coronary care units in the 1960s. It seems that the more pronounced decline in case-fatality in recent years may at least in part be explained by the increasing use of coronary revascularization in the 1970s, and by the increasing use of the new drugs

for acute treatment and for secondary prevention in the 1980s (beta-blockers, anticoagulants, antiplatelets, thrombolytics, nitroglycerin, ACE, lipid-lowering drugs). Since the early intervention studies in the 1960s and 1970s a lot of clinical trials have demonstrated the efficacy of these new drugs.

The effect of antihypertensive medication on the decline of stroke-mortality in the US is widely recognized. During the 1970s the detection and treatment of patients with hypertension in the US increased dramatically. Correspondingly, the decline of stroke-mortality increased from about 1% per year in the 1950s and 1960s, to 1.5% per year in the early 1970s, and to more than 5% per year during the 1970s (Levy 1981). Throughout the thrombolytic period, it is clear from the WHO MONICA Project (Tunstall-Pedoe *et al.* 2000) that changes in coronary care and secondary prevention were strongly linked with declining coronary endpoints. Several observational studies of normal clinical practice (Pashos, Newhouse, and McNeil 1993; Stevenson *et al.* 1993; Rogers *et al.* 1994; European Secondary Prevention Study Group 1996; Chandra *et al.* 1997; Tu *et al.* 1997; Tunstall-Pedoe *et al.* 2000) have confirmed the effect of thrombolytics, the other new drugs, and the new cardiac procedures documented in clinical trials. One-month survival in patients treated with thrombolytics was considerably higher compared to those without this treatment, even when controlled for contraindications, confounders, and severity.

It is not yet evident that one-year survival and especially long-term survival (more than five years) have increased. A comparison of the use of diagnostic and therapeutic interventions between hospitals in Canada and the USA participating in the Survival and Ventricular Enlargement (SAVE) study showed a much lower use of medical interventions in Canada than in the USA (Rouleau *et al.* 1993). In spite of this, the rate of reinfarction and mortality after one, two, and three years or more were almost the same; although there was a slightly lower incidence of activity-limiting angina in the USA than in Canada. Another later comparison between Canada and the USA of the use of invasive cardiac procedures among elderly patients (Tu *et al.* 1997) also showed a much lower use of coronary angiography and revascularization in Canada than in the USA. The 30-day case-fatality was slightly, but significantly, lower among USA-patients than among Canadian patients. However, the one-year mortality was identical. In the four communities of the USA participating in the ARIC study women and blacks were less likely to have invasive cardiac procedures and thrombolytic therapy (Weitzman *et al.* 1997).

Nevertheless, in most of the studies from the thrombolytic period the in-hospital case-fatality has declined to a level of about 15% or even lower. Even in southwestern France (the Tolouse center of the French MONICA study) where the IHD mortality is very low, the overall case-fatality declined among men from 38% to 27% in the period 1985–90, but not significantly among women. This decline was due almost only to a decline in in-hospital case-fatality (from 21% to 11%), and only in male patients with previous IHD (from 33% to 19%), but not among patients without a previous IHD (from 8% to 7%); the out-of-hospital decline was minor (from 21% to 18%) (Ferrières *et al.* 1995). In the same period the use of antiplatelets, beta-blockers, thrombolytics, and revascularizations doubled. Compared to southern Germany in the same period (the Augsbourg center of the German MONICA study), where both the declining incidence and mortality were higher, but the in-hospital case-fatality among men did not decrease, the increased use of these medi-

cations and revascularizations was much higher in southern France (Marques-Vidal *et al.* 1997).

Several of the studies mentioned above showed that only about a third of the AMI patients in most regions were treated with thrombolytics, although a majority of those who were not treated had no contraindications. In particular, smaller proportions of women and older patients were not treated with the new drugs. It seems that recent advances in the treatment of AMI have predominantly benefited male MI patients younger than 65 years. Most studies showed a smaller decline in in-hospital case-fatality among women than among men, except one study which found the same decline for women as for men (Pashos, Newhouse, and McNeil 1993). However, in a meta-analysis of 31 studies which all show a higher in-hospital case-fatality among women than among men, it was found that in the studies, in which age was controlled, the age-adjusted differences did not reach statistical significance (Nohria, Vaccarino, and Krumholz 1998). This study also suggests that factors other than the underuse of these treatments among women might contribute to explaining the differences—such as a higher presence of severe comorbidities, a lower efficacy of thrombolytics and antiplatelets, and a higher risk for reinfarction and bleedings after these treatments among women.

Most of the elderly, and especially the oldest-old today, are women with a high prevalence of comorbidities and therefore many contraindications for treatments with anticoagulants, antiplatelets and thrombolytics. Nevertheless, in spite of this higher proportion of elderly patients with contraindications, many more elderly patients may benefit from these treatments. In the 1990s there seems to be a tendency in clinical practice to treat an increasing number of elderly, including the oldest-old, with the new cardiovascular drugs, except lipid-lowering drugs. That is the case even for Danish centenarians of whom a high proportion take cardiovascular drugs, including antiplatelets, anticoagulants and beta-blockers (Table 4).

The more aggressive use of treatments and secondary prevention may also have had an impact on the recurrence of AMI and other sequelae after a first AMI. One third of all AMI events are recurrent events. The recent studies in which the recurrence rates have been estimated indicate a decline of at least 1% per year with a tendency to higher declines in the most recent years (McGovern *et al.* 1996; Salomaa *et al.* 1996; Rosamond *et al.* 1998;

Table 4. Cardiovascular drugs among Danish centenarians ($N = 207$).

	n	%
Cardiovascular drugs *	132	64
Diuretics **	123	59
Antihypertensives (thiazides included)	57	28
Digoxin	35	17
Thrombosis preventive drugs	30	15
Antihypertensives (thiazides not included)	12	6

*Diuretics, antihypertensives and vasodilators. ** Thiazides alone: N = 47 (23%).
Source: Andersen-Randerg et al. 2001.

Guidry *et al.* 1999; Lang *et al.* 1999; Bata *et al.* 2000; Goff *et al.* 2000). In Finland the decline in recurrent events in the period 1983–92 was very high—as high as 9% per year in both sexes in the Kuopio province—which explained the largest part of the mortality decline in this region, while the decline in case-fatality was very small (Salomaa *et al.* 1996). Also in France the decline in recurrent events was high in approximately the same period—almost 6% on average for the three participating centres (Lang *et al.* 1999).

Decline in the Risk Factors for CVD

The decline in incidence, severity, and case-fatality may in part be explained by the decrease in the well-established risk factors for cardiovascular diseases (cholesterol, tobacco, and hypertension), although coronary heart disease and stroke are not influenced to the same degree by these risk factors (MMWR 1999a). Public health interventions have sought to reduce the risk either by "the high-risk" or by "the population-wide" approach, but at the population level the impact of changes in these classical risk factors on the decline of CVD is difficult to assess (Dobson *et al.* 1998; Lang *et al.* 1999; Tunstall-Pedoe *et al.* 1999; Salomaa, Rosamond, and Mähönen 1999; Thorvaldsen *et al.* 1999; Kuulasmaa *et al.* 2000). But there is no doubt that the levels of the main risk factors have declined markedly in most Western populations during recent decades. Table 5 shows the changes in main coronary risk factors in different studies of middle-aged and younger elderly persons (Salomaa, Rosamond, and Mähönen 1999).

The contributions attributed to these major risk factors seem to decrease with advancing age (Larson 1995; Tervahauta, Pekkanen, and Nissinen 1995). According to the comparisons of 70-year-old Danes from three different cohorts born in 1897, 1914, and 1921, participating in the Glostrup Population Studies, the classical risk factors still seem to be

Table 5. Changes in main coronary heart disease risk factors in different studies (negative numbers indicate a decrease).

			Change in			
Area	**Age (years)**	**Period**	**Cholesterol (mol/l)**	**SBP (mmHg)**	**DBP (mmHg)**	**Smoking (%)**
Men						
Eastern Finland	30–59	1972–1992	–88		–86	–16
Framingham, USA	50–59	1950–1970	–18	–40	–10	–220
Iceland	45–64	1968–1988	–42	–155		–293
Gothenburg, Sweden	45–54	1963–1995	–60	–40		–270
Minnesota, USA	25–74	1986–1991	–13	–9		–3.4
Women						
Eastern Finland	30–59	1972–1992	–118		–122	+9.0
Iceland	45–64	1969–1988	–75	–193		–118
Gothenburg, Sweden	45–54	1970–1995	–130	–70		–110
Minnesota, USA	25–74	1986–1991	–10	–9		–1.9

Source: Salomaa *et al.* 1999.

important risk factors for younger-elderly (Thomsen 1999). The same has been found in other studies of younger-elderly, e.g., in the Framingham Heart Study and the SHEP study (Larson 1995; Frost *et al.* 1996). However, it is very controversial how important they are among the oldest-old. The problem in estimating their effect on CVD-mortality in the oldest-old is that the number of confounding and intermediate factors become more numerous with advancing age: low values of the major risk factors such as low cholesterol and low blood pressure may be associated with underlying lethal diseases. Even when controlling for underlying diseases, high values have been found associated with higher survival ("paradoxical survival") values rather than low and middle values among the oldest-old in some studies (Forette, Tortrat, and Wolmark 1989; Langer, Ganiats, and Barrett-Connor 1991; Casiglia *et al.* 1993; Curb *et al.* 1996a; Weverling-Rijnsburger *et al.* 1997; Oliver 1999; Forette 1999).

In the USA more than half of all middle-aged men were smokers in the 1960s, whereas in the 1990s about a quarter of all men were smokers, and the percentage of adults who never smoked increased form 44% in the mid-1960s to 55% in 1997 (MMWR 1999b). In most populations participating in the WHO MONICA Project the prevalence of cigarette smoking decreased among men in the 1980s, but varied among women (Dobson *et al.* 1998). In eastern Finland, the percentage of decline of smoking was 16% among men (from 53% to 37%) in the period 1972–92 which predicted a 10% decline in IHD mortality (Vartiainen *et al.* 1994). Even in Denmark, where life expectancy did not improve in the period 1975–95 as in comparable European countries, the decline among men in Denmark is substantial—from more than 70% in the 1960s to less than 40% today (Videbæk and Madsen 1999). However, the proportion among women has declined less—from more than 50% in 1960s to 37% in 1995—a proportion which is the highest among women in European countries. Furthermore, the proportion of heavy smokers has increased among women from less than 15% to more than 20%, while it decreased among men from more than 50% to less than 40% (Osler *et al.* 1998).

Due to the small number who survived to advanced ages in the ongoing cohort studies of middle-aged and younger-elderly persons, we do not know whether those who made it to the age of 85 or more have smoked less than their contemporaries. However, among Danish nonagenarians and centenarians about three-quarters of the men and more than a third of the women were smokers when they were middle-aged (Table 6). These proportions correspond to the proportion of smokers among men and women in the period 1960–70,

Table 6. Smokers among Danish nonagenarians and centenarians.

	Men		**Women**	
	93 years	**100 years**	**93 years**	**100 years**
Smokers	142 (25%)	10 (22%)	170 (10%)	22 (14%)
Former smokers	310 (55%)	23 (51%)	362 (22%)	48 (30%)
Never smoked	112 (20%)	10 (22%)	1105 (68%)	85 (52%)
Missing data		2 (5%)		7 (4%)
N	564	45	1637	162

although there may have been differences in the type and quantity, and in the proportion of heavy smokers and the proportion who inhaled the smoke. According to a meta-analysis of more than thirty studies the risk for stroke due to smoking declined beyond the age of 75 years (Shinton and Beevers 1989), although smoking was still a risk factor for CVD below the age of 85 in the Framingham Heart Study (Larson 1995).

A decrease in the prevalence of hypertension and in both systolic (SBP) and diastolic blood pressure (DBP) of several mmHG has been found in several studies (Tunstall-Pedoe *et al.* 1997; Dobson *et al.* 1998; MMWR 1999a; Salomaa, Rosamund, and Mähönen 1999). The decline in BP was substantial in the 1970s in Japan (more than 10 mmHG in SBP and 4 mmHG in DBP), and was probably the main contributor to the declining stroke incidence and mortality, especially the decline of cerebral haemorrhage (Shimamoto *et al.* 1989). In eastern Finland the decline of DBP by 9% among men in the period 1972–92 predicted a 15% decline in IHD mortality. In the Glostrup Population Studies of the three populations of 70-year-old people both the SBP and DBP decreased significantly from the 1960s to the 1990s in both sexes; and the proportion of medically treated hypertensive 70 year old patients doubled (Sjøl, Thomsen, and Schroll 1998; Thomsen 1999). In the USA the percentage of treated patients with hypertension increased more than twofold already in the 1960s (Goldman and Cook 1984). But it is not evident whether these trends were similar above the age of 80 years (Forette 1999). In the Honolulu Heart Program study of stroke among men, the percentage of strokes attributable to hypertension decreased from 50% in those aged 45–54 years to 18% in those over 65 years (Curb *et al.* 1996b). This less attributable risk in the elderly was not due to a decline in the risk for stroke associated with hypertension or due to the effect of treatment, but to the increasing incidence of stroke in normotensive men. This suggests that other factors associated with age play an increasing role in the risk of stroke with advancing age.

Several studies indicate a decrease in the mean level of cholesterol of about a half to one mmol/l, and clinical trials have estimated that a 1% decline leads to a 2% decline in the risk of IHD (Wilhelmsen 1997; Tunstall-Pedoe *et al.* 1997; Salomaa, Rosamond, and Mähönen 1999). This decrease is less consistent as the levels increased in several of the populations particpating in the WHO MONICA (Dobson *et al.* 1998). However, in eastern Finland, where the level in the 1970s was very high, the cholesterol level declined by 13% (almost 1 mmol/l) among men from 1972 to 1992, which predicted 26% of the decline in IHD mortality (Vartiainen *et al.* 1994). In the Glostrup Populations Studies of 70-year-old people while fasting, serum cholesterol decreased in both sexes by about a quarter from the 1960s to the 1990s (Sjøl, Grunnet, and Schroll 1991; Thomsen 1999). The mean level of serum cholesterol among Danish centenarians born in 1895–96 (unpublished data) was much lower than among 70-year-olds born in 1897 (5 vs. 8 mmol/l); and also a bit lower than 70-year-olds born in 1914 and 1921 (5.5–6 mmol/l). It is well known that cholesterol decreases with advancing age beyond 60. However, the impact of cholesterol on mortality in the oldest-old is intriguing. Forette, Tortrat, and Wolmark (1989) found that a low cholesterol level was much more risky than a high cholesterol level in the oldest-old without cancer. Although results from later studies are still controversial, most studies have found that the risk diminishes or becomes negatively associated with overall mortality and IHD with advancing ages (Weverling-Rijnsburger *et al.* 1997; Oliver 1999).

It seems that sex differences in these classical risk factors may contribute to the difference in mortality between the sexes, especially due to CVD up to the age of 65 (Salomaa, Rosamond, and Mähönen 1999). However, it is unclear whether the differences in these rist factors can explain the difference in sex mortality and CVD in the oldest-old. With advancing age the differences in risk factors between the sexes seem to diminish, although the differences in mortality increase steadily, leading to a very high proportion of women among nonagenarians and centenarians. It therefore seems more probable that the male mortality disadvantage among the oldest-old is related to type and severity of comorbidity and to treatments.

A number of other risk factors have been found to be associated with the risk and mortality of CVD such as socioeconomic factors, work activity, stress, type A behaviour, exercise, antioxidants, homocystein and fibronogen levels. Although the trends in the changes of these risk factors have been investigated less than those of the classical risk factors, it seems that especially leisure time activity and the intake of antioxidants (including red wine, nuts and chocolate) have increased in recent decades, and both incidence and survival after AMI and stroke differ among socioeconomic groups (Evans *et al.* 1995; Eagles, Gulati, and Martin 1996; Tunstall-Pedoe *et al.* 1997; Osler *et al.* 2000a; Peltonen *et al.* 2000).

It seems very probable that gene-environment interactions have changed with changes in life conditions and lifestyles (Yashin *et al.* 1998, 1999, 2000). It is evident that, for example, the ApoE polymorphism, which plays an important role in cholesterol metabolism, has a substantial effect on longevity (Gerdes *et al.* 2000), and that some other genes may be associated with longevity. This has been suggested in studies of centenarians (De Benedictis *et al.* 1998A, 1998B, 1999, Jeune and Andersen-Ranberg 2000). However, the lack of replicability and the lack of association between several high risk genes for CVD (Bladbjerg *et al.* 1999) indicate that the changing patterns of these interactions may be very complex.

Contributions to the Decline in CVD Mortality

Several studies have investigated the impact of the various contributors to the decline of CVD mortality (Stern 1979; Levy 1981; Goldman and Cook 1984; Shimamoto *et al.* 1989; Beaglehole 1990; Sytkowsky, Kannel, and d'Agostino 1990; Sigfusson *et al.* 1991; Whitney *et al.* 1992; Vartiainen *et al.* 1994; Bots and Grobbee 1996; McGovern *et al.* 1996; Salomaa *et al.* 1996; Bonneux *et al.* 1997; Hunink *et al.* 1997; Gregor *et al.* 1998; Lang *et al.* 1999; Salomaa, Rosamond, and Mahonen 1999; Reitsmaa *et al.* 1999; Thorvaldsen *et al.* 1999; Tu, Naylor, and Austin 1999; Tunstall-Pedoe *et al.* 1999; 2000, Bata *et al.* 2000; Kuulasmaa *et al.* 2000; Madsen, Rasmussen, and Juel 2000; Osler *et al.* 2000b).

Based on studies in the USA in the 1960s and 1970s, already Stern (1979), and Goldman and Cooklates (1984), estimated that changes in lifestyle accounted for most of the reduction in IHD mortality. For the period 1968 to 1976 Goldman and Cook (1984) estimated that 63% of the decline in IHD mortality was due to risk factor reductions, including the effect of antihypertensive treatments, and 31% owing to other treatments. In a review of studies mainly from the USA, Australia and New Zealand, based on data from the

prethrombolytic period, Beaglehole (1990) concluded that "the major part of the decline in mortality rates occurred in out-of-hospital ('sudden') deaths, much of this decline has been in incident case", and that "a reasonable judgement is that risk factor trends, particularly in diet and smoking, are the most important cause of the trends in mortality".

However, the Framingham Heart Study (Sytkowski, Kannel, and D'Agostino 1990) showed that even before 1980 medical interventions probably had a major impact as only a third of the decline in IHD mortality was a result of a declining incidence. In spite of a further decline in incidence in the USA from about 1% annually before 1980 to about 2% in the period 1980 to 1990, Hunink *et al.* (1997) found that the contribution of medical interventions was more significant than primary prevention. Based on a computer simulation model they estimated that "actual coronary mortality in 1990 was 34% (127,000 deaths) lower than would be predicted if risk factor levels, case-fatality rates, and event rates in those without coronary disease remained the same as in 1980". However, "only 25% was explained by primary prevention, while 29% was explained by secondary reduction in risk facors in patients with coronary disease and 43% by other improvements in treatment of patients with coronary disease". Of the various risk factors, changes in diet resulting in decreased cholesterol levels accounted for a third of the decline in IHD mortality; and it seems that lowering hyperlipedemia in patients with IHD by lipid-lowering medications was more cost-effective than changes in diet. This thorough study suggests that the contributions to the decline in IHD mortality may have shifted in favour of medical interventions during the 1980s in the USA, i.e. during the shift from the prethrombolytic to the thrombolytic period.

Still concerned with the prethrombolytic period (1978–1985), Bots and Grobbee (1996) estimated that, without the decline in IHD mortality, about 225,000 persons would have died instead of about 200,000 actual deaths in this period in the Netherlands. They estimated on the basis of data from the Dutch NIVEL study, international results from intervention studies, and clinical trials that about 5,000 of these 25,000 could have survived due to declining smoking habits, about 5,000 to antihypertensive treatment, about 4,000 to treatment with beta-blockers, about 4,000 to treatment with anticoagulants, about 1,500 to coronary bypass surgery, about 1,000 to treatment with antiplatelets, and almost 1,000 to the effect of coronary care unit facilities. Surprisingly the contribution of the declining cholesterol levels was very small (about 100 subjects) due to the fact that cholesterol levels only decreased among the younger-elderly but increased among the middle-aged. Although it is well-known that the results from clinical trials are very seldom repeated in routine clinical practice, this study indicates a substantial effect of treatments already before thrombolysis was used on a large scale.

In a recent review, Salomaa, Rosamond, and Mähönen (1999) concluded that during the 1970s and early 1980s the decline in incidence due to reduction of risk factors was the major contribution to the decline in IHD mortality; while during the latter half of the 1980s and the beginning of the 1990s, the contributions of treatment and secondary prevention have become increasingly important.

Nevertheless, divergent contributions of incidence and case-fatality to declining mortality have been found among various regions in Australia and New Zealand (Beaglehole *et al.* 1997), Canada (The Nova Scotia-Saskatchewan Cardiovascular Disease Epidemiology

Group 1992), Finland (Salomaa *et al.* 1996), France (Lang *et al.* 1999), Sweden (Malmstrøm *et al.* 1999; Peltonen *et al.* 2000) and the USA (Kimm *et al.* 1983; Wing *et al.* 1986; Ragland, Selvin, and Merrill 1988), and among different socioeconomic groups in England and Wales (Marmot *et al.* 1978; Rose and Marmot 1981, Marmot and McDowall 1986), France (Lang *et al.* 1999), and the USA (Wing *et al.* 1988; Barnett, Armstrong, and Caspar 1999).

It seems apparent that differences in lifestyle have contributed to the differences in CVD incidence and mortality between different regions. The Seven Countries Study (Keys 1970) and the Japanese migration studies (Kato *et al.* 1973) found a strong correlation between dietary fat intake and CVD. Also the influence of different blood pressure levels in different regions on CVD was demonstrated in these studies. The major importance of the declining blood pressure on stroke trends has since been evident in most countries, especially in Japan (Shimamoto *et al.* 1989), where it seems to have been a result of increasing antihypertensive treatment, decreasing salt intake, and other environmental changes.

In Finland, which about 1970 had the highest CVD mortality in the world, it seems that the decline in IHD-mortality during the 1970s was mainly due to the declining incidence, while the contributions to the decline during the 1980s was more complex. "Until the mid-1980s the trend of the observed mortality followed the predicted mortality but after that the decline in observed mortality accelerated more than was predicted from the changes in risk" (Vartianen *et al.* 1994). In eastern Finland, where the levels of the classical risk factors have been very high, three-quarters of the decline could be predicted on the basis of the changes in the three classical risk factors, and half of the decline was predicted by the change in serum cholesterol. While in southwestern Finland, where the risk factor levels and IHD mortality have been lower, "decline in case-fatality rates has had a more important contribution" (Salomaa *et al.* 1996). A very high contribution by the classical risk factors have been found in Iceland (Sigfusson *et al.* 1991), as the calculated reduction in risk for the age group 45–64 was about 35% which was closely similar to the observed decrease in IHD mortality.

In an editorial, "Autres pays, autres moeurs", Tunstall-Pedoe (1988) made a 'sentimental journey' from Scotland with a very high CVD mortality through England with a middle high CVD mortality to France with a very low CVD mortality, and reflected on what could be the causes of 'the French paradox'. He emphasized that French people drink more wine, eat more vegetables, including more garlic and onions, and despite a high fat intake consume more polyunsaturated fatty acids.

Several ecological analyses (St. Leger, Cochrane, and Moore 1979; Richard, Cambine, and Ducimetière 1981; Richard 1987; Renaud and De Lorgeril 1989, 1992, 1993; Artaud-Wild *et al.* 1993; Criqui and Ringel 1994) have compared the correlation between risk factors and IHD mortality. Even when misclassifications in the death certificates are considered, the IHD mortality is lower in France than in other European countries in spite of a similar high consumption of fat and the same level of the major risk factors. In France, compared to other mediterranean countries with low IHD mortality, the consumption of fat and the major risk factors are higher and the intake of vegetables lower, but the wine consumption clearly higher. Apparently, according to most of these ecological analyses only the wine

consumption explains the French paradox. However, it is still a matter for debate whether this could be due to non-ethanol beneficial effects of antioxidants in red wine either through an effect on atherosclerosis (inhibtion of oxidation of low-density lipoprotein) or through a hemostatic mechanism (inhibition of platelet aggregation), or is due to a healthier life style among wine drinkers (Renaud and De Lorgeril 1992, 1993; Frankel *et al.* 1993; Criqui and Ringel 1994; Grønbæk 1997; Simini 2000). In a recent review (Fagrell *et al.* 1999) it was concluded that light to moderate drinking independently of type of beverages has a protective effect on cardiovascular diseases. It was also concluded "that there is no strong evidence for a better protective effect on cardiovascular events from wine than from other types of liqueurs, but that confounding factors such as diet and lifestyle factors may play a role".

Comparisons of the nutritrional patterns of France with those of other European populations and within different regions in France have found some differences which apart from wine may contribute to an explanation. Comparing two MONICA centres, Belfast in Ireland and Toulouse in southwestern France with a fourfold difference in CVD mortality, Evans *et al.* (1995) in an article named "Autres pays, autres coeurs?" confirmed that the total fat intake did not differ. However, "carbohydrate and saturated fat intake was significantly higher in Belfast, while protein, dietary cholesterol and polyunsaturated fat, particularly linoleic acid intake, was significantly higher in Toulouse, as was consumption of wine, cheese, fruit and vegetables, but not potatoes".

The difference in coronary mortality between France and Finland was the highest in Europe in the 1970s, and they both deviated markedly from other countries in ecological analyses of the correlation between fat intake and IHD. "Differences in coronary mortality can be explained by differences in cholesterol and saturated fat intakes in 40 countries, but not in France and Finland" (Artaud-Wild *et al.* 1993). In spite of approximately the same total fat intake, there were substantial differences in food consumption between Finland and France, as the consumption of milk and butterfat was higher in Finland and the consumption of vegetables and vegetable oils was higher in France.

Comparison of risk factors (Douste-Blazy *et al.* 1988) and dietary patterns (Jost *et al.* 1990) among the three French MONICA centres has shown a higher intake of vegetable fat and a lower intake of animal fat in southwestern France than in the northern and eastern France. The amount of alcohol intake was the same but the alcohol intake in southwestern France was mainly wine whereas wine and beer was taken in about the same proportions in northern and eastern France. Additionally, the high total cholesterol in southwestern France was mainly due to a higher HDL-cholesterol (the "good cholesterol") which is known to be associated with a lower incidence of IHD and in part due to intake of wine. Finally, the proportion of smokers was the same but the proportion of hypertension and the Boby-Mass Index was lower in southwestern France.

In spite of the differences in dietary patterns and other risk factors among the three centres of the French MONICA study, "differences in case-fatality, much more than incidence", has accounted for the disparities of AMI mortality in France in the thrombolytic period (Lang *et al.* 1999). Also the Halifax center of the WHO MONICA Project found that by combining the risk factors to predict the trend of IHD mortality "the actual decrease of mortality was much larger than predicted" (Gregor *et al.* 1998).

The first analysis of the pooled data from the WHO MONICA Project for the period mid-80s to mid-90s, the thrombolytic period, shows that about two-thirds of the decline in IHD mortality were due to a decline in event rates (incidence and recurrent rates), and one third was due to a decline of case-fatality rates (Tunstall-Pedoe *et al.* 1999). However, a later analysis of the WHO MONICA data of the contribution by the classical risk factors (Kuulasmaa *et al.* 2000) showed less reliable estimates, especially for women. This was confirmed by the latest analysis of the WHO MONICA data (Tunstall-Pedoe *et al.* 2000) which found a higher contribution of coronary care and secondary prevention than previoulsy estimated. But it was not possible to estimate how much of the remaining variance was attributable to other factors, to time delay between risk factor changes, or to complexities of measurements. As Lang *et al.* (1999) emphasize, it is far from simple to assess what is behind the declining trends and the regional differences. Classical risk factors and medical care may not be the only important factors to have contributed to the decline in IHD-mortality (Kaplan *et al.* 1988).

We may learn also from paradoxes other than the French paradox, such as *the USA-paradox* of the oldest-old, i.e. a lower mortality among the oldest-old in the USA than in Japan, Sweden, France, and England in spite of the opposite among adults (Manton and Vaupel 1995); '*the Japanese paradox*' of declining IHD mortality in spite of a substantial increase in animal fat intake and cholesterol levels; and '*the Danish paradox*' of declining IHD mortality comparable to other western European countries in spite of a remarkable stagnation of life expectancy in Denmark in the period 1975–1995.

A recent study of Danish mortality in the period 1835 to 1995 (Andreev 1999) has shown that the Danish excess mortality in recent decades compared to Sweden, the Netherlands and Japan was mainly observed among the middle-aged. Compared to Sweden the disadvantageous trends were mainly due to cancer, especially lung and breast cancer, and respiratory diseases. Deaths from IHD was important compared with Japan, where the rate was very low, and only important for the age group 50–59 years but not among age groups beyond 60 years. Futhermore the level and decline of the IHD rate in the period 1970 to 1995 were the same as in Sweden both among the middle-aged, elderly and oldest-old.

Since 1950 the consumption of pure alcohol has quadrupled in Denmark—from 4 litres per adult inhabitant to 12 litres per year. However, since 1970 this increase is not due to beer, as beer has been replaced by wine. Although Denmark is still far away from France, a moderate wine consumption among Danes included in the Copenhagen City Heart Study has been found to be associated with lower over-all mortality and with a lower risk of coronary heart disease and stroke (Grønbæk *et al.* 1994, 1995; Truelsen *et al.* 1998), in particular among elderly people (Grønbæk *et al.* 1998). The Danes who preferred wine to beer had a healthier diet as they ate more fruit, fish, cooked vegetables, and salad, and they used more olive oil for cooking (Tjønneland *et al.* 1999). Furthermore, moderate wine intake was related to good self-perceived health (Grønbæk *et al.* 1999).

The USA paradox suggests that an earlier reduction of the classical risk factors, an earlier introduction of antihypertensives, and a greater use of medical interventions, also among elderly people, have resulted in an earlier and steeper decline of CVD mortality in the USA than in Europe. The Japanese and the Danish paradoxes indicate, like the French

paradox, that other risk factors than the classical risk factors are important, and that medical interventions, especially in the thrombolytic period, have contributed to approximately the same rate of decline in spite of different levels and reductions of the classical risk factors. Furthermore, these paradoxes suggest that the decline of CVD mortality in recent decades may explain a substantial part of the decline in total mortality among elderly populations, including the oldest-old.

High Prevalence of CVD in the Oldest-Old

In spite of these very favourable contributions to the declining mortality trends, we cannot finalize our conclusion without considering the fact that these improvements create new dilemmas in the care of the oldest-old in the future. The fact that the incidence of CVD declined less than mortality has led to a marked increase in the number of patients with chronic heart diseases and stroke-sequelae such as chronic coronary syndromes, congestive heart failure and vascular dementia (Davis *et al.* 1985; Whitney *et al.* 1992; Feinleib 1995; Bonneux *et al.* 1997; Salomaa, Rosamond, and Mähönen 1999; Reitsma *et al.* 1999; Guidry *et al.* 1999).

By 1968–78 the mortality of chronic ischaemic heart disease had increased in half of the more than five-hundred socioeconomic areas in the USA among men and in a quarter of these areas among women (Davis *et al.* 1985). Despite the dramatic decline of CVD mortality the percentage of total deaths caused by CVD in the US in this period did not decline much—only from 54.3% to 51.3% (Feinleib, Havlik, and Thom 1982). In the 1980s it became evident that hospital discharge rates for IHD diseases increased, especially due to an increase in patients with congestive heart failure but also due to an increase of other coronary syndromes, including unstable angina. In 1980 angina pectoris (both stable and unstable) accounted for only 15% of the total IHD discharges, whereas in 1989 they accounted for 37% in the USA. This shift in hospitalizations "away from AMI toward less severe ischaemic events may be due to earlier recognition, diagnosis and medical interventions" (Whitney *et al.* 1992). The Dutch study by Bonneux *et al.* (1997) "provides circumstantial evidence that the sharp drop in mortality from coronary heart disease between 1985 and 1992, the levelling off of mortality from stroke, and the increase in mortality from congestive heart failure are causally linked by the same process: the increased survival of patients with coronary heart disease".

In the Netherlands (Reitsmaa *et al.* 1999), the absolute number of hospital admissions for total CVD nearly doubled from 1975 to 1995—from about 10% of all admissions to almost 20%. The increase in the age-adjusted admission rates for heart failure more than doubled in Denmark from 1978 to 1996 (Videbæk and Madsen 1999). In addition, as a result of the ageing of the population, the numbers of CVD have decreased much less than what would be expected from the mortality decline. In the USA the death rate from IHD declined by almost 30% from 1985 to 1995; but the actual number of deaths only declined by about 10% (Salomaa, Rosamond, and Mähönen 1999). The Danish MONICA study of stroke (Thorvaldsen *et al.* 1999) has shown that the risk associated with ageing almost counterbalanced the effect of improved prevention. The end result seems therefore to be a dynamic balance between a tendency to a compression of morbidity due to a declining

Table 7. Cardiovascular diseases among Danish centenarians (N = 207).

	n	%
Hypertension (140/90)	108	52
Chronic heart failure	67	32
Angina pectoris/ischemia	57	28
Atrial fibrillation/flutter	36	17
Stroke	19	9

incidence and an expansion of morbidity due to declining case-fatalities. Consequently, the health care system experienced no substantial alleviation of the burden of CVD.

The high prevalence of cardiovascular diseases in the oldest-old is clearly illustrated in Danish centenarians (Table 7). These figures are minimum estimates as not all centenarians could be adequately clinically examined. About three-quarters of the centenarians had cardiovascular diseases. More than half of the centenarians had hypertension or were treated for that, and about half had diagnosed chronic heart failure or myocardial ischaemia. Most of the centenarians were being treated with drugs for cardiovascular diseases. A larger proportion of centenarians born in 1895/96 were treated for chronic heart failure than people aged 85 from the 1897-birth cohort of the Glostrup Population Studies (Andersen-Ranberg, Schroll, and Jeune 2001).

Although the increase in hospitalization admissions decelerates at very high ages as shown in one of our recent Danish register-based studies of a sample of 1 million inhabitants (Madsen and Serup-Hansen 2000), those who reach the age of 80 or more today may have benefited from medical improvements in treatments. A retrospective analysis of the hospitalization of Danish centenarians since they were 80-years-old showed a steady increase in hospitalization (Andersen-Ranberg, Schroll, and Jeune 2001). Nearly all centenarians added to the increasing hospitalization rate.

In recent years the oldest-old have been hospitalized and treated with surgery, which was not the case decades ago. The mortality after major operations on elderly people with, for example, hip fractures and cancer, has declined, due to improvements of anaesthetics and operation methods, including less invasive surgery. Furthermore, age limits for surgery on elderly people have been replaced by clinical criteria including functional ability to a degree that even centenarians are operated on with success today (Milliken and Milliken 1971; Katlic 1985; McCann and Smith 1990; Warner *et al.* 1998). A similar change is true for medical treatment of potentially fatal diseases, e.g. antibiotics for pneumonia, anticoagulants for arrhythmia, and influenza vaccination.

Most of the Danish centenarians have survived potentially fatal diseases like pneumonia, myocardial infarction, stroke, or malignant tumours, and have been through major surgery for hip fractures, gallstones, cancer, or other operable diseases (Table 8). About sixty percent of the Danish centenarians that we examined had survived an AMI, a stroke, a malignant cancer or a hip fracture—and three-quarters, if pneumonia was also considered.

Table 8. Number of former diagnoses confirmed in medical files among Danish centenarians (N = 207).

	n	%
Pneumonia	81	40
Fracture of hip	78	35
Myocardical infarction	56	27
Stroke of transient ischaemic attack	46	22
Skin cancer	42	20
Gastric ulcer	37	18
Gallbladder disease	36	17
Erysipelas	28	14
Other cancers	25	12

We have found centenarians who have survived operations for hip fractures and cancer at an advanced stage while they were in their nineties. One woman had been hospitalized more than 20 times and survived 7 major operations, including a hip fracture and an advanced colon cancer when she was 95 years. Most of these centenarians would not have reached the age of 100 fifty years ago. Improvement of medical interventions has made it possible for an increasing proportion of the oldest-old both to survive and to live with major diseases.

Conclusion

Despite the complexity of the search for an explanation of the decline in mortality among the oldest-old, it seems reasonable to summarize the results from the above-mentioned studies by the following general conclusion:

The declining CVD mortality is attributable to a combination of:

1. a declining incidence, including a substantial reduction in out-of-hospital deaths, due to improvement of primary prevention, especially in the prethrombolytic period:
2. a declining case-fatality due to improvement of treatment, which increased markedly in the thrombolytic period:
3. a declining recurrence rate due to improvement of secondary prevention, mainly in the thrombolytic period.

For the future we may expect further improvements in primary prevention. An interesting recent Danish assessment has shown that if the inhabitants in Denmark would all follow the official recommendations regarding the optimal intake of total and saturated fat, fish, fruits and vegetables, and alcohol, then between 3,000 and 6,000 ischaemic heart disease deaths could be avoided, i.e. 5–10% of the total annual number of deaths in Denmark (Osler *et al.* 2000b).

Although inprovements in primary prevention are far from exhausted, especially among elderly people, we may also expect an increasing contribution of improvements in treatments

and secondary prevention, particularly among the oldest-old. The gradual shift from "autres moeurs, autres coeurs" to "same care, same share" of the oldest-old seems to be an important new trend.

References

Aase, A. (1989) "Regionalizing mortality data: Ischaemic heart disease in Norway", *Social Science and Medicine*, 29(8):907–911.

al Roomi, K. A., Dobson, A. J., Hall, E., Heller, R. F., and Magnus, P. (1989) "Declining mortality from ischemic heart disease and cerebrovascular disease in Australia", *American Journal of Epidemiology*, 129(3):503–510.

Andersen-Ranberg, K., Christensen, K., Jeune, B., Skytthe, A., Vasegaard, L., and Vaupel, J. W. (1999) "Declining physical abilities with age: A cross-sectional study of older twins and centenarians in Denmark", *Age and Ageing*, 28(4):373–377.

Andersen-Ranberg, K., Schroll, M., and Jeune, B. (2001) "Healthy centenarians do not exist—but autonomous centenarians do. A population-based study of morbidity among Danish centenarians", *JAGS*, 49(7):900–908.

Andreev, K. (1999) *Demographic Surfaces: Estimation, Assessment and Presentation with Application to Danish Mortality, 1835–1995*, Ph.D. thesis, University of Southern Denmark.

Artaud-Wild, S. M., Connor, S. L., Sexton, G., and Connor, W. E. (1993) "Differences in coronary mortality can be explained by differences in cholesterol and saturated fat intakes in 40 countries but not in France and Finland. A paradox", *Circulation*, 88(6):2771–2779.

Asplund, K., Bonita, R., Kuulasmaa, K., Rajakangas, A. M., Schaedlich, H., Suzuki, K., Thorvaldsen, P., and Tuomilehto, J. (1995) "Multinational comparisons of stroke epidemiology. Evaluation of case ascertainment in the WHO MONICA Stroke Study. World Health Organization monitoring trends and determinants in cardiovascular disease [published erratum appears in *Stroke* 1995 Aug;26(8):1504]", *Stroke*, 26(3):355–360.

Barker, D. J. (1998) *Mothers, Babies and Health in Later Life*. Edinburg: Churchill Livingstone.

Barnett, E., Armstrong, D. L., and Casper, M. L. (1999) "Evidence of increasing coronary heart disease mortality among black men of lower social class", *Annals of Epidemiology*, 9(8):464–471.

Bata, I. R., Eastwood, B. J., Gregor, R. D., Guernsey, J. R., Klassen, G. A., MacKenzie, B. R., and Wolf, H. K. (1997) "Decreasing mortality from acute myocardial infarctions: Effect of attack rates and case severity", *Journal of Clinical Epidemiology*, 50(7):787–791.

Bata, I. R., Gregor, R. D., Eastwood, B. J., and Wolf, H. K. (2000) "Trends in the incidence of acute myocardial infarction between 1984 and 1993—The Halifax County MONICA Project", *Canadian Journal of Cardiology*, 16(5):589–595.

Beaglehole, R. (1990) "International trends in coronary heart disease mortality, morbidity, and risk factors", *Epidemiologic Review*, 12:1–15.

Beaglehole, R., Stewart, A. W., Jackson, R., Dobson, A. J., McElduff, P., D'Este, K., Heller, R. F., Jamrozik, K. D., Hobbs, M. S., Parsons, R., and Broadhurst, R. (1997) "Declining rates of coronary heart disease in New Zealand and Australia, 1983–1993", *American Journal of Epidemiology*, 145(8):707–713.

Bladbjerg, E. M., Andersen, R. K., de Maat, M. P., Kristensen, S. R., Jeune, B., Gram, J., and Jespersen, J. (1999) "Longevity is independent of common variations in genes associated with cardiovascular risk", *Thrombosis and Haemostasis*, 82(3):1100–1105.

Bonita, R., Stewart, A., and Beaglehole, R. (1990) "International trends in stroke mortality: 1970–1985", *Stroke*, 21(7):989–992.

Bonita, R. (1993) “Stroke trends in Australia and New Zealand: Mortality, morbidity, and risk factors”, *Annals of Epidemiology*, 3(5):529–533.

Bonita, R., Broad, J. B., and Beaglehole, R. (1993) “Changes in stroke incidence and case-fatality in Auckland, New Zealand, 1981–91”, *Lancet*, 342(8885):1470–1473.

Bonneux, L., Looman, C. W., Barendregt, J. J., and van der Maas, P. J. (1997) “Regression analysis of recent changes in cardiovascular morbidity and mortality in the Netherlands”, *British Medical Journal*, 314(7083):789–792.

Borhani, N. O., and Hechter, H. H. (1964) “Recent changes in CVR disease mortality in California”, *Public Health Reports*, (79):146–160.

Bots, M. L., and Grobbee, D. E. (1996) “Decline of coronary heart disease mortality in the Netherlands from 1978 to 1985: Contribution of medical care and changes over time in presence of major cardiovascular risk factors”, *Journal of CardiovascularRisk*, 3(3):271–276.

Broderick, J. P. (1993) “Stroke trends in Rochester, Minnesota, during 1945 to 1984”, *Annals of Epidemiology*, 3(5):476–479.

Brophy, J. M. (1997) “The epidemiology of acute myocardial infarction and ischemic heart disease in Canada: Data from 1976 to 1991”, *Canadian Journal of Cardiology*, 13(5):474–478.

Brown, R. D., Whisnant, J. P., Sicks, J. D., O’Fallon, W. M., and Wiebers, D. O. (1996) “Stroke incidence, prevalence, and survival: Secular trends in Rochester, Minnesota, through 1989”, *Stroke*, 27(3):373–380.

Burke, G. L., Edlavitch, S. A., and Crow, R. S. (1989) “The effects of diagnostic criteria on trends in coronary heart disease morbidity: The Minnesota Heart Survey”, *Journal of Clinical Epidemiology*, 42(1):17–24.

Burnand, B., and Feinstein, A. R. (1992) “The role of diagnostic inconsistency in changing rates of occurrence for coronary heart disease”, *Journal of Clinical Epidemiology*, 45(9):929–940.

Casiglia, E., Spolaore, P., Ginocchio, G., Colangeli, G., Di Menza, G., Marchioro, M., Mazza, A., and Ambrosio, G. B. (1993) “Predictors of mortality in very old subjects aged 80 years or over”, *European Journal of Epidemiology*, 9(6):577–586.

Chambless, L., Keil, U., Dobson, A., Mahonen, M., Kuulasmaa, K., Rajakangas, A. M., Lowel, H., and Tunstall, P. H. (1997) “Population versus clinical view of case-fatality from acute coronary heart disease: Results from the WHO MONICA project 1985–1990. Multinational monitoring of trends and determinants in cardiovascular disease”, *Circulation*, 96(11):3849–3859.

Chandra, H., Yarzebski, J., Goldberg, R. J., Savageau, J., Singleton, C., Gurwitz, J. H., and Gore, J. M. (1997) “Age-related trends (1986–1993) in the use of thrombolytic agents in patients with acute myocardial infarction. The Worcester Heart Attack Study”, *Archives of Internal Medicine*, 157(7):741–746.

Christensen, K., Vaupel, J. W., Holm, N. V., and Yashin, A. I. (1995) “Mortality among twins after age 6: Fetal origins hypothesis versus twin method”, *British Medical Journal*, 310(6977):432–436.

Cooper, R., Stamler, J., Dyer, A., and Garside, D. (1978) “The decline in mortality from coronary heart disease, U.S.A., 1968–1975”, *Journal of Chronic Disorders*, 31(12):709–720.

Criqui, M. H., and Ringel, B. L. (1994) “Does diet or alcohol explain the French paradox?” *Lancet*, 344(8939–8940):1719–1723.

Curb, J. D., Masaki, K., Rodriguez, B. L., Abbott, R. D., Burchfiel, C. M., Chen, R., Petrovitch, H., Sharp, D., and Yano, K. (1996a) “Peripheral artery disease and cardiovascular risk factors in the elderly. The Honolulu Heart Program”, *Arteriosclerosis, Thrombosis, and Vascular Biology*, 16(12):1495–1500.

Curb, J. D., Abbott, R. D., MacLean, C. J., Rodriguez, B. L., Burchfiel, C. M., Sharp, D. S., Ross, G. W., and Yano, K. (1996b) "Age-related changes in stroke risk in men with hypertension and normal blood pressure", *Stroke*, 27(5):819–824.

Davis, W. B., Hayes, C. G., Knowles, M., Riggan, W. B., Van Bruggen, J., and Tyroler, H. A. (1985) "Geographic variation in declining ischemic heart disease mortality in the United States, 1968–1978. I. Rates and change, whites aged 35–74 years", *American Journal of Epidemiology*, 122(4):657–672.

De Benedictis, G., Carotenuto, L., Carrieri, G., De Luca, M., Falcone, E., Rose, G., Yashin, A. I., Bonafe, M., and Franceschi, C. (1998a) "Age-related changes of the 3'APOB-VNTR genotype pool in ageing cohorts", *Annals of Human Genetics*, 62(Pt 2):115–122.

De Benedictis, G., Carotenuto, L., Carrieri, G., De Luca, M., Falcone, E., Rose, G., Cavalcanti, S., Corsonello, F., Feraco, E., Baggio, G., Bertolini, S., Mari, D., Mattace, R., Yashin, A. I., Bonafe, M., and Franceschi, C. (1998b) "Gene/longevity association studies at four autosomal loci (REN, THO, PARP, SOD2)", *European Journal of Human Genetics*, 6(6):534–541.

De Benedictis, G., Rose, G., Carrieri, G., De Luca, M., Falcone, E., Passarino, G., Bonafe, M., Monti, D., Baggio, G., Bertolini, S., Mari, D., Mattace, R., and Franceschi, C. (1999) "Mitochondrial DNA inherited variants are associated with successful aging and longevity in humans", *The FASEB Journal*, 13(12):1532–1536.

De Henauw, S., de Smet, P., Aelvoet, W., Kornitzer, M., and De Backer, G. (1998) "Misclassification of coronary heart disease in mortality statistics. Evidence from the WHO-MONICA Ghent-Charleroi Study in Belgium", *Journal of Epidemiology and Community Health*, 52(8):513–519.

de Vreede, J. J., Gorgels, A. P., Verstraaten, G. M., Vermeer, F., Dassen, W. R., and Wellens, H. J. (1991) "Did prognosis after acute myocardial infarction change during the past 30 years? A meta-analysis", *Journal of the American College of Cardiology*, 18(3):698–706.

Desai, M. M., Zhang, P., and Hennessy, C. H. (1999) "Surveillance for morbidity and mortality among older adults–United States, 1995–1996", *Morbidity and Mortality Weekly Report CDC Surveillance Summaries*, 48(8):7–25.

Dobson, A. J., Alexander, H. M., Al Roomi, K., Gibberd, R. W., Heller, R. F., Leeder, S. R., Lloyd, D. M., Malcolm, J. A., and Steele, P. L. (1988) "Coronary events in the Hunter region of New South Wales, Australia: 1984–1986", *Acta Medica Scandinavica Supplement*, 728:84–89.

Dobson, A. J., Alexander, H. M., Al Roomi, K., Gibberd, R. W., Heller, R. F., Malcolm, J. A., and Steele, P. L. (1990) "Methodological issues in interpreting trends in MONICA event rates", *Revue d'epidemiologie et de sante publique*, 38(5–6):397–402.

Dobson, A. J., Evans, A., Ferrario, M., Kuulasmaa, K. A., Moltchanov, V. A., Sans, S., Tunstall, P. H., Tuomilehto, J. O., Wedel, H., and Yarnell, J. (1998) "Changes in estimated coronary risk in the 1980s: Data from 38 populations in the WHO MONICA Project. World Health Organization. Monitoring trends and determinants in cardiovascular diseases", *Annals of Medicine*, 30(2):199–205.

Douste, B. P., Ruidavets, J. B., Arveiler, D., Bingham, A., Camare, R., Schaffer, P., Aby, M. A., and Richard, J. L. (1988) "Comparison of cardiovascular risk factor levels in two French populations: Haute-Garonne (Toulouse) and Bas-Rhin (Strasbourg)", *Acta Medica Scandinavica Supplement*, 728:137–143.

Ducimetière, P., Richard, J. L., Cambien, F., Rakotovao, R., and Claude, J. R. (1980) "Coronary heart disease in middle-aged Frenchmen. Comparisons between Paris prospective study, seven countries study, and pooling project", *Lancet*, 1(8182):1346–1350.

Eagles, C. J., Gulati, R., and Martin, U. (1996) "Non-pharmacological modification of cardiac risk factors: Part 1", *Journal of Clinical Pharmacology and Therapeutics*, 21(5):289–296.

Epstein, F. H. (1989) "The relationship of lifestyle to international trends in CHD", *International Journal of Epidemiology*, 18(3) Suppl 1: S203–S209.

European Secondary Prevention Study Group. (1996) “Translation of clinical trials into practice: A European population-based study of the use of thrombolysis for acute myocardial infarction.”, *Lancet*, 347(9010):1203–1207.

Evans, A. E., Ruidavets, J. B., McCrum, E. E., Cambou, J. P., McClean, R., Douste, B. P., McMaster, D., Bingham, A., Patterson, C. C., Richard, J. L., *et al.* (1995) “Autres pays, autres coeurs? Dietary patterns, risk factors and ischaemic heart disease in Belfast and Toulouse”, *Quarterly Journal of Medicine*, 88(7):469-477.

Fagrell, B., De Faire, U., Bondy, S., Criqui, M., Gaziano, M., Gronbaek, M., Jackson, R., Klatsky, A., Salonen, J., and Shaper, A. G. (1999) “The effects of light to moderate drinking on cardiovascular diseases”, *Journal of Internal Medicine*, 246(4):331–340.

Feinleib, M., Havlik, R. J., and Thom, T. J. (1982) “The changing pattern of ischemic heart disease”, *Journal of Cardiovascular Medicine*, 7(2):139–146.

Feinleib, M., Ingster, L., Rosenberg, H., Maurer, J., Singh, G., and Kochanek, K. (1993) “Time trends, cohort effects, and geographic patterns in stroke mortality–United States”, *Annals of Epidemiology*, 3(5):458–465.

Feinleib, M. (1995) “Trends in heart disease in the United States”, *American Journal of Medical Science*, 310 (Suppl 1): S8–14.

Ferrieres, J., Cambou, J. P., Ruidavets, J. B., and Pous, J. (1995) “Trends in acute myocardial infarction prognosis and treatment in southwestern France between 1985 and 1990 (the MONICA Project-Toulouse)”, *American Journal Cardiology*, 75(17):1202–1205.

Fitzgerald, A. P., and Jarrett, R. J. (1992) “Body weight and coronary heart disease mortality: An analysis in relation to age and smoking habit. 15 years follow-up data from the Whitehall Study”, *International Journal of Obesity and Related Metabolic Disorders*, 16(2):119–123.

Forette, B., Tortrat, D., and Wolmark, Y. (1989) “Cholesterol as risk factor for mortality in elderly women”, *Lancet*, 1(8643):868–870.

Forette, B. (1999) “Hypertension in very old subjects”, *Clinical and Experimental Hypertension*, 21(5-6):917–925.

Frankel, E. N., Kanner, J., German, J. B., Parks, E., and Kinsella, J. E. (1993) “Inhibition of oxidation of human low-density lipoprotein by phenolic substances in red wine”, *Lancet*, 341(8843):454–457.

Frost, P. H., Davis, B. R., Burlando, A. J., Curb, J. D., Guthrie, G. P., Isaacsohn, J. L., Wassertheil, S. S., Wilson, A. C., and Stamler, J. (1996) “Coronary heart disease risk factors in men and women aged 60 years and older: Findings from the Systolic Hypertension in the Elderly Program”, *Circulation*, 94(1):26–34.

Gerdes, L. U., Jeune, B., Andersen-Ranberg, K., Nybo, H., and Vaupel, J. W. (2000) “Estimation of Apolipoprotein E genotype-specific relative mortality risks from the distribution of genotypes in centenarians and middle-aged men: Apolipoprotein E gene is a “frailty gene” not a “longevity gene””, *Genetic Epidemiology*, 19:202–210.

Goff, D. C. J., Howard, G., Wang, C. H., Folsom, A. R., Rosamond, W. D., Cooper, L. S., and Chambless, L. E. (2000) “Trends in severity of hospitalized myocardial infarction: The atherosclerosis risk in communities (ARIC) study, 1987–1994”, *American Heart Journal*, 139(5):874–880.

Goldberg, R. J., Gore, J. M., Alpert, J. S., and Dalen, J. E. (1988) “Incidence and case-fatality rates of acute myocardial infarction (1975–1984): The Worcester Heart Attack Study”, *American Heart Journal*, 115(4):761–767.

Goldman, L., Cook, F., Hashimotso, B., Stone, P., Muller, J., and Loscalzo, A. (1982) “Evidence that hospital care for acute myocardial infarction has not contributed to the decline in coronary mortality between 1973–1974 and 1978–1979”, *Circulation*, 65(5):936–942.

Goldman, L., and Cook, E. F. (1984) "The decline in ischemic heart disease mortality rates. An analysis of the comparative effects of medical interventions and changes in lifestyle", *Annals of Internal Medicine*, 101(6):825–836.

Gordon, T., and Thom, T. (1975) "The recent decrease in CHD mortality", *Preventive Medicine*, 4(2):115–125.

Gregor, R. D., Bata, I. R., Eastwood, B. J., and Wolf, H. K. (1998) "Ten-year trends of heart disease risk factors in the Halifax County MONICA population. MONItoring of trends and determinants in CArdiovascular disease", *Canadian Journal of Cardiology*, 14(8):1017–1024.

Gronbaek, M., Deis, A., Sorensen, T. I., Becker, U., Borch, J. K., Muller, C., Schnohr, P., and Jensen, G. (1994) "Influence of sex, age, body mass index, and smoking on alcohol intake and mortality", *British Medical Journal*, 308(6924):302–306.

Gronbaek, M., Deis, A., Sorensen, T. I., Becker, U., Schnohr, P., and Jensen, G. (1995) "Mortality associated with moderate intakes of wine, beer, or spirits", *British Medical Journal*, 310(6988):1165–1169.

Gronbaek, M. (1997) "Wine and mortality", *Biofactors*, 6(4):377–383.

Gronbaek, M., Deis, A., Becker, U., Hein, H. O., Schnohr, P., Jensen, G., Borch, J. K., and Sorensen, T. I. (1998) "Alcohol and mortality: Is there a U-shaped relation in elderly people?", *Age and Ageing*, 27(6):739–744.

Gronbaek, M., Mortensen, E. L., Mygind, K., Andersen, A. T., Becker, U., Gluud, C., and Sorensen, T. I. (1999) "Beer, wine, spirits and subjective health", *Journal of Epidemiology and Community Health*, 53(11):721–724.

Guidry, U. C., Evans, J. C., Larson, M. G., Wilson, P. W., Murabito, J. M., and Levy, D. (1999) "Temporal trends in event rates after Q-wave myocardial infarction: The Framingham Heart Study", *Circulation*, 100(20): 2054–2059.

Harmsen, P., Tsipogianni, A., and Wilhelmsen, L. (1992) "Stroke incidence rates were unchanged, while fatality rates declined, during 1971–1987 in Goteborg, Sweden", *Stroke*, 23(10):1410–1415.

Heller, R. F., Chinn, S., Pedoe, H. D., and Rose, G. (1984) "How well can we predict coronary heart disease? Findings in the United Kingdom heart disease prevention project", *British Medical Journal and Clinical Research Ed*, 288(6428):1409–1411.

Homer, D., Whisnant, J. P., and Schoenberg, B. S. (1987) "Trends in the incidence rates of stroke in Rochester, Minnesota, since 1935", *Annals of Neurology*, 22(2):245–251.

Hopper, J. L., Pathik, B., Hunt, D., and Chan, W. W. (1989) "Improved prognosis since 1969 of myocardial infarction treated in a coronary care unit: Lack of relation with changes in severity", *British Medical Journal*, 299(6704):892–896.

Hunink, M. G., Goldman, L., Tosteson, A. N., Mittleman, M. A., Goldman, P. A., Williams, L. W., Tsevat, J., and Weinstein, M. C. (1997) "The recent decline in mortality from coronary heart disease, 1980–1990. The effect of secular trends in risk factors and treatment", *The Journal of the American Medical Association*, 277(7): 535–542.

Jackson, R., Stewart, A., and Beaglehole, R. (1990) "Trends in coronary heart disease mortality and morbidity in Auckland, New Zealand, 1974–1986", *International Journal of Epidemiology*, 19(2):279–283.

Jeune, B. and Kannisto V. (1997) "Emergence of centenarians and supercentenarians". In: Robine, J-M., *et al*., (eds.), *Longevity: To the Limits and Beyond,* Springer -Verlag, Berlin, pp. 77–90.

Jeune, B. and Andersen-Ranberg, K. (2000) "What can we learn from centenarians?" In: Martin, P., *et al*. (eds.), *Centenarians. Autonomy versus Dependence in the Oldest Old*. New York: Serdi Edition and Springer Publishing, pp. 9–24.

Jones, D. W., Sempos, C. T., Thom, T. J., Harrington, A. M., Taylor-HA, J., Fletcher, B. W., Mehrotra, B. D., Wyatt, S. B., and Davis, C. E. (2000) "Rising levels of cardiovascular mortality in Mississippi, 1979–1995", *American Journal of Medical Science*, 319(3):131–137.

Jorgensen, H. S., Plesner, A. M., Hubbe, P., and Larsen, K. (1992) "Marked increase of stroke incidence in men between 1972 and 1990 in Frederiksberg, Denmark", *Stroke*, 23(12):1701–1704.

Jost, J. P., Simon, C., Nuttens, M. C., Bingham, A., Ruidavets, J. B., Cambou, J. P., Arveiler, D., Lecerf, J. M., Schlienger, J. L., and Douste, B. P. (1990) "Comparison of dietary patterns between population samples in the three French MONICA nutritional surveys", *Revue d'epidemiologie et de sante publique*, 38(5–6):517–523.

Juel, K., and Sjol, A. (1995) "Decline in mortality from heart disease in Denmark: Some methodological problems", *Journal of Clinical Epidemiology*, 48(4):467–472.

Kannisto, V. (1994) *Development of oldest-old mortality, 1950–1990: Evidence from 28 developed countries*. Odense: Odense University Press.

Kannisto, V. (1996) *The Advancing Frontier of Survival. Life Tables for Old Age*. Odense: Odense University Press.

Kannisto, V., Christensen, K., and Vaupel, J. W. (1997) "No increased mortality in later life for cohorts born during famine", *American Journal of Epidemiology*, 145(11):987–994.

Kaplan, G. A., Cohn, B.A., Cohen, R.D., and Guralnik, J. (1988) "The decline of ischemic heart disease mortality: Prospective evidence from the Alameda County Study", *American Journal of Epidemiology*, 127(6):1131–1142.

Katlic, M. R. (1985) "Surgery in centenarians", *The Journal of the American Medical Association*, 253(21):3139–3141.

Kato, H., Tillotson, J., Nichaman, M. Z., Rhoads, G. G., and Hamilton, H. B. (1973) "Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii, and California. Serum lipids and diet". *American Journal of Epidemiology*, 97:327–385.

Keys A, (ed), (1970) "Coronary heart disease in seven countries". *Circulation*, 41(Suppl. 1):1–211.

Kimm, S. Y., Ornstein, S. M., DeLong, E. R., and Grufferman, S. (1983) "Secular trends in ischemic heart disease mortality: Regional variation", *Circulation*, 68(1):3–8.

Kirchhoff, M., Davidsen, M., Bronnum, H. H., Hansen, B., Schnack, H., Eriksen, L. S., Madsen, M., and Schroll, M. (1999) "Incidence of myocardial infarction in the Danish MONICA population 1982–1991", *International Journal of Epidemiology*, 28(2):211–218.

Kodama, K. (1993) "Stroke trends in Japan", *Annals of Epidemiology*, 3(5):524–528.

Kuulasmaa, K., Tunstall, P. H., Dobson, A., Fortmann, S., Sans, S., Tolonen, H., Evans, A., Ferrario, M., and Tuomilehto, J. (2000) "Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations", *Lancet*, 355(9205):675–687.

Lackland, D. T., Egan, B. M., and Jones, P. J. (1999) "Impact of nativity and race on "Stroke Belt" mortality", *Hypertension*, 34(1):57–62.

Lang, T., Ducimetiere, P., Arveiler, D., Amouyel, P., Ferrieres, J., Ruidavets, J. B., Montaye, M., Haas, B., and Bingham, A. (1999) "Trends and geographical disparities in coronary heart disease in France: Are results concordant when different definitions of events are used?", *International Journal of Epidemiology*, 28(6):1050–1058.

Langer, R. D., Ganiats, T. G., and Barrett, C. E. (1991) "Factors associated with paradoxical survival at higher blood pressures in the very old [published erratum appears in Am J Epidemiol 1993 Nov 1;138(9):774]", *American Journal of Epidemiology*, 134(1):29–38.

Lanska, D. J. (1993) "Geographic distribution of stroke mortality in the United States: 1939–1941 to 1979–1981", *Neurology*, 43(9):1839–1851.

Lanska, D. J., and Peterson, P. M. (1995) "Effects of interstate migration on the geographic distribution of stroke mortality in the United States", *Stroke*, 26(4):554–561.

Larson, M. G. (1995) "Assessment of cardiovascular risk factors in the elderly: The Framingham Heart Study", *Statistics of MedIcine*, 14(16):1745–1756.

Levy, D., and Thom, T. J. (1998) "Death rates from coronary disease–progress and a puzzling paradox [editorial]", *New England Journal of Medicine*, 339(13):915–917.

Levy, R. I. (1981) "The decline in cardiovascular disease mortality", *Annual Review of Public Health*, 2: 49–70.

Lindenstrom, E., Boysen, G., Nyboe, J., and Appleyard, M. (1992) "Stroke incidence in Copenhagen, 1976–1988", *Stroke*, 23(1):28–32.

Mackenbach, J. P., Looman, C. W., Kunst, A. E., Habbema, J. D., and van der Maas, P. J. (1988) "Regional differences in decline of mortality from selected conditions: The Netherlands, 1969–1984", *International Journal of Epidemiology*, 17(4):821–829.

Madsen, J., and Serup-Hansen, N. (2000) Alder, død og sundhedsomkostninger. [Age, death, and health service costs]. Odense, Faculty of Social Sciences, University of Southern Denmark. Health Economics Papers 4.

Madsen, M., Balling, H., and Eriksen, L. S. (1990) "The validity of the diagnosis of acute myocardial infarction in 2 registries: The Heart Registry compared to the National Patient Registry", *Ugeskr.Laeger*, 152(5): 308–314.

Madsen, M., Rasmussen, S., and Juel, K. (2000) "Acute myocardial infarction in Denmark. The development in incidence and prognosis in 20 years", *Ugeskr.Laeger*, 162(44):5918–5923.

Mahonen, M., Salomaa, V., Torppa, J., Miettinen, H., Pyorala, K., Immonen, R. P., Niemela, M., Ketonen, M., Arstila, M., Kaarsalo, E., Lehto, S., Mustaniemi, H., Palomaki, P., Puska, P., Vuorenmaa, T., and Tuomilehto, J. (1999) "The validity of the routine mortality statistics on coronary heart disease in Finland: Comparison with the FINMONICA MI register data for the years 1983–1992. Finnish multinational MONItoring of trends and determinants in CArdiovascular disease", *Journal of Clinical Epidemiology*, 52(2):157–166.

Malmstrom, M., Sundquist, J., Bajekal, M., and Johansson, S. E. (1999) "Ten-year trends in all-cause mortality and coronary heart disease mortality in socio-economically diverse neighbourhoods", *Public Health*, 113(6):279–284.

Manton, K. G., and Vaupel, J. W. (1995) "Survival after the age of 80 in the United States, Sweden, France, England, and Japan", *New England Journal of Medicine*, 333(18):1232–1235.

Manton, K. G., and Yashin, A. I. (2000) *Mechanisms of Aging and Mortality: The Search for New Paradigms.* Odense: Odense University Press.

Marmot, M. G., Adelstein, A. M., Robinson, N., and Rose, G. A. (1978) "Changing social-class distribution of heart disease", *British Medical Journal*, 2(6145):1109–1112.

Marmot, M. G., and McDowall, M. E. (1986) "Mortality decline and widening social inequalities [published erratum appears in Lancet 1987 Feb 14;1(8529):394]", *Lancet*, 2(8501):274–276.

Marques-Vidal P., Ferrieres, J., Metzger, M. H., Cambou, J. P., Filipiak, B., Lowel, H., and Keil, U. (1997) "Trends in coronary heart disease morbidity and mortality and acute coronary care and case-fatality from 1985–1989 in southern Germany and south-western France", *European Heart Journal*, 18(5):816–821.

McCann, W. J., and Smith, J. W. (1990) "The surgical care of centenarians", *Current Surgery*, 47(1):2–3.

McGovern, P. G., Burke, G. L., Sprafka, J. M., Xue, S., Folsom, A. R., and Blackburn, H. (1992) "Trends in mortality, morbidity, and risk factor levels for stroke from 1960 through 1990. The Minnesota Heart Survey", *The Journal of the American Medical Association*, 268(6):753–759.

McGovern, P. G., Shahar, E., Sprafka, J. M., and Pankow, J. S. (1993) "The role of stroke attack rate and case-fatality in the decline of stroke mortality. The Minnesota Heart Survey", *Annals of Epidemiology*, 3(5):483–487.

McGovern, P. G., Pankow, J. S., Shahar, E., Doliszny, K. M., Folsom, A. R., Blackburn, H., and Luepker, R. V. (1996) "Recent trends in acute coronary heart disease–mortality, morbidity, medical care, and risk factors. The Minnesota Heart Survey Investigators", *New England Journal of Medicine*, 334(14):884–890.

McKeown, T. (1965) *Medicine in Modern Society. Medical planning based on evaluation of medical achievement* New York: Hafner Publishing Company.

Milliken, R. A., and Milliken, G. M. (1971) "Centenarian surgery", *The Journal of the American Medical Association*, 218(9):1435–1436.

MMWR (1999a) "Decline in deaths from heart disease and stroke–United States, 1900–1999", *Morbidity and Mortality Weekly Report*, 48(30):649–656.

MMRW (1999b) "Tobacco use–United States, 1900–1999", *Morbidity, Mortality Weekly Report*, 48(43):986–993.

Nohria, A., Vaccarino, V., and Krumholz, H. M. (1998) "Gender differences in mortality after myocardial infarction. Why women fare worse than men", *Cardiology Clinics*, 16(1):45–57.

Numminen, H., Kotila, M., Waltimo, O., Aho, K., and Kaste, M. (1996) "Declining incidence and mortality rates of stroke in Finland from 1972 to 1991. Results of three population-based stroke registers", *Stroke*, 27(9):1487–1491.

Nyboe, J., Jensen, G., Appleyard, M., and Schnohr, P. (1989) "Risk factors for acute myocardial infarction in Copenhagen. I: Hereditary, educational and socioeconomic factors. Copenhagen City Heart Study", *European Heart Journal*, 10(10):910–916.

Oliver, M. F. (1999) "Lowering cholesterol in old age", *J.R.College Physicians London* 33(3):252–253.

Osler, M., Sorensen, T. I., Sorensen, S., Rostgaard, K., Jensen, G., Iversen, L., Kristensen, T. S., and Madsen, M. (1996) "Trends in mortality, incidence and case-fatality of ischaemic heart disease in Denmark, 1982–1992", *International Journal Epidemiology*, 25(6):1154–1161.

Osler, M., Prescott, E., Gottschau, A., Bjerg, A., Hein, H. O., Sjol, A., and Schnohr, P. (1998) "Trends in smoking prevalence in Danish adults, 1964–1994. The influence of gender, age, and education", *Scandinavian Journal of Social Medicine*, 26(4):293–298.

Osler, M., Rostgaard, K., Sorensen, T. I., and Madsen, M. (1999) "The effect of recurrent events on register-based estimates of level and trends in incidence of acute myocardial infarction", *Journal of Clinical Epidemiology*, 52(7):595–600.

Osler, M., Gerdes, L. U., Davidsen, M., Bronnum, H. H., Madsen, M., Jorgensen, T., and Schroll, M. (2000a) "Socioeconomic status and trends in risk factors for cardiovascular diseases in the Danish MONICA population, 1982–1992", *Journal of Epidemiology and Community Health*, 54(2):108–113.

Osler, M., Godtfredsen, J., Gronbaek, M., Marckmann, P., and Overvad, O. K. (2000b) "En kvantitativ vurdering af kostens betydning for dødeligheden af hjertesygdomme i Danmark. Beregning af ætiologisk fraktion. [A quantitative assessment of the impact of diet on the mortality of heart disease in Denmark. Estimation of etiologic fraction]", *Ugeskr.Laeger*, 162(37):4921–4925.

Pashos, C. L., Newhouse, J. P., and McNeil, B. J. (1993) "Temporal changes in the care and outcomes of elderly patients with acute myocardial infarction, 1987 through 1990", *The Journal of the American Medical Association*, 270(15):1832–1836.

Pell, S. and Fayerweather, W. E. (1985) "Trends in the incidence of myocardial infarction and in associated mortality and morbidity in a large employed population, 1957–1983", *New England Journal of Medicine*, 312(16):1005–1011.

Peltonen, M., Rosen, M., Lundberg, V., and Asplund, K. (2000) "Social patterning of myocardial infarction and stroke in Sweden: Incidence and survival", *American Journal of Epidemiology*, 151(3):283–292.

Perry, H. M., and Roccella, E. J. (1998) "Conference report on stroke mortality in the southeastern United States", *Hypertension* , 31(6):1206–1215.

Poikolainen, K. and Eskola, J. (1986) "The effect of health services on mortality: Decline in death rates from amenable and non-amenable causes in Finland, 1969–1981", *Lancet*, 1(8474):199–202.

Puska, P., Tuomilehto, J., Nissinen, A., and Salonen, J. (1985) "Ten years of the North Karelia project", *Acta Medica Scandinavica Supplement*, 701:66–71.

Ragland, K. E., Selvin, S., and Merrill, D. W. (1988) "The onset of decline in ischemic heart disease mortality in the United States", *American Journal of Epidemiology*, 127(3):516–531.

Rapola, J. M., Virtamo, J., Korhonen, P., Haapakoski, J., Hartman, A. M., Edwards, B. K., and Heinonen, O. P. (1997) "Validity of diagnoses of major coronary events in national registers of hospital diagnoses and deaths in Finland", *European Journal of Epidemiology*, 13(2):133–138.

Reitsma, J. B., Limburg, M., Kleijnen, J., Bonsel, G. J., and Tijssen, J. G. (1998) "Epidemiology of stroke in The Netherlands from 1972 to 1994: The end of the decline in stroke mortality", *Neuroepidemiology*, 17(3):121–131.

Reitsma, J. B., Dalstra, J. A., Bonsel, G. J., van der Meulen, J. H., Koster, R. W., Gunning-Schepers, L. J., and Tijssen, J. G. (1999) "Cardiovascular disease in the Netherlands, 1975 to 1995: Decline in mortality, but increasing numbers of patients with chronic conditions", *Heart*, 82(1):52–56.

Renaud, S., and de Lorgeril, M. (1989) "Dietary lipids and their relation to ischaemic heart disease: From epidemiology to prevention", *Journal of Internal Medicine Supplement*, 225(731):39–46.

Renaud, S., and de Lorgeril, M. (1992) "Wine, alcohol, platelets, and the French paradox for coronary heart disease", *Lancet*, 339(8808):1523–1526.

Renaud, S., and de Lorgeril, M. (1993) "The French paradox: Dietary factors and cigarette smoking-related health risks", *Annals of New York Academy of Sciences*, 686:299–309.

Richard, J. L., Cambien, F., and Ducimetiere, P. (1981) "Particuliarités épidémiologiques de la maladie coronarienne en France. [Epidemiologic characteristics of coronary disease in France]", *Nouvelle Presse Medicale*, 10(14):1111–1114.

Robine, J.-M., Forette, B., Franceschi, C., and Allard, M. e. (1999) *The Paradoxes of Longevity*. Berlin, Springer.

Roger, V. L., Jacobsen, S. J., Weston, S. A., Bailey, K. R., Kottke, T. E., and Frye, R. L. (1999) "Trends in heart disease deaths in Olmsted County, Minnesota, 1979–1994", *Mayo Clinic Proceedings*, 74(7): 651–657.

Rogers, W. J., Bowlby, L. J., Chandra, N. C., French, W. J., Gore, J. M., Lambrew, C. T., Rubison, R. M., Tiefenbrunn, A. J., and Weaver, W. D. (1994) "Treatment of myocardial infarction in the United States (1990 to 1993). Observations from the National Registry of Myocardial Infarction", *Circulation*, 90(4):2103–2114.

Rosamond, W. D., Shahar, E., and Luepker, R. V. (1996) "Assessing medical history in coronary heart disease surveillance: Agreement between contemporaneous and retrospective methods", *Epidemiology*, 7(4):447–449.

Rosamond, W. D., Chambless, L. E., Folsom, A. R., Cooper, L. S., Conwill, D. E., Clegg, L., Wang, C. H., and Heiss, G. (1998) "Trends in the incidence of myocardial infarction and in mortality due to coronary heart disease, 1987 to 1994", *New England Journal of Medicine*, 339:13:861–867.

Rose, G. and Marmot, M. G. (1981) "Social class and coronary heart disease", *British Heart Journal*, 45(1):13–19.

Rouleau, J. L., Moye, L. A., Pfeffer, M. A., Arnold, J. M., Bernstein, V., Cuddy, T. E., Dagenais, G. R., Geltman, E. M., Goldman, S., Gordon, D., *et al*. (1993) "A comparison of management patterns after acute myocardial infarction in Canada and the United States. The SAVE investigators", *New England Journal of Medicine*, 328(11):779–784.

Ryglewicz, D., Polakowska, M., Lechowicz, W., Broda, G., Roszkiewicz, M., Jasinski, B., and Hier, D. B. (1997) "Stroke mortality rates in Poland did not decline between 1984 and 1992", *Stroke*, 28(4):752–757.

Sakata, K., and Labarthe, D. R. (1996) "Changes in cardiovascular disease risk factors in three Japanese national surveys 1971–1990", *Journal of Epidemiology*, 6(2):93–107.

Salomaa, V., Arstila, M., Kaarsalo, E., Ketonen, M., Kuulasmaa, K., Lehto, S., Miettinen, H., Mustaniemi, H., Niemela, M., Palomaki, P., *et al*. (1992) "Trends in the incidence of and mortality from coronary heart disease in Finland, 1983–1988", *American Journal of Epidemiology*, 136(11):1303–1315.

Salomaa, V., Miettinen, H., Palomaki, P., Arstila, M., Mustaniemi, H., Kuulasmaa, K., and Tuomilehto, J. (1995) "Diagnostic features of acute myocardial infarction–changes over time from 1983 to 1990: Results from the FINMONICA AMI Register Study", *Journal of Internal Medicine*, 237(2):151–159.

Salomaa, V., Miettinen, H., Kuulasmaa, K., Niemela, M., Ketonen, M., Vuorenmaa, T., Lehto, S., Palomaki, P., Mahonen, M., Immonen, R. P., Arstila, M., Kaarsalo, E., Mustaniemi, H., Torppa, J., Tuomilehto, J., Puska, P., and Pyorala, K. (1996) "Decline of coronary heart disease mortality in Finland during 1983 to 1992: Roles of incidence, recurrence, and case-fatality. The FINMONICA MI Register Study", *Circulation*, 94(12):3130–3137.

Salomaa, V., Dobson, A., Miettinen, H., Rajakangas, A. M., and Kuulasmaa, K. (1997) "Mild myocardial infarction–a classification problem in epidemiologic studies. WHO MONICA Project", *Journal of Clinical Epidemiology*, 50(1):3–13.

Salomaa, V., Rosamond, W., and Mahonen, M. (1999) "Decreasing mortality from acute myocardial infarction: Effect of incidence and prognosis", *Journal of Cardiovascular Risk*, 6(2):69–75.

Salonen, J. T., Puska, P., Kottke, T. E., Tuomilehto, J., and Nissinen, A. (1983) "Decline in mortality from coronary heart disease in Finland from 1969 to 1979", *British Medical Journal and Clinical Research Ed*, 286(6381):1857–1860.

Sans, S., Kesteloot, H., and Kromhout, D. (1997) "The burden of cardiovascular diseases mortality in Europe. Task force of the European society of cardiology on cardiovascular mortality and morbidity statistics in Europe [corrected and republished in Eur Heart J 1997 Dec;18(12):1231–48]", *European Heart Journal*, 18(8):1231–1248.

Sarti, C., Tuomilehto, J., Sivenius, J., Kaarsalo, E., Narva, E. V., Salmi, K., Torppa, J., and Salomaa, V. (1994) "Declining trends in incidence, case-fatality and mortality of stroke in three geographic areas of Finland during 1983–1989. Results from the FINMONICA stroke register", *Journal of Clinical Epidemiology*, 47(11):1259–1269.

Schneider, J. (1984) "Lipid- and lipoprotein values in octo- and nonagenarians free from overt degenerative arterial disease", *Clinica Chimica Acta*, 143(1):1–5.

Shahar, E., McGovern, P. G., Pankow, J. S., Doliszny, K. M., Smith, M. A., Blackburn, H., and Luepker, R. V. (1997) "Stroke rates during the 1980s. The Minnesota Stroke Survey", *Stroke*, 28(2):275–279.

Shimamoto, T., Komachi, Y., Inada, H., Doi, M., Iso, H., Sato, S., Kitamura, A., Iida, M., Konishi, M., Nakanishi, N., *et al*. (1989) "Trends for coronary heart disease and stroke and their risk factors in Japan", *Circulation*, 79(3):503–515.

Shinton, R. and Beevers, G. (1989) "Meta-analysis of relation between cigarette smoking and stroke", *British Medical Journal*, 298(6676):789–794.

Sigfusson, N., Sigvaldason, H., Steingrimsdottir, L., Gudmundsdottir, I. I., Stefansdottir, I., Thorsteinsson, T., and Sigurdsson, G. (1991) "Decline in ischaemic heart disease in Iceland and change in risk factor levels", *British Medical Journal*, 302(6789):1371–1375.

Simini, B. (2000) "Serge Renaud: From French paradox to Cretan miracle [news]", *Lancet*, 355(9197):48–1957.

Sjol, A., Grunnet, K., and Schroll, M. (1991) "Secular trends in serum cholesterol, high density lipoproteins and triglycerides 1964–1987", *International Journal of Epidemiology*, 20(1):105–113.

Sjol, A., Thomsen, K. K., and Schroll, M. (1998) "Secular trends in blood pressure levels in Denmark 1964–1991", *International Journal of Epidemiology*, 27(4):614–622.

St.Leger, A. S., Cochrane, A. L., and Moore, F. (1979) "Factors associated with cardiac mortality in developed countries with particular reference to the consumption of wine", *Lancet*, 1(8124):1017–1020.

Stallones, R. A. (1980) "The rise and fall of ischemic heart disease", *Scientific American*, 243(5):53–59.

Stamler, J. (1989) "Opportunities and pitfalls in international comparisons related to patterns, trends and determinants of CHD mortality", *Internatioanl Journal of Epidemiology*, 18(3 Suppl 1):S3–18.

Stanner, S. A., Bulmer, K., Andres, C., Lantseva, O. E., Borodina, V., Poteen, V. V., and Yudkin, J. S. (1997) "Does malnutrition in utero determine diabetes and coronary heart disease in adulthood? Results from the Leningrad siege study, a cross sectional study", *British Medical Journal*, 315(7119):1342–1348.

Stegmayr, B., Asplund, K., and Wester, P. O. (1994) "Trends in incidence, case-fatality rate, and severity of stroke in northern Sweden, 1985–1991", *Stroke*, 25(9):1738–1745.

Stegmayr, B., Asplund, K., Kuulasmaa, K., Rajakangas, A. M., Thorvaldsen, P., and Tuomilehto, J. (1997) "Stroke incidence and mortality correlated to stroke risk factors in the WHO MONICA Project. An ecological study of 18 populations", *Stroke*, 28(7):1367–1374.

Stehbens, W. E. (1987) "An appraisal of the epidemic rise of coronary heart disease and its decline", *Lancet*, 1(8533):606–611.

Stehbens, W. E. (1991) "Imprecision of the clinical diagnosis of coronary heart disease in epidemiological studies and atherogenesis", *Journal of Clinical Epidemiology*, 44(10):999–1006.

Stern, M. P. (1979) "The recent decline in ischemic heart disease mortality", *Annals of Internal Medicine*, 91(4):630–640.

Stevenson, R., Ranjadayalan, K., Wilkinson, P., Roberts, R., and Timmis, A. D. (1993) "Short and long term prognosis of acute myocardial infarction since introduction of thrombolysis [published erratum appears in BMJ 1993 Oct 9;307(6909):909]", *British Medical Journal*, 307(6900):349–353.

Sytkowski, P. A., Kannel, W. B., and D'Agostino, R. B. (1990) "Changes in risk factors and the decline in mortality from cardiovascular disease. The Framingham Heart Study", *New England Journal of Medicine*, 322(23):1635–1641.

Terent, A. (1988) "Increasing incidence of stroke among Swedish women", *Stroke*, 19(5):598–603.

Tervahauta, M., Pekkanen, J., and Nissinen, A. (1995) "Risk factors of coronary heart disease and total mortality among elderly men with and without preexisting coronary heart disease. Finnish cohorts of the Seven Countries Study", *Journal of American College of Cardiology*, 26(7):1623–1629.

The Centers for Disease Control and Prevention (1999) "Decline in deaths from heart disease and stroke–United States, 1900–1999", *The Journal of the American Medical Association*, 282(8):724–726.

The Nova Scotia-Saskatchewan Cardiovascular Disease Epidemiology Group (1992) "Trends in incidence and mortality from acute myocardial infarction in Nova Scotia and Saskatchewan 1974 to 1985.", *Canadian Journal of Cardiology*, 8(3):253–258.

Thom, T. J., Epstein, F. H., Feldman, J. J., and Leaverton, P. E. (1985) "Trends in total mortality and mortality from heart disease in 26 countries from 1950 to 1978", *International Journal of Epidemiology*, 14(4):510–520.

Thom, T. J. (1989) "International mortality from heart disease: Rates and trends", *International Journal of Epidemiology*, 18(3 Suppl 1):S20–S28.

Thom, T. J. (1993) "Stroke mortality trends. An international perspective", *Annals of Epidemiology*, 3(5):509–518.

Thom, T. J., and Epstein, F. H. (1994) "Heart disease, cancer, and stroke mortality trends and their interrelations. An international perspective", *Circulation*, 90(1):574–582.

Thomsen, K. K. (1999) *The Influence of Age, Period and Cohort Effects on Prevalence and Prognostic Implications of Coronary Risk Factors in Elderly Men and Women*. Ph.D. Thesis, Centre of Preventive Medicine, University Hospital of Copenhagen, Glostrup, and Cardiovascular Research Unit, Faculty of Health Sciences, University of Southern Denmark.

Thorvaldsen, P., Asplund, K., Kuulasmaa, K., Rajakangas, A. M., and Schroll, M. (1995) "Stroke incidence, case-fatality, and mortality in the WHO MONICA project. World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease [published errata appear in Stroke 1995 Aug;26(8):1504 and 1995 Dec;26(12):2376]", *Stroke*, 26(3):361–367.

Thorvaldsen, P., Kuulasmaa, K., Rajakangas, A. M., Rastenyte, D., Sarti, C., and Wilhelmsen, L. (1997) "Stroke trends in the WHO MONICA project", *Stroke*, 28(3):500–506.

Thorvaldsen, P., Davidsen, M., Bronnum, H. H., and Schroll, M. (1999) "Stable stroke occurrence despite incidence reduction in an aging population: Stroke trends in the danish monitoring trends and determinants in cardiovascular disease (MONICA) population", *Stroke*, 30(12):2529–2534.

Tjonneland, A., Gronbaek, M., Stripp, C., and Overvad, K. (1999) "Wine intake and diet in a random sample of 48763 Danish men and women", *American Journal of Clinical Nutrition*, 69(1):49–54.

Truelsen, T., Prescott, E., Gronbaek, M., Schnohr, P., and Boysen, G. (1997) "Trends in stroke incidence. The Copenhagen city heart study", *Stroke*, 28(10):1903–1907.

Truelsen, T., Gronbaek, M., Schnohr, P., and Boysen, G. (1998) "Intake of beer, wine, and spirits and risk of stroke : The copenhagen city heart study", *Stroke*, 29(12):2467–2472.

Tu, J. V., Pashos, C. L., Naylor, C. D., Chen, E., Normand, S. L., Newhouse, J. P., and McNeil, B. J. (1997) "Use of cardiac procedures and outcomes in elderly patients with myocardial infarction in the United States and Canada [published erratum appears in N Engl J Med 1997 Jul 10;337(2):139]", *New England Journal of Medicine*, 336(21):1500–1505.

Tu, J. V., Naylor, C. D., and Austin, P. (1999) "Temporal changes in the outcomes of acute myocardial infarction in Ontario, 1992–1996", *Canadian Medical Association Journal*, 161(10):1257–1261.

Tunstall-Pedoe H. (1988) "Autres pays, autres moeurs [editorial]", *British Medical Journal*, 297(6663):1559–1560.

Tunstall-Pedoe H. (1989) "Diagnosis, measurement and surveillance of coronary events", *International Journal of Epidemiology*, 18(3 Suppl 1):S169–S173.

Tunstall-Pedoe H., Kuulasmaa, K., Amouyel, P., Arveiler, D., Rajakangas, A. M., and Pajak, A. (1994) "Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents", *Circulation*, 90(1):583–612.

Tunstall-Pedoe H., Woodward, M., Tavendale, R., A'Brook, R., and McCluskey, M. K. (1997) "Comparison of the prediction by 27 different factors of coronary heart disease and death in men and women of the Scottish Heart Health Study: Cohort study [published erratum appears in BMJ 1998 Jun 20;316(7148):1881]", *British Medical Journal*, 315(7110):722–729.

Tunstall-Pedoe H. (1998) "Perspectives on trends in mortality and case-fatality from coronary heart attacks: The need for a better definition of acute myocardial infarction [editorial]", *Heart*, 80(2):112–113.

Tunstall-Pedoe H., Kuulasmaa, K., Mahonen, M., Tolonen, H., Ruokokoski, E., and Amouyel, P. (1999) "Contribution of trends in survival and coronary-event rates to changes in coronary heart disease mortality: 10-year results from 37 WHO MONICA project populations. Monitoring trends and determinants in cardiovascular disease", *Lancet*, 353(9164):1547–1557.

Tunstall-Pedoe H., Vanuzzo, D., Hobbs, M., Mahonen, M., Cepaitis, Z., Kuulasmaa, K., and Keil, U. (2000) "Estimation of contribution of changes in coronary care to improving survival, event rates, and coronary heart disease mortality across the WHO MONICA Project populations", *Lancet*, 355(9205):688–700.

Tuomilehto, J., Rastenyte, D., Sivenius, J., Sarti, C., Immonen, R. P., Kaarsalo, E., Kuulasmaa, K., Narva, E. V., Salomaa, V., Salmi, K., and Torppa, J. (1996) "Ten-year trends in stroke incidence and mortality in the FINMONICA Stroke Study", *Stroke*, 27(5):825–832.

Ueda, K., Omae, T., Hirota, Y., Takeshita, M., Katsuki, S., Tanaka, K., and Enjoji, M. (1981) "Decreasing trend in incidence and mortality from stroke in Hisayama residents, Japan", *Stroke*, 12(2):154–160.

Uemura, K. and Pisa, Z. (1988) "Trends in cardiovascular disease mortality in industrialized countries since 1950", *World Health Statistics Quarterly*, 41(3–4):155–178.

Vartiainen, E., Puska, P., Pekkanen, J., Tuomilehto, J., and Jousilahti, P. (1994) "Changes in risk factors explain changes in mortality from ischaemic heart disease in Finland", *British Medical Journal*, 309(6946):23–27.

Vaupel, J. W. and Jeune, B. (1995) "The emergence and proliferation of centenarians". In: Jeune, B., Vaupel, J. W., (eds.), *Exceptional Longevity: From Prehistory to the Present*. Odense: Odense University Press, pp. 109–115.

Vaupel, J. W., Carey, J. R., Christensen, K., Johnson, T. E., Yashin, A. I., Holm, N. V., Iachine, I. A., Kannisto, V., Khazaeli, A. A., Liedo, P., Longo, V. D., Zeng, Y., Manton, K. G., and Curtsinger, J. W. (1998)"Biodemographic trajectories of longevity", *Science*, 280(5365):855–860.

Videbæk, J., and Madsen M. (1999) "HjerteStatistik [Heart Statistics]", Hjerteforeningen, Copenhagen.

Walker, W. J. (1974) "Coronary mortality: what is going on?", *The Journal of the American Medical Association*, 227(9):1045–1046.

Warner, M. A., Hosking, M. P., Lobdell, C. M., Offord, K. P., and Melton, L. J. (1988) "Surgical procedures among those greater than or equal to 90 years of age. A population-based study in Olmsted County, Minnesota, 1975–1985", *Ann.Surg.*, 207(4):380–386.

Weitzman, S., Cooper, L., Chambless, L., Rosamond, W., Clegg, L., Marcucci, G., Romm, F., and White, A. (1997) "Gender, racial, and geographic differences in the performance of cardiac diagnostic and therapeutic procedures for hospitalized acute myocardial infarction in four states", *American Journal of Cardiology*, 79(6):722–726.

Weverling-Rijnsburger, A. W., Blauw, G. J., Lagaay, A. M., Knook, D. L., Meinders, A. E., and Westendorp, R. G. (1997) "Total cholesterol and risk of mortality in the oldest old [published erratum appears in Lancet 1998 Jan 3;351(9095):70]", *Lancet*, 350(9085):1119–1123.

Whisnant, J. P. (1984) "The decline of stroke", *Stroke*, 15(1):160–168.

Whitney, E. J., Shear, C. L., Mantell, G., Lydick, E., and Wolf, R. (1992) "The case for unstable angina pectoris as a primary end point in primary prevention studies", *American Journal of Cardiology*, 70(7):738–743.

WHO MONICA Project Principal Investigators (1988) "The World Health Organization MONICA Project (monitoring trends and determinants in cardiovascular disease): A major international collaboration.", *Journal of Clinical Epidemiology*, 41(2):105–114.

Wilhelmsen, L., Johansson, S., Ulvenstam, G., Welin, L., Rosengren, A., Eriksson, H., Larsson, B., Tsipogianni, A., and Wedel, H. (1989) "CHD in Sweden: Mortality, incidence and risk factors over 20 years in Gothenburg", *International Journal of Epidemiology*, 18(3 Suppl 1): S101–S108.

Wilhelmsen, L. (1997) "ESC Population Studies Lecture (1996) Cardiovascular monitoring of a city over 30 years", *European Heart Journal*, 18(8):1220–1230.

Wilhelmsen, L., Rosengren, A., Johansson, S., and Lappas, G. (1997) "Coronary heart disease attack rate, incidence and mortality 1975–1994 in Goteborg, Sweden", *European Heart Journal*, 18(4):572–581.

Wilmoth, J. R., Deegan, L. J., Lundstrom, H., and Horiuchi, S. (2000) "Increase of maximum life-span in Sweden, 1861–1999", *Science*, 289:2366–2368.

Wing, S., Hayes, C., Heiss, G., John, E., Knowles, M., Riggan, W., and Tyroler, H. A. (1986) "Geographic variation in the onset of decline of ischemic heart disease mortality in the United States", *American Journal of Public Health*, 76(12):1404–1408.

Wing, S. (1988) "Social inequalities in the decline of coronary mortality [editorial]", *American Journal of Public Health*, 78(11):1415–1416.

Wing, S., Casper, M., Riggan, W., Hayes, C., and Tyroler, H. A. (1988) "Socioenvironmental characteristics associated with the onset of decline of ischemic heart disease mortality in the United States", *American Journal of Public Health*, 78(8):923–926.

Wing, S., Barnett, E., Casper, M., and Tyroler, H. A. (1992) "Geographic and socioeconomic variation in the onset of decline of coronary heart disease mortality in white women", *American Journal of Public Health*, 82(2):204–209.

Wolf, P. A., D'Agostino, R. B., O'Neal, M. A., Sytkowski, P., Kase, C. S., Belanger, A. J., and Kannel, W. B. (1992) "Secular trends in stroke incidence and mortality. The Framingham Study", *Stroke*, 23(11):1551–1555.

Yashin, A. I., Vaupel, J. W., Andreev, K. F., Tan, Q., Iachine, I. A., Carotenuto, L., De Benedictis, G., Bonafe, M., Valensin, S., and Franceschi, C. (1998) "Combining genetic and demographic information in population studies of aging and longevity", *Journal of Epidemiology Biostatistics*, 3(3):289–294.

Yashin, A. I., De Benedictis, G., Vaupel, J. W., Tan, Q., Andreev, K. F., Iachine, I. A., Bonafe, M., De Luca, M., Valensin, S., Carotenuto, L., and Franceschi, C. (1999) "Genes, demography, and life span: The contribution of demographic data in genetic studies on aging and longevity", *American Journal of Human Genetics*, 65(4):1178–1193.

Yashin, A. I., De Benedictis, G., Vaupel, J. W., Tan, Q., Andreev, K. F., Iachine, I. A., Bonafe, M., Valensin, S., De Luca, M., Carotenuto, L., and Franceschi, C. (2000) "Genes and longevity: Lessons from studies of centenarians", *The Journals of Gerontology: Series A Biological Science and Medical Science*, 55(7): B319–B328.

CHAPTER 17. EXPLANATION OF THE DECLINE IN MORTALITY AMONG THE OLDEST-OLD: A DEMOGRAPHIC POINT OF VIEW[1]

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Introduction

In many highly developed countries, remarkable progress has been made in recent decades in reducing death rates, especially at older ages. New statistical data on mortality over time and up to the highest ages have revealed the time and age pattern of these improvements. These data have permitted reliable estimation of the age-trajectory of mortality, which turns out to follow a logistic pattern with deceleration at advanced ages. Individuals are heterogeneous with regard to their chances of death, and the frail tend to die first. Deeper understanding of the age-trajectory of mortality and the pattern of mortality improvements hinges on the development of statistical models that incorporate such mortality selection. This paper surveys the dynamics of mortality over age and time, reviews some "frailty model" approaches to analysing these dynamics, and presents some illustrative findings from studies of Danish twins and of the surface of Italian mortality over age and since 1895. Our goal is to participate in the debate on longevity from a demographic point of view and disclose the underlying features of accelerating human longevity. We are of the opinion that an analysis of this nature could help reveal the triggering factors. The study is a first step towards achieving this goal.

1. The New Frontier of Survival

During the second half of the twentieth century, and particularly after 1970, progress in the socioeconomic and medical-health spheres, together with changes in individual and group lifestyles, all ensured major gains in terms of life expectancy. A child born today in Italy may expect to live until aged 82 if a girl and almost 76 if a boy. Thirty years ago this was respectively 75 and 69 years, thus an average gain of 7 years for women and 6

[1] Part of this paper is an update of the one published four years ago (Caselli, G., Vaupel, J., and Yashin, A. 2000, "Longevity, heterogeneity and selection", in *Atti della XL Riunione Scientifica della Società Italiana di Statistica,* pp. 49–72, SIS 2000: Florence.

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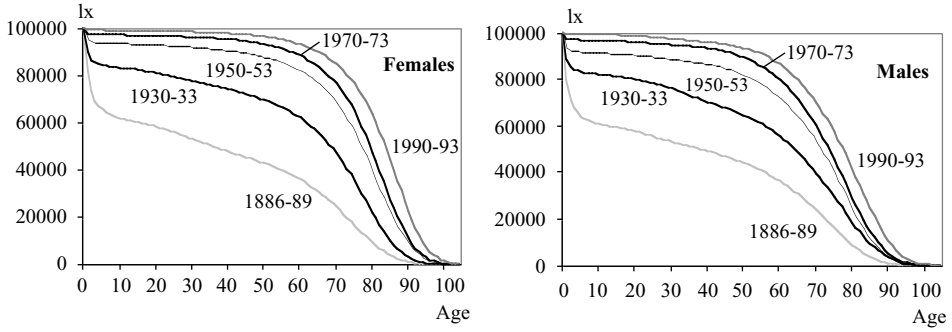

Figure 1. Trends among survivors from mortality tables for selected years, 1886–1993, females and males, Italy.

for men. What we are witnessing is a real revolution, made possible by major gains in life expectancy among the elderly. In less than thirty years over-sixty-year-old women have added 4 years to their average life span (from 20 to 24 years) and men 2 years (from 18 to 20 years). Over-eighty-year-olds gained 2 (from 6.9 to 8.9 years) and 1 year (from 6.1 to 7.1 years), respectively. However, since the '80s the developed world has experienced a renewed increase in survival for men and women of the fourth age.

According to the most recently available Italian life tables (ISTAT, 2004), 65% of women and 48% of men are expected to be alive at 80 years of age. What this implies is that more than half the population dies after their 80th birthday. For women, it should be noted, 29% of these deaths take place after they have reached 90 years of age (only 13% for men). Figure 1 shows how the number of people still alive between 90 and 100 years increases over time, while the curve is continually pushed forwards in favour of older and older ages.

It is evident that the survival curve reflects this postponed appointment with death. A brief examination of mortality data provided by the National Institute of Statistics shows not only that the total number of deaths after 100 has more than doubled (1038 to 2183) between 1989 and 1997, with a constant number of births for the cohorts of origin (see Figure 2); but also that the numbers of those dying after 105 years is growing all the time at a higher rate of increase than that for preceding age groups (100–104 years, see Figure 2).

Thus, people have smaller chances of death during young and adult ages, implying that more and more people reach old age and, once the old age threshold is crossed, death occurs less frequently and continually later (Kannisto 1996). Recently, in fact, the decline in mortality at this age, particularly for women, has been given a new impetus in all developed countries, even in those at a disadvantage, and in those which appeared to have reached the lowest mortality levels possible (France and Japan, for example: Figure 3). Is there any stop in sight? When? What are the decisive factors? There is no clear cut answer as of yet. However, all eyes are focused on this trend. A trend which arouses a certain amount of perplexity given its impact, without precedence, on the increase in the number of elderly and on population ageing. In Italy, for example, the over 65-year-old

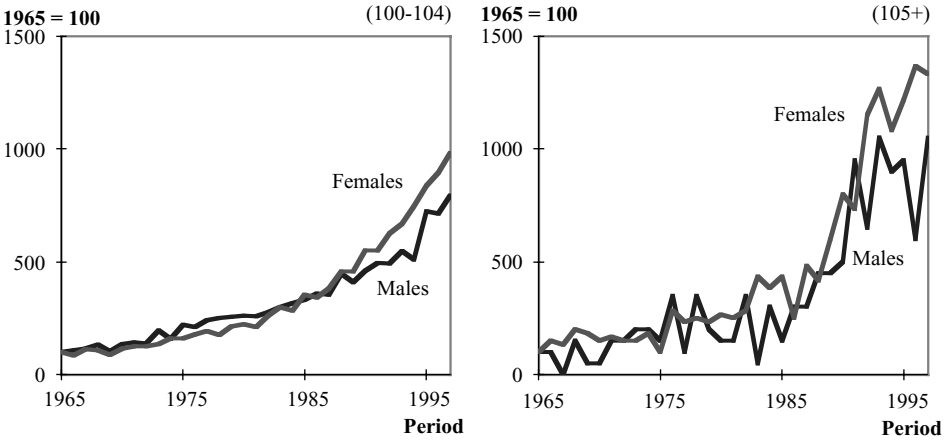

Figure 2. Italian deaths ratio trends by age 100–104 (left) and at ages 105 and over (right), from 1965 to 1997 (1965 = 100).

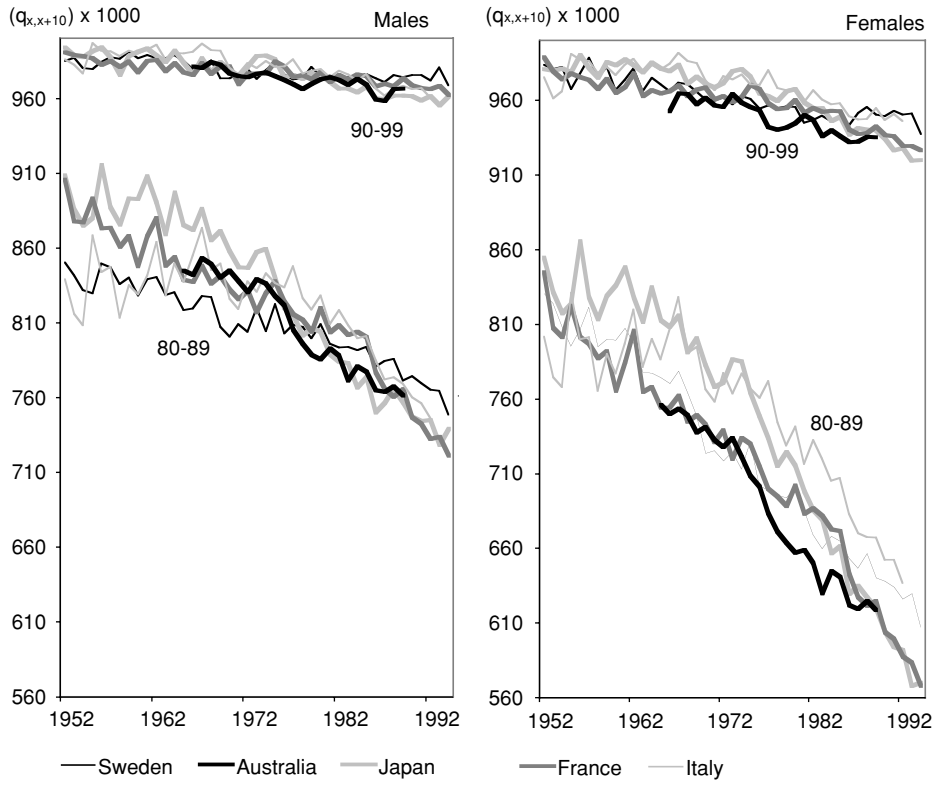

Figure 3. Female and male mortality trends among the 80–89 and 90–99 age groups in selected developed countries from 1952 to 1994–96.

population has topped the under 15-year-old population (17.6% compared with 14.6%); and the number of oldest-old is growing all the time. As we all know, ageing, both absolute and relative, involves considerable social and individual costs, causing difficulties for the welfare state, the family system, and inter-generation relationships. Nor should we overlook the fact that the older the person is the more he will have to grapple with late-onset diseases.

Note that in Figure 3 improvements in mortality at ages 90–99 are slower than improvements at age 80–89. This raises the question of whether it is difficult or even impossible to substantially reduce the risk of death.

2. New Trajectories of Mortality for the Oldest-Old: The Search for An Explanation

Ageing and longevity are very topical questions on today's agenda. The two processes are closely intertwined. Biologists and geneticists who study the implied mechanisms and try to establish at what stage one is old, as well as the real possibilities of further extending longevity, have come up with 300 or so theories on ageing. According to Medvedev (1990) these can be grouped under four main theories: programmed genetic ageing; age associated changes; primary damage; evolutionary theories (Marigliano 1995). Some of these theories focus on "how we age", i.e., on the mechanisms of free-radical damage, telomere shortening, errors in cell division, hardening of the arteries, etc. that characterize ageing. Other theories focus on "why we age", i.e., on the fundamental evolutionary forces that underlie the fact that humans and other species are not immortal (see, e.g., Williams 1957; Kirkwood 1990; Rose 1991; Finch and Kirkwood 2000). Demographers are interested in "when we die". That is, demographers want to know why some people die at age 60, others at 80, and a few at 100, and why the number of people dying at older ages is rapidly increasing. The theories of how we age have not yet shed much light on this kind of question. The current theories of why we age are so abstract and general that these theories shed virtually no light at all on the age-patterns of mortality and changes in these patterns over time.

Hence, with little or no theory to guide them, demographers have focused on empirical observations of changes in mortality over age and time. New observations based on highly reliable data on mortality after age 90 have caused demographers to question the validity of Benjamin Gompertz' Law (1825) when applied to older ages. The curve describing the increase in mortality rates with age (the parameter which defines the speed of ageing) instead of inexorably obeying an inexorable exponential law, tends to decelerate after 75–80 years (Manton and Vaupel 1995; Thatcher *et al.* 1998; Horiuchi and Wilmoth 1998). In other words, the mortality rate which increases during the post-reproductive stage until about 75 years of age, then gradually slows down (Horiuchi and Coale 1990). This phenomenon had been noted in the past, but was blamed on the data's lack of reliability. Taking age-specific rates of mortality change with age for French and Italian women in three different periods, this deceleration process can be clearly seen (Figure 4). This phenomenon is also observed in other species, such as insects and worms, where the deceleration occurs well past the normal productive ages (Vaupel *et al.* 1998). Thus, it may said that this is not a Gompertzian curve, but a logistic curve that fits the data of mortality well from 80 to 105 years, indicating that death rates may reach a plateau. Some studies show how a

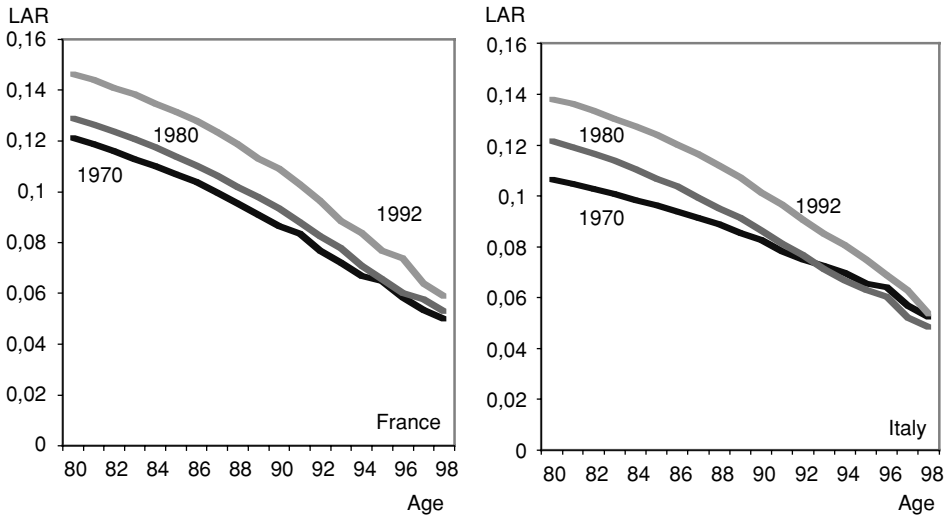

Figure 4. Estimated life tables ageing rate after 80 years for French and Italian women, in 1970, 1980 and 1992.

quadratic curve fits the data at age 105, suggesting a decline in mortality after the age of 110 (Thatcher *et al.* 1998).

Neither Gompertz' Law nor any violations which occur have any known theoretical explanation (Klarsfeld and Revah 2000). Consequently, demographers focus on the fact that the mortality curve is, by its very nature, statistical. This can trace a population's extinction (a group of individuals), even if no one of these individuals behaves as the population as a whole. A deceleration in the curve does not imply that the speed of individual ageing changes with age. One explanation may be that individuals in the same generation may be vulnerable in different ways to death (Vaupel *et al.* 1979). Thus the observed deceleration in the force of mortality may be traced to changes in the composition of heterogeneous populations. There are frailer individuals who age quicker and are eliminated earlier; and there are more robust individuals who age slower and live longer. Population ageing slows down, similar to the mortality curve, when frailer individuals have been almost totally eliminated and only the robust survive. However, their mortality, whether frail or robust, follows Gompertz' Law.

Thus, the population's observed mortality trends may be related to different (unobserved) individual processes. Individuals differ in their susceptibility to illness and death and some of these differences are not measured in demographic and epidemiological studies. Unobserved heterogeneity, also called frailty, is a major concern in applications to survival analysis where hidden individual variations cannot be safely ignored. Compelling evidence currently exists showing that lifestyle, environmental and living conditions may change individual frailty (susceptibility to disease and death), and that the life spans of related individuals are correlated. Changes in individual frailty (e.g. the debilitation of individual

organisms with age) make their contribution to observed population characteristics (Yashin and Manton 1997).

The goal of this study is to show what has been and what will continue to be the demographer's role in the study of longevity (Caselli *et al.* 2000). The Italian context and other forerunner countries in terms of survival levels were taken as an example here to emphasise the importance and topicality of the issues raised. Let us now assume that no empirical observation is fully acceptable until made explicable (Vaupel *et al.* 1998) and seek new interpretations. Nor should we overlook the fact that explanations require hypotheses, not to mention appropriate methodologies for the data available.

In the next section we describe some frailty models and explain how they can be used to estimate the relationship between the observed trajectory of mortality for a population and the underlying trajectory of mortality for the individuals in the population. It turns out that important insights can be gained by studying twins, and in particular by considering the application of the correlated frailty model to statistical analysis of genetic and environmental factors influencing the survival of identical (MZ) and fraternal (DZ) twins.

Then we turn to mortality surfaces. The influence of many factors on mortality and longevity is summarized in these surfaces. For Italy and some other countries, death rates are available by year of age from birth to advanced old age, and by year of time for a century or more. Analysis of the pattern of mortality over age and time can deepen understanding of how mortality changes with age, with time, and for successive generations. By combining the results from twin studies with mortality-surface data, a new perspective can be opened concerning how heterogeneous populations are, how steeply death rates rise with age for individuals, and how quickly death rates are falling over time, and thanks to the results hypotheses may be forwarded regarding the causes triggering the changes observed.

3. Insights from Frailty Models: Nonparametric Models and Individual Data

Vaupel, Manton, and Stallard (1979) proposed a simple frailty model for studying mortality. Let $\bar{\mu}(x)$ be the force of mortality (hazard of death) in a population at age x. Let $\mu(x, z)$ be the force of mortality at age x for an individual of unobserved frailty z. Assume that z is a proportional hazard such that $\mu(x, z) = z\mu(x, 1) \equiv z\mu_o(x)$, where $\mu_o(x)$ is the standard or baseline force of mortality at age x. Then $\bar{\mu}(x) = \bar{z}(x)\mu_o(x)$, where $\bar{z}(x)$is the average value of frailty among those individuals who are alive at age x. If frailty is gamma distributed with mean 1 and variance σ^2, then:

$$\bar{\mu}(x) = \frac{\mu_o(x)}{\left[1 + \sigma^2 \int_0^x \mu_o(t)dt\right]}$$

If a functional form is specified for the force of mortality, e.g., that the force of mortality increases exponentially with age—the Gompertz assumption—then maximum likelihood methods can be used to estimate the variance in frailty as well as the parameters of the mortality function. There is, however, no compelling evidence concerning the shape of the

age-trajectory of mortality for individuals. Alternative assumptions can produce radically different estimates of the variance of frailty and the pace of mortality increase with age (Vaupel and Carey 1993).

To circumvent this fundamental difficulty, data on twins or other related individuals can be used in "correlated frailty models" (Yashin and Iachine 1994). Remarkably, these models permit nonparametric estimation of the age-trajectory of mortality for individuals as well as providing parametric estimates of the variance in frailty and the correlation of the frailties of the related individuals (Yashin *et al*. 1995).

3.1. DANISH TWIN DATA

In this paper we apply methods of bivariate frailty modelling using the analysis data on life spans of Danish identical (MZ) and fraternal (DZ) male and female twins born between 1870 and 1900. The data were taken from the Danish Twin Register, which was created in 1954 (Hauge 1981). The register contains survival data on all twins born in Denmark between 1870 and 1930, if both survived age 6. The studies of ageing discussed here were completed in two stages. At the first stage data on like-sex twins born in 1870–1900 both surviving at age 30 were used. All together we have 470 male MZ twin pairs, and 780 male DZ twin pairs, 475 female MZ twin pairs, and 835 female DZ twin pairs. To simplify calculations ten pairs with censored information were not included in the analysis at the first stage. For both male and female MZ twins life expectancy is higher than for respective DZ twins (72.4 and 75.3 years vs. 72.0 and 73.9 years respectively). For the same cohorts of the Danish population life expectancy is 72 years for males and 73 years for females.

Correlation coefficients show higher association between the life spans of MZ than those of DZ twins in a pair. The Pearson's correlation for MZ twins (0.23) is almost three times higher than for DZ twins (0.07) for both sexes, which suggests the presence of a non-additive genetic effect on the life span (Neale *et al.* 1992). The mean absolute values of differences between the life spans are about two years smaller for MZ than for DZ twins. It has been shown (Christensen *et al.* 1995; Yashin and Iachine 1995) that the chances of survival for twin-individuals are almost the same as the respective chances calculated from standard demographic life tables for the same cohorts of the Danish population. The chances of survival for MZ individuals are close to respective chances of DZ individuals for both sexes. This similarity justifies the use of the inclusive survival model and the integration of data sets for MZ and DZ twins. Such a strategy plays a crucial role in identification of the genetic parameters of the survival model.

3.2. BIVARIATE FRAILTY MODELS

To analyse data on the life spans of twins and other relatives, Hougaard *et al*. (1992) proposed a shared frailty model, based on a model for estimating association in a random-effects framework proposed by Clayton (1978) and Clayton and Cuzick (1985). Versions of the shared frailty model have been used successfully in the analysis of bivariate survival data, e.g., by Vaupel *et al.* (1992) who showed that the life spans of MZ twins are more similar than the life spans of DZ twins. The shared frailty model, however, suffers from some severe problems. The definition of frailty in the univariate model differs from the

definition in the shared frailty model, making comparisons difficult. More seriously, use of the shared frailty model will in general result in biased estimates of parameter values (Yashin *et al.* 1995).

Hence, Yashin and colleagues developed the correlated frailty model (Yashin and Iachine 1994; Yashin *et al*. 1995). One version of this model, which assumes that frailty is gamma distributed, has turned out to be particularly useful. Let $\mu_i(z_i, x) = z_i\, \mu_{0i}(x)$, i =1,2 be the hazard functions for two related individuals. Assume that frailties z_i, $i = 1, 2$ are gamma-distributed with means 1, variances σ_1^2, σ_2^2 and the correlation coefficient ρ_z. Yashin and Iachine (1994) found that the bivariate survival function $\bar{s}(x_1, x_2)$ can be expressed in terms of the relevant survival functions for the cohorts the two individuals belong to, as follows:

$$\bar{s}(x_1, x_2) = \bar{s}_1(x_1)^{1-\frac{\sigma_1}{\sigma_2}\rho_z}\, \bar{s}_2(x_2)^{1-\frac{\sigma_2}{\sigma_1}\rho_z} \left(\bar{s}_1(x_1)^{-\sigma_1^2} + \bar{s}_2(x_2)^{-\sigma_2^2} - 1\right)^{-\frac{\rho_z}{\sigma_1\sigma_2}},$$

where the cohort survival function is given by:

$$\bar{s}(x) = \exp\left\{-\int_0^x \bar{\mu}(t)dt\right\}.$$

If the distribution of frailty can be assumed to be the same for the two individuals, e.g., in the case of identical twins of the same sex, then this formula can be further simplified. Instead of assuming that frailty is gamma distributed, other assumptions can be made (Yashin *et al.* 1998).

Estimation of the variance in frailty, σ^2, from bivariate data using the correlated gamma-frailty model with $\sigma_1^2 = \sigma_2^2 = \sigma^2$ does not involve any assumptions about the age-trajectory of the force of mortality for individuals, $\mu_o(x)$. When estimates are available concerning the proportion of a cohort that has survived to various ages x, then the force of mortality for the standard individual can be calculated by:

$$\mu_0(x) = \bar{\mu}(x)\bar{s}\,(x)^{-\sigma_z^2},$$

where $\bar{\mu}(x)$ is the estimated force of mortality for the population and σ^2 has been estimated from the equation in the previous paragraph.

Thus, the information provided by bivariate data permits nonparametric estimation of the underlying hazard or force of mortality for individuals, based on an estimate of the parameter σ^2, the variance in frailty. Application of this approach to Danish twin data led to estimates of variance of frailty of about 1.5. This, in turn, led to the nonparametric estimates of the age-trajectory of morality for males show in Figure 5 and for females shown in Figure 6. Note that the pace of mortality increase for individuals,$\mu_o(x)$, is much more rapid than the pace of increase for the population, $\bar{\mu}(x)$. A Gompertz pattern of mortality, involving exponential increase with age, would be a straight line on the semi-log scale of the two figures, so the estimated trajectory of individual mortality is also much steeper than a Gompertz trajectory. This example suggests that correction for unobserved

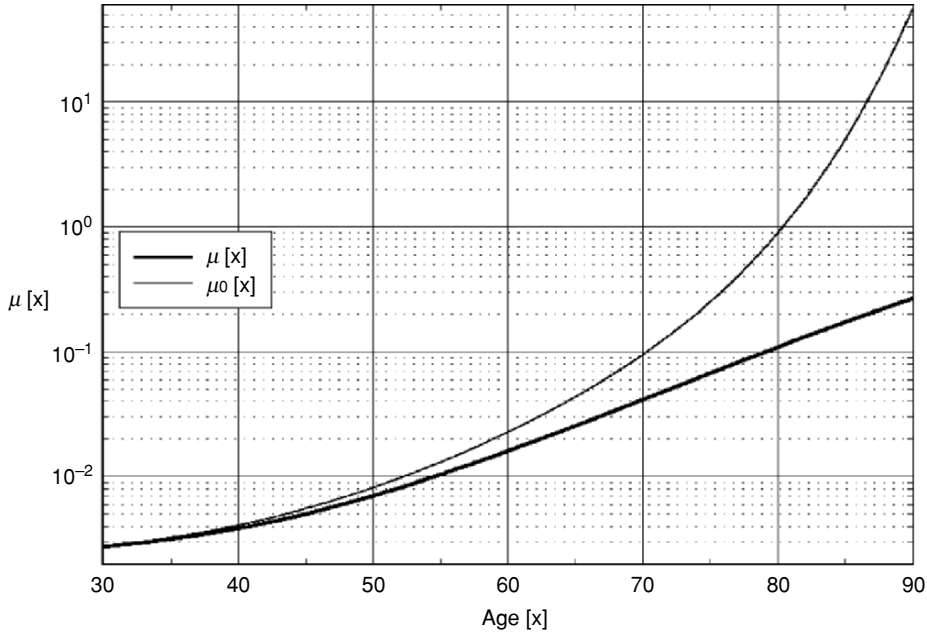

Figure 5. The force of mortality for the population (thick line) and the estimated force of mortality for the standard individual (thin line) calculated from survival data on Danish male twins born in 1870–1900 using the correlated gamma-frailty model (Yashin and Iachine 1997).

heterogeneity in demographic life tables may be needed not only for the oldest old but also for the traditional interval of ageing between 35 and 85 years of age, for which the observed trajectory of mortality appears to be well described by a Gompertz curve.

3.3. GENETIC MODELS OF FRAILTY

Here we consider the application of the correlated frailty model to statistical analysis of genetic factors influencing the survival of MZ and DZ twins. In particular, calculate semi-parametric estimates for the six genetic models of frailty which correspond to six different assumptions about its structure. We refer to the notations used in McGue *et al.* (1993) and in Yashin and Iachine (1994) for such models. To be more specific, let *A, D, I, C, E*, and *H* be the six components of frailty which represent additive genetic effects, dominance genetic effects, epistatic genetic effects, common environmental effects, uncommon environmental effects, and total genetic effects, respectively, in additive decomposition of frailty. From the estimation point of view not more than three components should be represented in the model when MZ and DZ data are analysed (more components can be considered if, in addition, data about adopted children and twins reared apart are available). In these notations an ACE model refers to the decomposition of frailty $Z = A + C + E$. An AE model refers to the decomposition $Z = A + E$. ADE, DE, DCE, and HE models are

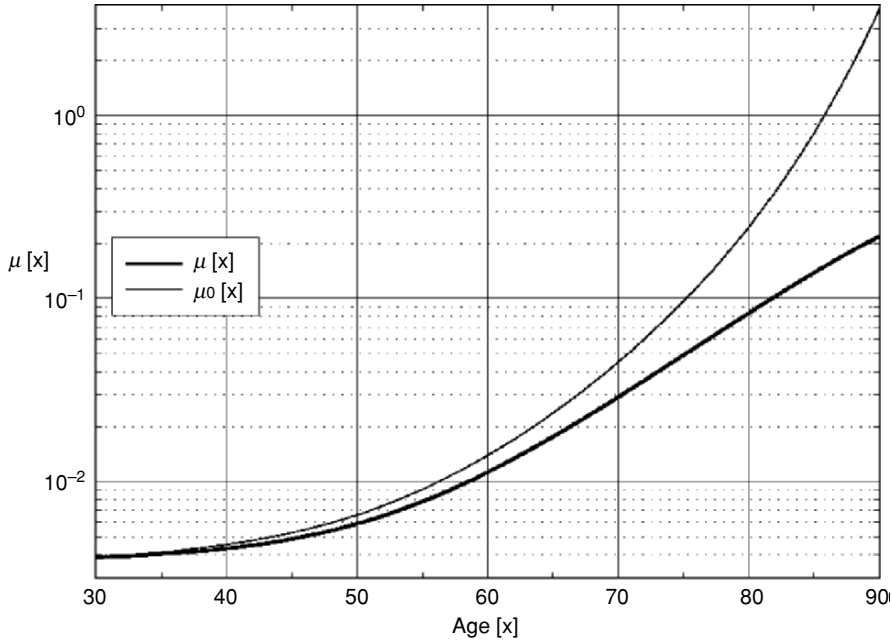

Figure 6. The force of mortality for the population (thick line) and the estimated force of mortality for the standard individual (thin line) calculated from survival data on Danish female twins born in 1870–1900 using the correlated gamma-frailty model (Yashin and Iachine 1997).

defined similarly. We use small letters a^2, d^2, i^2, c^2, e^2 instead of $\gamma_j (j = 1, 2, \ldots, n)$ to refer to the respective proportions of variance. For example, the relationship:

$$1 = a^2 + c^2 + e^2$$

corresponds to the decomposition of variance in the ACE model of frailty. Yashin and Iachine (1994) use the assumption that the correlation coefficient of the bivariate frailty distribution for this model admits decomposition:

$$\rho = \rho_1 a^2 + \rho_4 c^2 + \rho_5 e^2$$

where a^2 is the proportion of the variance associated with additive genetic effects, called narrow-sense heritability; c^2 is the proportion of variance associated with shared environmental factors; e^2 is the proportion of variance with nonshared environmental factors; and ρ_1, ρ_4 , and ρ_5 are correlations between additive genetic, common environmental, and uncommon environmental components for related individuals. Similarly, ρ_2 and ρ_3 are correlation coefficients between dominant genetic and epistatic genetic components, respectively. H^2 is used for the broad-sense heritability coefficient $H^2 = a^2 + d^2 + i^2$. The model for broad-sense heritability includes genetic component, H, common environmental,

Table 1. Genetic and environmental components of frailty for Danish male twins surviving to age 30*.

Model	a^2	d^2	H^2	k	c^2	e^2	LogLik	AIC
ACEs	0.479				0.000	0.521	−17876.5686	2.0000
	—				—	—		
Aes	0.479					0.521	−17876.5686	0.0000
	(0.111)					(0.111)		
ADEs	0.247	0.258				0.494	−17876.0955	1.0538
	(0.333)	(0.355)				(0.292)		
Des		0.519				0.481	−17876.5788	0.0205
		(0.124)				(0.124)		
DCEs		0.423			0.082	0.494	−17876.0955	1.0538
		(0.169)			(0.115)	(0.136)		
Hes			0.506	0.372		0.494	−17876.0955	1.0538
			(0.122)	(0.147)		(0.122)		

*Semiparametric estimation with correlated frailty model.

C, and independent environmental, E, components (the HCE-model). Respective equations for proportions of variance and correlation coefficient are:

$$1 = H^2 + c^2 + e^2$$
$$\rho = RH^2 + \rho_4 c^2 + \rho_5 e^2$$

where R is the correlation coefficient between total genetic components of the phenotype. We use semiparametric representation for the marginal bivariate survival function with respective decompositions of the correlation coefficients of frailty. Standard assumptions of the quantitative genetics specify different values of ρ_i ($i = 1, 2, \ldots, 5$) and R for MZ and DZ twins. For MZ twins $\rho_i = 1$ ($i = 1, 2, 3, 4$), $\rho_5, = 0$, $R = 1$. For DZ twins $\rho_i = 0.5$, $\rho_2 = 0.25$, $\rho_3 = m$, $\rho_4 = 1$, $\rho_5 = 0$, $R = k$. Here $0 \leq = m \leq 0.25$ and $0 \leq k \leq 0.5$ are unknown parameters. Note that the one more important assumption is that the variances of the phenotypic traits for MZ and DZ twins are the same. This hypothesis was tested and confirmed with Danish twin data for both sexes.

Since our data deal with individuals who survived to age 30, we need to adjust the bivariate survival function to consider conditional survival distribution. The results of the semiparametric estimation procedure for six models of frailty (ACE, AE, ADE, DE, DCE, and HE) are shown in Table 1 for male and in Table 2 for female twins. Small "s" after models in these Tables indicates that the semiparametric procedure was used for parameter estimation.

One can see from Table 1 that for male twins the ACE model converges to the AE model since the estimate of c^2 tends to zero (standard errors for the ACE model are not shown in Table 1, since 0 is the boundary of the parametric space). Note that the value of the likelihood function for the ADE model is higher than for the AE model. However, the AE

Table 2. Genetic and environmental components of frailty for Danish female twins surviving to age 30.

Model	a^2	d^2	H^2	k	c^2	e^2	LogLik	AIC
ACEs	0.405				0.111	0.484	−18878.6591	1.4747
	(0.168)				(0.145)	(0.174)		
Aes	0.525					0.475	−18878.9218	0.0000
	(0.168)					(0.168)		
ADEs	0.525	0.000				0.475	−18878.9218	2.0000
	—	—				—		
Des		0.509				0.491	−18878.8840	5.9244
		(0.152)				(0.152)		
DCEs		0.270			0.246	0.484	−18878.6591	1.4747
		(0.139)			(0.152)	(0.173)		
Hes			0.516	0.607		0.484	−18878.6591	1.4747
			(0.174)	(0.148)		(0.174)		

model is better than the ADE model according to the likelihood-ratio test. For females the value of ACE likelihood is higher than AE likelihood.

However, the AE model is better according to the likelihood-ratio test. The ADE model converges to the AE model since the estimate of d^2 tends to zero. Standard errors are not shown for the same reason as before. Since not all of our models are nested we used the Akaike Information Criteria (AIC) to compare different models. According to AIC the AE model gives the best fit to the bivariate data for both sexes.

It is curious that in all six models the estimate of e^2 (i.e., uncommon environmental component of variation in frailty) is close to 0.5 for both sexes. These results support the main finding of our previous study based on parametric estimation procedure: environmental factors determine not less than 50% of variability in individual frailty (Yashin and Iachine 1994, unpublished observations).

Standard deviations of the parameter estimates given in Tables 2 and 3 do not take into account the errors in nonparametric estimations of the univariate survival functions, so they are not real standard errors. However, the estimates calculated in the parametric estimation procedure (Yashin and Iachine 1994) are very close to the semiparametric estimates given in Tables 2 and 3 and have almost the same standard deviations.

4. Mortality Surfaces to Better Understand Mortality for the Oldest-Old

As noted above, observed patterns of mortality in a population result from the complicated interaction of the process of ageing on the individual level and a process of mortality selection on the population level (Manton and Yashin 2000). In addition, mortality levels

change over time as environmental conditions change and as health progress is made. It should be emphasized that a consideration of events as they occurred during different calendar years is somewhat limiting. Mortality, for example, may not be viewed apart from what happened prior to the fatal event, from the moment of conception to death. Data from a period life table summarise average variations in risks due to biological ageing (the age factor) as well as the average impact of environmental factors, influenced by socio-economic and medical progress (period effect). An individual's vulnerability at a given age is not only the outcome of his vital biological function at that specific age and health status during the period of observation. Other aspects are also important, such as his initial genetic map and the improvement or deterioration in the "vital capital" of the previous life history of his cohort of origin. This third component, the cohort effect, is crucial in understanding how selection processes operate and in order to study the effects of variations in both initial and acquired, frailty, on mortality levels, and longevity. To consider these components (age, period, and cohort components) what is needed is long mortality data series and suitable methods of analysis (Caselli and Capocaccia 1989; Caselli 1996).

The influence of many factors on mortality and longevity can be summarised in mortality surfaces, representing mortality rate as a function of age and time. Figure 7 portrays over a century's mortality in Italy for men and women. The serious crises in mortality due to the two World Wars (period effects) can easily be traced on the maps in the elongated shafts of high mortality penetrating all ages. For men these effects linger on for some years after the war among cohorts who were born or grew up during the war years (Caselli *et al.* 1985; Wilmoth *et al.* 1990). As can be seen in Figure 3, the slow progress in reducing mortality rates among older ages, particularly for men, until the 1970's, contrasts with the recent marked decrease.

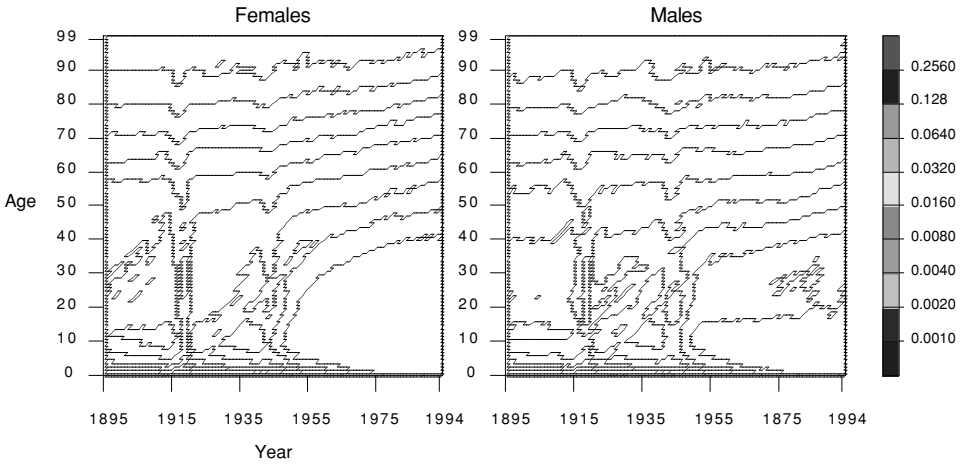

Figure 7. Surfaces of the observed annual, age-specific probabilities of death for Italian females and males from 1895 to 1994.

The analysis of such surfaces requires new models. These models should help identify influential factors responsible for period and cohort effects observed on mortality surfaces. They will allow us to evaluate distribution of hidden heterogeneity and its dynamic properties. They will also play a crucial role in estimating the details of interaction of physiological, environmental and genetic factors and their role in producing age and time specific patterns of mortality and survival.

Let $\bar{\mu}(x, y)$denote the surface of the force of mortality for a population, defined over age x and year y. Let $\mu_o(x, y)$similarly define the baseline surface that describes the dynamics of how mortality changes over age and time for individuals, in a frailty model framework. If frailty is gamma distributed with mean 1 and variance σ^2, then, as shown by Vaupel, Manton, and Stallard (1979):

$$\mu_o(x, y) = \bar{\mu}(x, y)\bar{s}(x, y - x)^{-\sigma^2},$$

where the cohort survivorship function is defined by:

$$\bar{s}(x, y - x) = \int_0^x \bar{\mu}(t, y - x + t)dt.$$

Hence, given sufficient information about cohort survival experiences and given a specific value for the variance in frailty, mortality surfaces for populations can be transformed into mortality surfaces for individuals.

Figure 8 illustrates this. Figure 8-left gives the mortality surface for the population of Italian females for ages 50 to 99 and years 1965–1994. Figure 8-right gives the corresponding

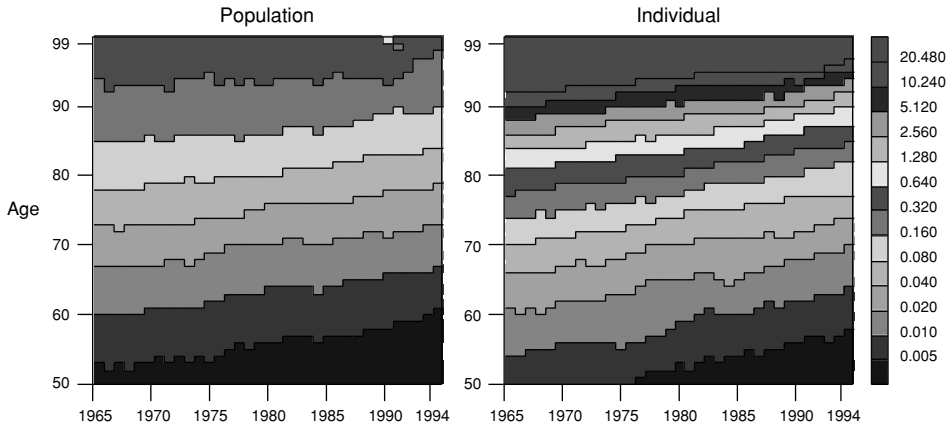

Figure 8. Surfaces of the estimated force of mortality for Italian females from 1965 to 1994, at the population level (left) and at the individual level with variance of frailty equal to one (right).

Table 3. Rates of Mortality Improvement (in %) for Italian Females for various values of the variance of frailty, averaged over ten-year age categories and ten-year time periods.

AGE and σ^2	1965–1974	1975–1984	1985–1994	AGE and σ^2	1965–1974	1975–1984	1985–1994
$\sigma^2 = 0$				$\sigma^2 = 0.5$			
50–59	1.1	3.1	1.6	50–59	1.5	4.0	2.0
60–69	1.7	3.0	1.3	60–69	2.4	3.5	2.2
70–79	1.4	3.2	1.9	70–79	2.6	4.2	2.6
80–89	0.9	0.5	2.9	80–89	2.9	2.0	5.2
90–99	0.04	0.02	1.1	90–99	2.6	2.9	3.1
$\sigma^2 = 1$				$\sigma^2 = 1.5$			
50–59	1.8	4.8	2.4	50–59	2.2	5.7	2.8
60–69	3.1	4.0	3.1	60–69	3.8	4.5	4.0
70–79	3.9	5.4	3.4	70–79	5.1	6.6	4.2
80–89	5.0	3.6	7.6	80–89	7.4	5.4	10.2
90–99	4.6	5.8	4.8	90–99	6.7	8.9	6.3

mortality surface for individuals, under the assumption that $\sigma^2 = 1$. Note how different the surfaces are, especially at advanced ages. Also note the much more rapid rate of mortality improvement, again especially at advanced ages, in the surface for individuals.

The rate of mortality improvement is given by:

$$\rho(x, y) = 1 - \mu_o(x, y + 1)/\mu_o(x, y).$$

Table 3 gives the average value of this rate for Italian females over ten-year periods of time and age, for four values of the variance in frailty. When this variance is zero, then the mortality surface for individuals is identical to the surface for the population. In the correlated frailty models applied to Danish twin data, estimated values of this variance were about 1.5.

Consider in Table 3 the rates of mortality progress when the variance in frailty is zero: these are the observed rates of improvement for the population. Note that in 1965–74 and in 1975–84 rates of improvement are much more rapid at younger ages than at the most advanced ages. In 1985–1994 there was a remarkable surge in progress in reducing mortality at oldest-old ages, but even in this decade the rate of improvement fell sharply from octogenarians to nonagenarians.

Now consider the values when the variance in frailty is 0.5, 1, or 1.5. Note that the rates of improvement are larger, especially at the highest ages. And note that this increase is particularly pronounced the larger the variance in frailty. The basic reason for this is as follows. As we know, in a heterogeneous population the frail tend to die first. If, for a cohort of individuals, death rates are reduced at younger ages, then frail individuals who would have died now survive to older ages. This influx of frail individuals will tend to

raise death rates. Hence to make mortality improvements this effect must be neutralized and then additional progress must be made. The greater the heterogeneity in frailty, the bigger this effect. Consequently, even small improvements in observed death rates at the population level may reflect very large improvements in mortality at the individual level.

When the variance in frailty is 0.5, then for each of the three decades of time the rates of improvements in different ages categories are roughly the same. Indeed, all 15 rates of improvement are very roughly comparable, averaging about 2.9%. The rates within any decade of time as well as the rates across time have considerably less variance than the corresponding rates for the population mortality surface (i.e., when the variance of frailty is zero). This greater simplicity adds support to the hypothesis that simple frailty models may help explain some of the features of mortality surfaces.

We estimated the value of the variance in frailty that minimized the variance in rates of mortality improvement. For both Italian females and Italian males, between ages 50 and 99 and from 1965 and 1994, this value was close to 0.5. Variance in rates of progress increased as the variance in frailty increased above 0.5. This can be seen in the bottom two panels of Table 3.

Also note that when the variance of frailty is 1 or 1.5, then some of the estimates rates of mortality improvement are very large. The estimated pace of reduction is more than 10% per year for octogenarians if the variance of frailty is 1.5. Such a rapid rate of progress seems implausible. The age-trajectory of the force of mortality for female Danish twins shown in Figure 6 is based on an estimated variance of frailty of about 1.5. If the variance was 0.5, then the trajectory would still rise somewhat faster than a Gompertz, exponential trajectory, but not nearly so dramatically.

Conclusion

Death rates in recent decades have fallen dramatically, especially at older ages. Death rates increase with age, but at a slower and slower pace at advanced ages. The remarkable improvements in mortality and the deceleration of the age-trajectory of mortality are puzzling phenomenon. Deeper comprehension of underlying causes hinges on the development of new analytical approaches. One promising direction for research is the application of models that incorporate the effects of mortality selection resulting from heterogeneity in frailty. As discussed and illustrated in this paper, such models can be used to nonparametrically estimate mortality trajectories for individuals, to decompose genetic and environmental influences, and to transform surfaces of mortality over age and time from observed surfaces for populations to estimated surfaces for individuals.

These results merely suggest the potential for further research by demographers. That much remains to be done is indicated by the apparent inconsistency of two key findings presented in this paper. On the one hand, analysis of Danish twin data suggests that the variance in frailty may be high, perhaps 1.5 or so, and that there is an extremely rapid increase in the force of mortality with age at older ages. On the other hand, analysis of patterns of mortality improvement in Italian surfaces of mortality over age and time suggest

a more modest value for the variance in frailty, perhaps 0.5 or so, and a pattern of mortality increase with age that is only somewhat faster than exponential increase.

We have set ourselves the target of further developing the analysis by means of surfaces, applying both the illustrated model and other methods, with reference to women's and men's mortality and especially mortality by cause of death. Following the knowledge of the mortality for a specific cause, hypotheses may be made about links with the originating risk factors, be they bio-genetic or generated by lifestyles or the individual's living environment.

In such analyses, the methods that combine genetic and demographic information may be extremely useful. These methods can use data about genetic markers obtained in centenarian studies. The analysis may also be performed on larger populations. For instance, the Italian regions collect individual morbidity histories (clinical and pharmaceutical data) and mortality for the whole population. Italy, thanks to its geographical features, the long tradition of separate regions, migratory flows, and the well-known existence of perceptible geographical differences in elderly mortality, the relationships highlighted between genetic distances (Soliani 1984), eating habits, smoking, environmental contexts (Caselli and Egidi 1981), and mortality levels among the oldest-old (Soliani 1984), could provide the right conditions necessary for identifying the factors which have an impact on population longevity.

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References

Caselli, G. (1996) "Future longevity among the elderly". In: Caselli, G., Lopez, A. D. (eds.), *Health and Mortality Among Elderly Populations*. Oxford: Clarendon Press, pp. 235–265.

Caselli, G., and Capocaccia, R. (1989) "Age, period, cohort and early mortality: An analysis of adult mortality in Italy", *Population Studies*, 43:133–153.

Caselli, G., and Egidi, V. (1981) "L'analyse des données multidimensionelles dans l'étude des rélations entre mortalité et variables socio-économiques, d'environnement, et de comportement individuel", *Genus*, 37(3–4):57–91.

Caselli, G., Vaupel, J. W., and Yashin, A. I. (1985) "Mortality in Italy: Contours of a century of evolution", *Genus*, 41:39–55.

Caselli, G., Vaupel, J. W., and Yashin, A. I. (2000) "Longevity, heterogeneity and selection". *Atti della XL Riunione Scientifica della Società Italiana di Statistica*, pp. 49–72, SIS 2000, Florence, p. 437.

Christensen, K. (1995) "Mortality among twin after age 6: Foetal origins hypothesis versus twin method", *British Medical Journal*, 310(6777):432–436.

Clayton, D. G. (1978) "A model for association in bivariate life tables and its application in epidemiological studies of familial tendency in chronic disease incidence", *Biometrica*, 65:141–151.

Clayton, D. G., and Cuzick, J. (1985) "Multivariate generalizations of the proportional hazards model (with discussion)", *Journal of Royal Statistical Society Series A*, 148:82–117.

Finch, C. E., and Kirkwood, T. B. L. (2000) *Chance, Development, and Aging*. Oxford: Oxford University Press.

Gompertz, B. (1825) "On the nature of the function expressive of the law of human mortality", *Philosophical Transactions*, 27:513–585.

Hauge, M. (1981) "The Danish twin register". In: Mednick, S. A., Baert, A. E., Backmann, B. P. (eds.), *Prospective Longitudinal Research, An Empirical Basis for the Primary Prevention of Psychiological Disorders*. London: Oxford University Press, pp. 218–221.

Horiuchi, S., and Coale, A. (1990) "Age patterns of mortality for older women: An analysis using the age-specific rate of mortality change with age", *Mathematical Population Studies*, 42:389–406.

Horiuchi, S., and Wilmoth, J. R. (1998) "Deceleration in the age pattern of mortality at older ages", *Demography*, 35(4):391–412.

Hougaard, P., Bent, H., and Holm, N. V. (1992) "Assessment of dependence in the life times of twins". In: Klein, G. P., Goel, P. K. (eds.), *Survival Analysis: State of the Art*. Dordrecht: Kluwer Academic Publishers, pp. 77–97.

ISTAT. (2004) *Tavole di mortalità della popolazione italiana per provincia e per regione di residenza. Anno 2000*, *http://demo.istat.it*.

Kannisto, V. (1996) *The Advancing Frontier of Survival*, Vol. 3, Odense: Odense University Press. (Odense Monographs on Population Aging).

Kirkwood, T. B. L. (1990) "The disposable soma theory of aging". In: Harrison, D. E., (ed.), *Genetic Effects on Aging II.* Caldwell: NJ Telford Press, pp. 9–19.

Kirkwood, T. B. L., and Rose, M. R. (1991) "Evolution of senescence: Late survival sacrificed for reproduction", *Philosophical Transactions of the Royal Society of London B. Biological Science*, 332:15–24.

Klarsfeld, A., and Revah, F. (2000) *Biologie de la mort.* Paris: Edition Odile Jacob.

Manton, K. G., Vaupel, J. W. (1995) "Survival after the age of 80 in the United States, Sweden, France, England and Japan", *New England Journal of Medicine*, 333(18):1232–1235.

Manton, K. G., and Yashin, A. I. (2000) *Mechanisms of Aging and Mortality: A Search for New Paradigms*, Denmark: Odense University Press. (Odense Monographs on Population Aging no. 7).

Marigliano, V. (1995) *Invecchiamento e longevità*. Roma: CESI.

McGue, M., Vaupel, J. W., Holm, N. V., and Harvald, B. (1993). "Longevity is moderately heritable in a sample of Danish twins born 1870–1880". *Journals of Gerontology Biological Science*, 48(6):B237–B244.

Medvedev, Z. A. (1990) "An attempt at a rational classification of theories of ageing", *Biology Review*, 65:375–398.

Neale, M. C., and Cardon, L. R. (1992) *Methodology for Genetic Studies of Twins and Familie*. Dordrecht: Kluwer Academic Publishers.

Robine, J.-M., Vaupel, J. W., Jeune, B., and Allard, M. (1997) *Longevity: To the Limits and Beyond*. New York: Springer.

Rose, M. R. (1991) *The Evolutionary Biology of Aging*. Oxford: Oxford University Press.

Soliani, L., and Lucchetti, E. (1997) Les facteurs genetiques de la mortalite. In: *Démographie: analyse et synthèse. Causes et conséquences des évolutions démographiques*, Actes du Séminaire de San Miniato, Vol. I, pp. 71–84,

Materiali di studi e di ricerche, numero speciale, Dipartimento di Scienze Demografiche and Institut national d'études démographiques-INED, Rome, Paris.

Thacter, A. R., Kannisto, V., and Vaupel, J. W. (1998) *The Force of Mortality at Ages 80 to 120*, Vol. 5. Odense: Odense University Press. (Odense Monographs on Population Aging).

Vaupel, J. W., and Carey, J. R. (1993) "Compositional interpretations of medfly mortality", *Science*, 260:1666–1667.

Vaupel, J. W., Manton, K. G., and Stallard, E. (1979) "The impact of heterogeneity in individual frailty on the dynamics of mortality", *Demography*, 16:439–454.

Vaupel, J. W., Bent, H., Holm, N., Yashin, A. I., and Xiu, L. (1992) "Survival analysis in genetics: Danish twin data applied to a gerontological question". In: Klein, J. P., Goel, P. K. (eds.), *Survival Analysis: State of the Art*. Dordrecht: Kluwer Academic Publishers, pp. 121–140.

Vaupel, J. W., Carey, J. R., Christensen, K., Johnson, T. E., Yashin, A. I., Holm, N. V., Iachine, I. A., Kannisto, V., Khanzaeli, A. A., Liedo, P., Longo, V. D., Zeng, Y., Manton, K. G., and Curtsinger, J. W. (1998) "Biodemographic trajectories of longevity", *Science*, 280:855–860.

Williams, G. C. (1957) "Pleiotropy, natural selection and the evolution of senescence", *Evolution*, 11:398–411.

Wilmoth, J., Vallin, J., and Caselli, G. (1989) "When does a cohort's mortality differ from what we might expected?", *Population* (english edn.), 12:93–126.

Yashin, A. I., and Iachine, I. A. (1994) "Mortality models with application to twin survival data. In: Halin, J., Karplus, W., Rimane, R. (eds.), *CISS-First Joint Conference of International Simulation Societies Proceedings.* Zurich, Switzerland: Simulation Councils, Inc. pp. 567–571.

Yashin, A. I., and Iachine, I. A. (1995) "Genetic analysis of durations: Correlated frailty model applied to survival of Danish twins", *Genetic Epidemiology*, 12:529–538.

Yashin, A. I., and Iachine, I. A. (1997) "How frailty models can be used for evaluating longevity limits: Taking advantage of an interdisciplinary approach", *Demography*, 34(1):31–48.

Yashin, A. I., Vaupel, J. W., and Iachine, I. A. (1995) "Correlated individual frailty: An advantageous approach to survival analysis of bivariate data", *Mathematical Population Studies*, 5(2):145–159.

Yashin, A. I., and Manton, K. G. (1997) "Effects of unobserved and partially observed covariate processes on system failure: A review of models and estimation strategies", *Statistical Science*, 12(1):20–34.

Yashin, A. I., Iachine, I. A., Christensen, K., Holm, N. V., and Vaupel, J. W. (1998) "Genetic component of discrete disability traits: An analysis using liability models with age-dependent thresholds", *Behaviour Genetics*, 28(3):207–214.

CHAPTER 18. MARITAL STATUS AND FAMILY SUPPORT FOR THE OLDEST-OLD IN GREAT BRITAIN

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Introduction

In many developed countries those aged 80 years and over constitute the fastest growing section of the population. The well-being and support of this group is therefore of increasing significance and the availability of family support for the oldest-old a matter of keen concern to policy makers. Studies of the social networks of older people, including the oldest-old, have shown that friendships are very important for well-being and morale (and so for health) and that those lacking close kin develop stronger relationships with more distant relatives and with friends (Wenger 1984, 1996). Nevertheless, friends play only a minor role in the provision of personal and domestic care to older people in need of assistance. In Britain, other Northern European countries and North America most of this care is provided by close relatives and to a lesser extent by professional care workers (Arber and Ginn 1990; Sundström 1994; Havens 1997).

As the oldest-old population is growing so rapidly, even quite small changes in either care needs or the availability of family support may have a potentially large effect on demand for formal services of various kinds. As shown in Table 1, the 1997 survey of disability in Great Britain found that among persons aged 80 and over with some degree of disability[1] and living in a private household, over a quarter needed daily help of one kind or another. Six percent of men and 10% of women reported needing help every night with one or more personal care activities, such as getting in and out of bed, turning over in bed, getting to and using the toilet, and similar tasks. Such care is very hard to provide from outside the household and in the absence of co-residents, institutional care may be the only alternative. Providing extra-household support to those with dementia (who may be unable to co-operate with a timetable of episodic care) is even more difficult. This condition is strongly age-related with very high rates of prevalence reported for those aged 90 or

[1] Disability was assessed using a detailed schedule based on the ICIDH and further developed by ONS (Martin *et al*. 1988). Seventy-six percent of those aged 80 and over were classified as disabled on the basis of responses to this schedule.

J.-M. Robine et al. (eds.), Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population, 415–436

Table 1. Reported need for daily help with practical care, day-time personal care and night-time personal care among men and women aged 80 and over with some degree of disability, Great Britain 1997.

% reporting need for daily help with:	Men	Women
Practical care	22	27
Day-time personal care	13	18
Night-time personal care	6	10
N	304	607

Source: 1996/7 Survey of Disability in Great Britain (Grundy *et al.* 1999, p. 103). (Private household population only).
Practical care = tasks which are important for daily life but not the essentials of self-care and may be delegated to others, e.g. preparing a hot meal.
Day-time personal care = e.g. washing hands and face; dressing and undressing; getting to and using toilet.
Night-time personal care = e.g. getting in and out of bed; turning over in bed; changing sheets/night-clothes; getting to and using toilet.

more (Saunders *et al*. 1993). For these types of reason policy makers have major worries about possible declines in the provision of family support at a time when the oldest-old population is rapidly growing.

Marital status has been emphasised as a socially and demographically important variable first and foremost because in Western populations marriage has in the past, if less so today, signified the formation of a new family unit and the start of socially approved childbearing. Those who are currently married have potential support in the form of a spouse, which the unmarried lack, and those who have ever-married are far more likely than the never-married to have a child or children. Spouses, children, and grandchildren are providers of emotional support and companionship, as well as practical help, and so may contribute substantially to the well-being and quality of life of the oldest-old. In this paper we examine several dimensions of the marital status and family support of the British population[2] aged 80 and over or 85 and over. Firstly we consider the current and future marital status distribution of the oldest-old population. In this section we also present some information on trends in the availability of at least one child, based on existing empirical data and projections of the proportion of women with no, one, and two or more children under various mortality assumptions. One of the important influences of marital status in later life is its strong effect on living arrangements. The second section of the paper deals with the household characteristics of those aged 85 and over and with transitions between different types of household. In the third section we examine associations between marital status and household type and perceived social support. We conclude with a discussion of the implications of our results for the future.

[2] Some analyses are restricted to England and Wales (excluding Scotland) or England (excluding Scotland and Wales).

Data Sources and Limitations

The oldest-old, although growing more numerous, still form only a small proportion of the total population and the numbers included in many surveys are too small for detailed analysis. A further important limitation of many surveys is that they are restricted to the population in private households and exclude the quite large minority of the oldest-old living in institutions (this is an issue considered in more detail in a later section of this paper). For these reasons much of the analysis in this paper is based on census microdata which have the advantage of large sample size and inclusion of those in institutions. Against this advantage must be set the limited range of information collected in the census. The census microdata source we use is the Office for National Statistics Longitudinal Study (ONS LS), a record linkage study originally based on 1% of the population enumerated in the 1971 Census of England and Wales. Sample members have been followed by adding to their records information from vital registration sources (births and deaths) and subsequent censuses. Additionally 1% of new births and immigrants have been added to the sample: so it remains representative and may be used for cross-sectional as well as longitudinal analyses.

We also present analyses of variations in perceived social support using data from a national sample survey—the Health Survey for England. We have combined data from three rounds of this fairly large survey in order to derive a reasonable sample of people aged 80 and over. This survey does not include the population in institutions and, as we discuss, this is a potential source of bias. We have also used data from another national Government sponsored survey, the General Household Survey, to produce, in conjunction with official mortality projections, estimates of the proportions of older people with specified numbers of children.

Marital Status of the Oldest-Old Population

In the older population the proportions married depend not just on historical nuptiality rates, but also on past rates of marital breakdown and, importantly, on the incidence and duration of widowhood. This itself will be determined by sex differentials in mortality, age differences between husbands and wives, and the extent of remarriage. Several, if not all, of these parameters have changed over time with consequent changes in the marital status distribution of the population. Published official projections by marital status use ages 75 and over as the open ended band (Shaw and Haskey 1999; National Statistics 2005), although recently projections with 90 and over as the open-ended band have been made available at http://www.gad.gov.uk/marital status projections. Changing mortality and marriage experiences might be expected to lead to different patterns among the oldest-old cohorts and, of course, the supply and demand for care varies substantially according to marital status. We therefore undertook our own projections of the marital status of those ages 85 and over by single year of age up to 2035. We based our projection on the joint distribution of partners' ages from the 1991 Census of England and Wales. These values were then updated to 2001 to make them consistent with the 2001 marital status projections for England and Wales using an Iterative Proportional Fitting (IPF) algorithm approach (Murphy and Wang, 1999). Since we were interested in patterns up to 2035, our analysis is

confined to those aged 50 and over in 2001: above this age, rates of international migration, divorce, and remarriage are comparatively low, so we have ignored these components. Each combination of spousal ages was projected separately, with four possible outcomes in any year: both survive; the husband dies and the wife becomes a widow; the wife dies and the husband becomes a widower; or both die in the period. Bereaved spouses were added to the appropriate widowed category and projected subsequently. This method projects each combination of spouses' ages, unlike the widely used LIPRO program (Van Imhoff and Keilman 1991), which produces overall consistent numbers within each marital status group, but bases this on only marginal, rather than joint, distributions of marital status.

Table 2 shows the 1991 and projected marital status distribution of the oldest-old population of Britain. The legacy of the European marriage system and high sex ratios in young adulthood in the early decades of the twentieth century, which depressed the marriage chances of young women, are evident in the relatively high proportions of never-married oldest-old women in 1991. The passage to later older age of the cohorts born in the inter war period, who had much higher nuptiality rates after World War II, is evident in the projected decline in this proportion. Projected changes in mortality, and in sex differentials

Table 2. Distribution (%) and projected distribution of the oldest-old population of England and Wales (per cent) by age and gender.

	Males				Females			
	85–89	**90–94**	**95+**	**85+**	**85–89**	**90–94**	**95+**	**85+**
Married								
1991	41.3	26.0	13.4	37.6	8.5	2.8	1.0	6.7
2011	37.4	24.8	13.4	32.4	12.0	4.7	1.1	8.5
2035	41.6	29.1	16.8	35.8	20.8	9.4	2.4	15.1
Single								
1991	7.1	6.7	8.6	7.1	13.1	13.9	15.7	13.5
2011	7.3	5.7	5.2	6.7	7.5	8.0	9.7	7.9
2035	8.9	6.9	5.7	8.1	6.7	6.1	6.4	6.5
Widowed								
1991	50.9	66.8	77.4	54.6	77.8	83.0	83.0	79.4
2011	53.1	68.0	80.4	58.9	77.8	85.4	88.0	81.3
2035	44.0	59.2	73.7	51.0	64.1	76.8	84.9	70.5
Divorced								
1991	0.7	0.5	0.6	0.7	0.5	0.3	0.3	0.5
2011	2.3	1.5	1.0	2.0	2.7	1.9	1.2	2.3
2035	5.5	4.8	3.8	5.1	8.4	7.7	6.3	7.9
Total(000s)(=100%)								
1991	146.9	34.5	6.0	187.4	398.2	138.3	34.6	571.1
2011	302.9	111.2	33.5	447.6	451.6	213.8	102.8	768.9
2035	540.1	219.7	87.9	847.7	655.6	293.4	158.1	1107.0

Source: Own projections based on unpublished data supplied by GAD, see text for explanation.

in mortality, as well as past variations in nuptiality, are reflected in projected increases in the proportion currently married. This will have more impact on women: for example, among women aged 90–94 in the 1991 Census, only 2.8 per cent were married, whereas the projected figure for 2035 is 9.4 per cent. Conversely there are projected declines in the proportions never-married, especially for women, and for the widowed, where, for example, the figure for 85–89-year-old women is expected to fall by 14 percentage points between 1991 and 2035.

The overall numbers of the oldest-old are expected to rise, with those of men rising at a faster rate than those of women. However, the numbers of single (never-married) people will remain effectively constant in the first two decades of the twenty-first century, since in these age groups the increased proportions surviving are offset by the smaller proportions who never married. Thus the number of never-married people aged 85 and over projected for 2021 is 91,800 compared with 90,300 in 1991; but by 2035 it is projected to reach 140,400. All of this increase will be in the number of single men; the number of single women is projected to continue declining throughout the period considered here, despite the large increase in the total number of oldest-old women. As a result, by 2035 never-married oldest-old men will outnumber their female counterparts, a very marked change from the 1991 situation when never-married women aged 85 and over outnumbered never-married men of the same age by nearly 6:1 (76,970:13,320). The effect of nuptiality and mortality change is that there is likely to be a somewhat smaller proportion of the oldest-old without a partner, but the overall increase in numbers will mean that the absolute numbers who are unpartnered will also rise.

The rise in proportions married is partially offset by the emergence of the group that shows the fastest rise, the divorced population, but this group starts from a very low baseline. By the end of the period, there will be broadly similar proportions of divorced and single people aged 85 and over. Marriage peaked around 1970 in Britain; and the birth cohorts of the 1950s and later who were to experience the much lower marriage rates of the last three decades only start to appear among the oldest-old at the end of the period we are considering. The sharp increase in divorce that took place from the late 1960s in Britain means that this will impact on the oldest-old progressively from about 2020; and when combined with the lower current rates of marriage, proportions unmarried will rise again. It is likely that the oldest-old in the early part of the twenty-first century will have experienced the highest rates of partnership of any cohort, before or after.

After spouses, children constitute the major kin resource for the oldest-old population. The availability of at least one child is important not just because of the potential support that children may provide, but also because having children is a necessary prerequisite for having biological-grandchildren and great grandchildren. Current estimates, based on the 1999 Omnibus Survey of living kin, are that 74% of the British population aged 80 years and over are members of families containing at least three living generations and that 32% have at least one living child, grandchild and great-grandchild (Grundy, Murphy, and Shelton 1999).

Differences in the nuptiality patterns of cohorts, and in marital fertility, mean that fluctuations in the proportion of oldest-old who have at least one child may be considerable.

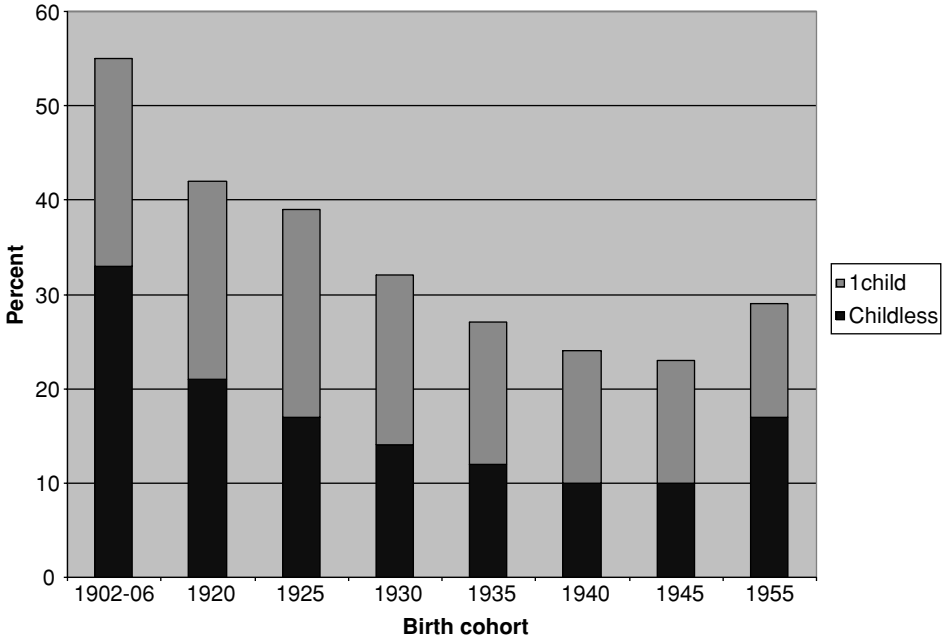

Figure 1. Per cent of women with no or only 1 child at age 45 by birth cohort, England and Wales. *Source:* Data from 1951 Census 1% tables and OPCS PP2 no. 12 and FM1 no. 13 presented in Grundy 1996.

Figure 1 shows the proportion of women childless, or with one child only, at age 45 for cohorts born in the first half of the twentieth century. Rates of childlessness were high among those born in the first decades of the twentieth century, low in the 1935–45 birth cohorts, and are increasing again in more recent cohorts. Similar trends are evident in a number of developed countries (Prioux 1993). The childbearing pattern of the twentieth century is one determinant of the availability of children among the oldest-old in the first part of the twenty-first century, whether the oldest-old have children alive also depends on the mortality experienced by these children.

In order to examine how these trends are likely to evolve in the next 50 years or so and their sensitivity to mortality change, we estimated the proportions with no, one, and two or more living children at different ages according to the projected sex-specific mortality levels of the 1996 British Official Projections (Shaw 1999), and the distributions expected if the mortality rates of 1990 were to hold. We use a series of birth histories of women aged under 60 obtained from the General Household Survey (GHS) for 1986 to 1995 as the base population. These data collected the survival status of the children at survey date and we projected the expected number of surviving children for cohorts who were born between 1925 and 1955 (we assume that childbearing is effectively complete by age 40). The results are shown in Figure 2.

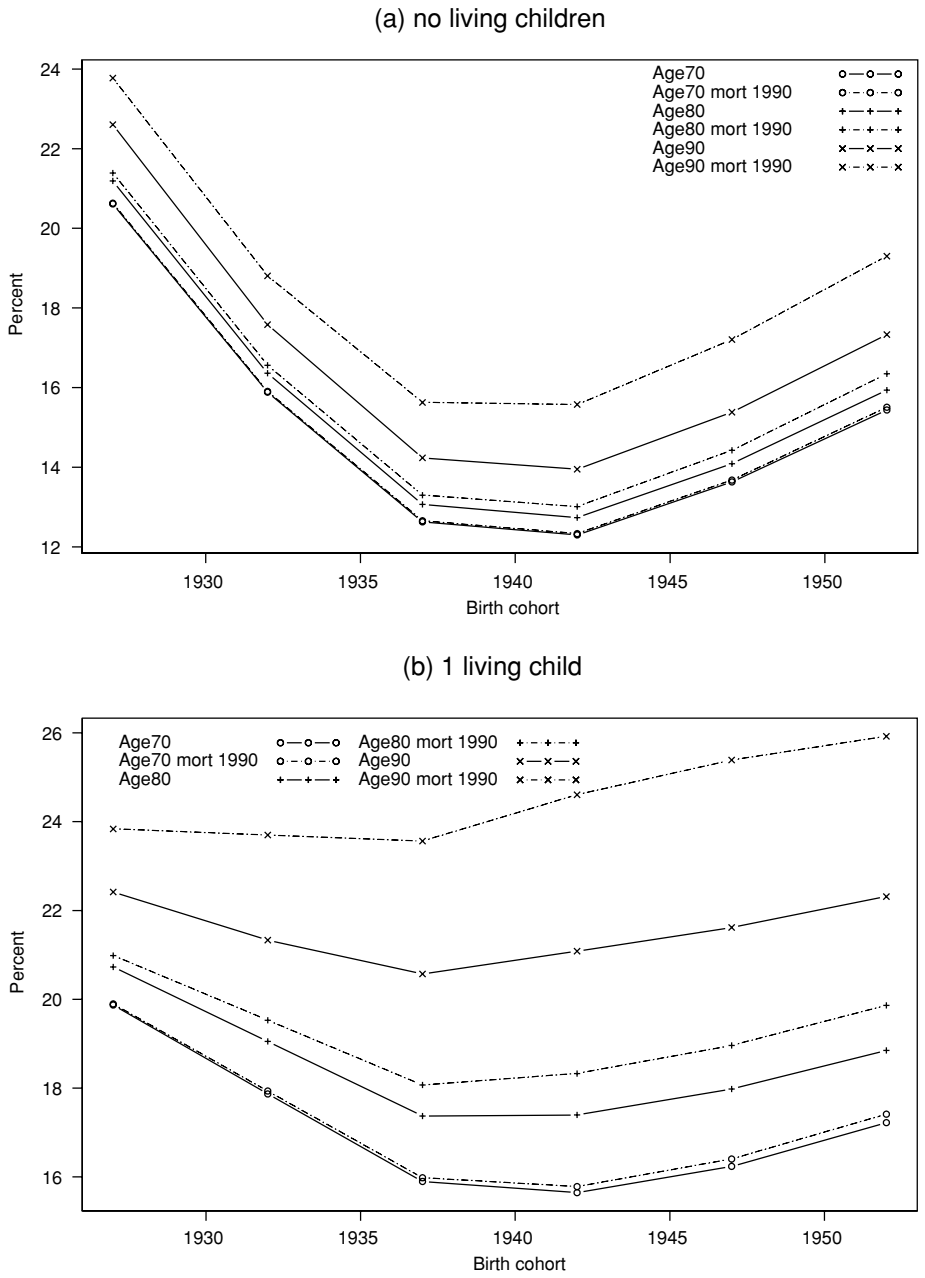

Figure 2. Proportions of women (%) with no, one, and two or more living children by age, cohort, and projected mortality level, England and Wales. (a) Proportions with no living children; (b) Proportions with one living child; (c) Proportions with 2+ living children. *Source:* Authors' projections based on birth history data from General Household Survey: see text.

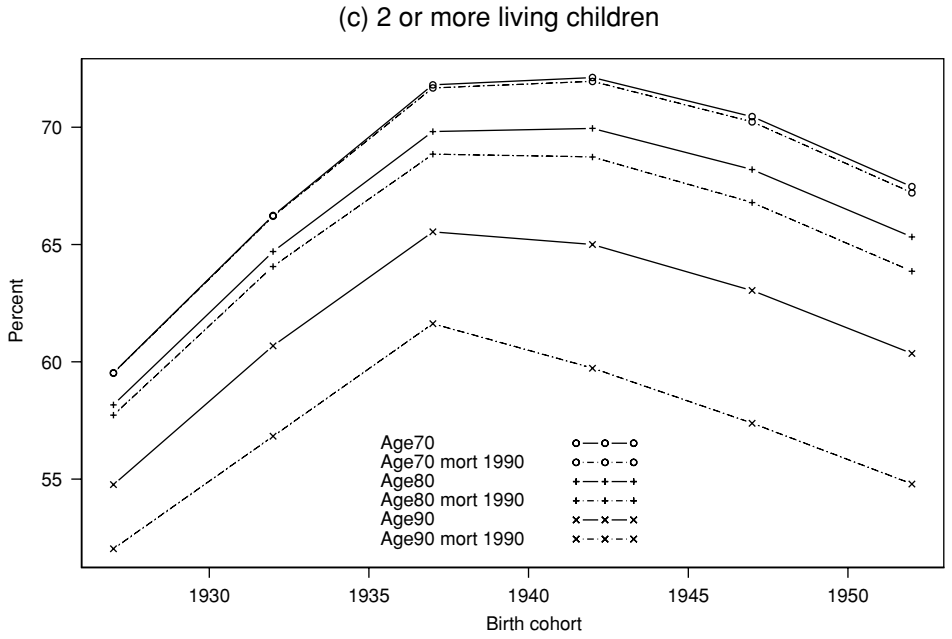

Figure 2. (*Continued*)

Although the sources of Figures 1 and 2 are different, they show a high degree of consistency, with slightly higher proportions childless in Figure 2 than in Figure 1, reflecting the fact that the latter takes account of intervening mortality of children. The trends in childlessness are similar with both sources showing a trough for the birth cohort of the early 1940s.

Figure 2 shows that the numbers with surviving children are sensitive to rates of mortality improvement only for the oldest-old. The effect for the 'younger-old' is less, reflecting the fact that changing mortality rates have a strong effect only when the children themselves are aged around 60 or over (as risks of death at earlier ages are low). In 2050, the proportion of women aged 90 who would have no surviving child would be about two per cent lower with the expected mortality improvement than if mortality rates remained at the 1990 levels (Figure 2a). However, these differences are small compared with the effect of fertility, which means that the proportion of 90-year-olds born 1926–30 without surviving children is likely to be about 23 percent, but will fall to 14 percent for those born around 1940, before rising again in later cohorts.

The effect of mortality on number of children of the oldest-old is more substantial. The proportions of those aged 90 with two or more living children would be about five percentage points higher around the middle of this century, if mortality continues to improve in line with expectations, than if it were to remain at 1990 levels (Figure 2c).

Marital Status, Household Type and Household Transitions

In Britain and other Western populations marital status has a major effect on the living arrangements of older people. All developed countries have shown a marked trend towards growing residential independence in older age groups, including the oldest-old, with living alone or just with a spouse now the predominant living arrangement for those in private households (Wall 1989; Kramarow 1995; Ogawa and Retherford 1997; Grundy 1999). As shown in Figure 3, the mean number of co-residents of men and women aged 85–89

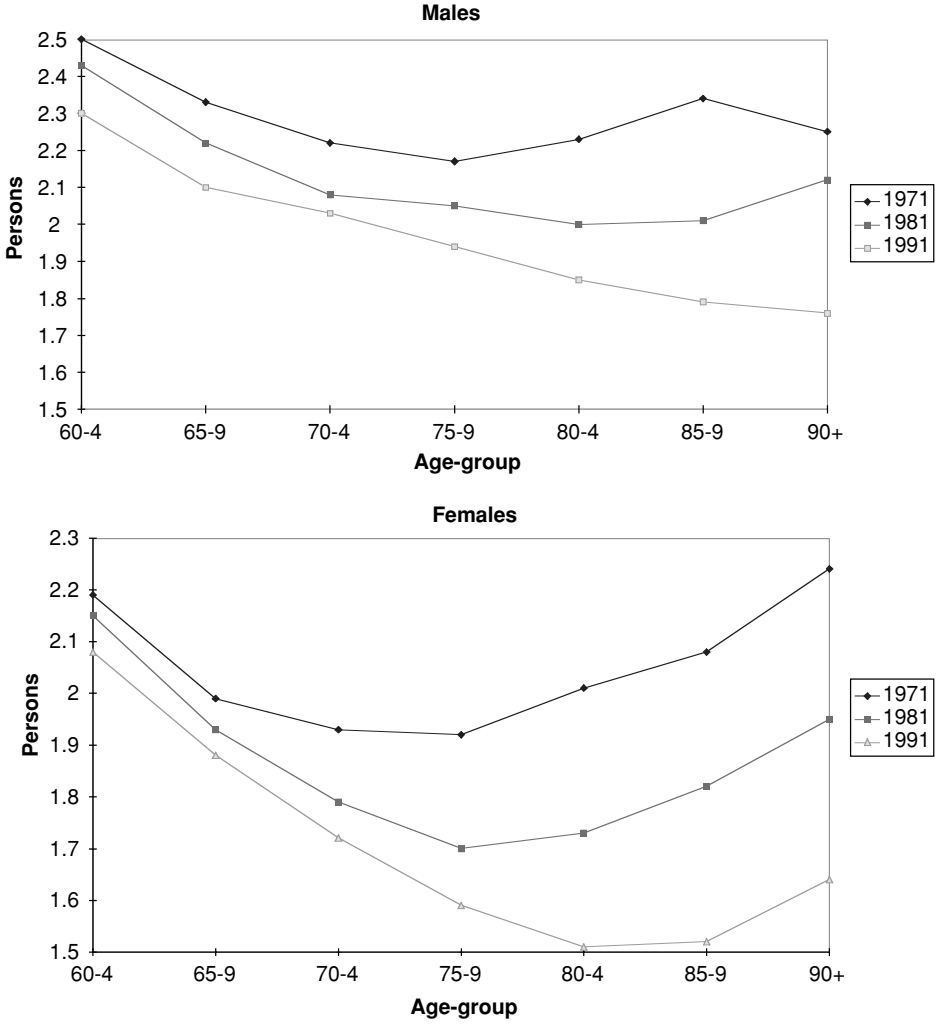

Figure 3. Average household size lived in by age, England and Wales, 1971, 1981 and 1991. ***Source:*** **Analysis of ONS Longitudinal Study data reported in Grundy 1996.**

Table 3. Distribution (%) of the population aged 85 and over by family/household type, England and Wales 2001.

Family/household type	Men	Women
Solitary	32.3	54.6
Couple only	37.5	7.7
Couple + others	4.2	0.9
Lives with a child[a]	7.3	11.1
Lives with other relative	2.0	2.1
Lives with non relative	0.7	0.7
Institution	13.2	23.0
Total	100	100
N	2911	7669

Source: Analysis of data from ONS Longitudinal Study (cross sectional data).
[a] with married or unmarried child of any age (but not with own spouse).

or 90 and over was considerably lower in 1991 than in 1971, even though the proportion unmarried was slightly lower. It is also noteworthy that in 1991 there is much less evidence of a late age increase in household size than in earlier years. This indicates a decrease in the proportion of oldest-old moving in with relatives, a conclusion supported by analyses of household transitions (Grundy and Glaser 1997). The distribution of the oldest-old population by detailed family/household type is shown in Table 3. The large effect of gender differentials in marital status is evident in the very different proportions of men and women living with a spouse. More than half of all women and a third of all men lived alone (these proportions represent 71% of women and 37% of men in private households). Among women living in an institution (defined as an establishment in which meals and services are centrally provided) was the second most usual residential arrangement; fewer than a quarter of women aged 85 and over lived in a private household with other household members. The proportions of both men and women who lived with a child (and not with a spouse) were low, although among these very old women living with a child was more usual (11.1%) than living with a spouse (8.6%).

The longitudinal data in the ONS LS make it possible to analyse household dynamics by looking at changes in the households in which individual sample members lived in successive censuses. This analysis is of course restricted to survivors and only allows comparison of points in time ten years apart, which means that not all intercensal changes are captured. Table 4 shows for those aged 75 and over in 1991 (and so 85 and over in 2001), who in 1991 were living in private (non institutional) households, the proportion who lived in the same broad family/household type in 2001 as in 1991; the proportion in a different type of private household; and the proportion who by 2001 were resident in institutions. Only permanent residents in the various categories are considered (defined as resident there for at least six months or having no other address) and the pre-dominant types of institution were nursing homes or residential homes for older people. Most of those entering these types of homes have chronic mentally or physically disabling conditions, such as Alzheimer's disease or stroke. In this analysis we have distinguished those who lived in a lone parent family in 1991—that is without their own spouse but with a

Table 4. Changes in household type 1991–2001 among men and women aged 75 and over in 1991 by family/household type in 1991, England and Wales.

	Family/household type in 2001				
Family/household type in 1991	**Same**	**Other private**	**Institution**	**All**	**N**
Men					
Solitary	71.6	7.2	21.1	100	525
Couple only	56.2	33.7	10.2	100	1592
Couple + others	35.2	58.6	6.2	100	162
Lone parent family[a]	64.6	20.8	14.6	100	48
Complex	39.1	43.8	17.2	100	128
All	57.4	29.9	12.7	100	2455
Women					
Solitary	70.3	5.7	24.1	100	3667
Couple only	26.4	56.8	16.8	100	1704
Couple + others	15.6	71.4	13.0	100	154
Lone parent family[a]	70.1	14.1	15.8	100	304
Complex	39.1	37.4	23.5	100	580
All	54.5	24.1	21.4	100	6409

Source: Analysis of ONS Longitudinal Study (longitudinal data)
[a] Lives with never-married child of any age (but not with own spouse).
Complex = Lives with ever-married child, other relative or non-relative.

never-married child—from those living with ever-married children who are here grouped with those living with other relatives or non-relatives (in the category labelled 'complex'). This is because household dynamics among those with a child who has never-married (and often never left the parental home) are rather different from those among older people living with a married child, in most cases because the parent has moved to join them (Grundy 1999). Among both women and men those living alone or in a lone parent family in 1991 were the most likely to be in the same type of private household ten years later. Transitions to institutions were highest among those living alone or in complex households, predominantly comprising unmarried elderly people living with ever-married children, and lowest among those who in 1991 lived with a spouse and one or more others. Multivariate analyses including all those aged 65 and over in 1991 (Table 5) show clearly the strong association between family/household type and transitions to residence in an institution. Those who lived with just with spouse or with a spouse and others in 1991 were much less likely to reside in an institution in 2001 than were those who lived alone in 1991.

The 'protective' effect of living with a spouse in 1991 appears higher for men than for women; however for women initial marital status may be a poorer indicator of actual marital status at time of moving to an institution. Table 6 shows transitions to institutions by marital status at the end of the period (2001) and shows clearly the high risk among the unmarried, particularly the never-married. Thirty-eight percent of never-married women aged 80 and over, and 28% of never-married men, who were living in private households in 1991 were resident in an institution ten years later, compared with 16% of women (and 7% of men) who were married in 2001.

Table 5. Odds ratios from logistic regression models of the proportion of those aged 65 and over in 1991 and then living in private households and who by 2001 were resident in institutions.

Sex and age in 1991	Odds ratio	95% confidence interval
Men		
65–9(Ref)	1.00	
70–4	1.99	1.56–2.53
75–9	5.21	4.12–6.60
80+	11.19	8.57–14.61
Family/household type 1991		
Solitary (Ref)	1.00	
Couple only	0.40	0.33–0.49
Couple + other	0.19	0.12–0.31
Lone parent family	1.00	0.58–1.71
Complex	0.88	0.63–1.24
N	13562	
Women		
65–9 (Ref)	1.00	
70–4	2.26	1.95–2.63
75–9	5.09	4.39–5.88
80+	11.78	10.12–13.72
Family/household type 1991		
Solitary (Ref)	1.00	
Couple only	0.67	0.60–0.75
Couple + other	0.39	0.29–0.55
Lone parent family	0.52	0.40–0.68
Complex	0.94	0.79–1.11
N	23158	

Source: Analysis of ONS Longitudinal Study Data.
Complex = living with ever married child, other relative or non relative in 1991
Controlling for presence of limiting longstanding illness and housing tenure in 1991.

Table 6. Transitions to institutions, England and Wales 1991–2001: Percent of those in private households in 1991 who by 2001 were resident in an institution, by marital status in 2001.

		Marital status in 2001				
	Age in 1991	Never-married	Married	Wid/Div	All	N
Women	75–9	22.4	6.1	16.6	15.8	4230
	80+	37.7	15.5	32.2	31.9	2233
Men	75–9	14.9	4.4	15.3	9.9	1857
	80+	28.1	6.7	27.1	20.1	647

Source: Analysis of ONS Longitudinal Study Data.

These results show that, as would be expected, having a spouse reduces the likelihood of moving to an institution. Similar findings have been reported in studies from other developed countries (Dolinsky and Rosenwaike 1989; Carriere and Pelletier 1995). As already noted, in these analyses we considered only permanent residents of institutions (or other types of households) and the predominant institutional residences were nursing or residential homes offering long term care to disabled older people. Having a spouse has also been shown to be associated with chance of dying at home, a preferred option for many with terminal conditions such as cancer, rather than in hospital (Grundy *et al.* 2004). Using information from the ONS Longitudinal Study on place of death, recorded at death registration, we found that 18% of people who died at ages of 80 or over during the period 1991–95 died at home. For those dying of cancer (but not from other causes), chance of a home death was significantly raised for those who in 1991 were living with a partner.

The strong associations between marital status and institutional residence and marital status and place of death for those dying from cancer, have a number of implications for both policy makers and researchers. For the former, the possible effects of changes in the marital status distribution on demand for long-term institutional care and shorter term hospice or hospital care for cancer patients are clearly paramount. For the latter, another very important issue is how to take account of a range of selection effects, including marital status and health related transitions to institutions, when analysing association between marital status, family support, and indicators of well-being. In Britain, as such large proportions of the never-married oldest-old population with health problems live in institutions, those that remain living alone are selected for good health.

Marital Status, Household Type and Health: Selection and Protection Effects

The marital status, household type, and wider social networks of the oldest-old are important not just because they are indicative of potential support available, but also because they may have more direct effects on health and well-being**.** A long and extensive literature has shown associations between marital status and indicators of health with the married, having the best health, followed by the never-married and then the formerly married (Vebrugge 1979; Hu and Goldman 1990; Cheung 2000). This association is hypothesised to reflect both positive health selection (unhealthy people are less likely to marry, stay married, or remarry) and the protective effects of companionship, care when ill, sexual intimacy, material advantages (especially for women), domestic services, and control of unhealthy behaviours (especially for men) (Umberson 1992; Hahn 1993; Waite 1995; Murphy, Glaser, and Grundy 1997; Lund *et al.* 2002). It has been suggested that this association may weaken, or even be reversed, in older women. Goldman, Korenmen, and Weinstein (1995) found that never-married older women had better health outcomes than their married counterparts, a result the authors attributed to more extensive social ties built up as an alternative to marriage. Grundy and Sloggett (2003), analysing English data on a range of health indicators among people 65–84 also found that, after control for socioeconomic indicators, social support, and smoking behaviour, never-married women had significantly better outcomes on several health indicators than married women. Both these analyses were based on private household samples; and, as we have already discussed, as institutional residence is associated both with marital status and health, the exclusion of those in institutions is

thus likely to lead to some bias. Analyses of British census data including the institutional population have shown a continuing, although weaker, advantage for the married, even in the oldest age groups in proportions reporting limiting long-term illness (Murphy, Glaser, and Grundy 1997). These rather divergent results suggest that cohort and context factors, extent of control for possibly confounding variables and choice of health indicator are all likely to influence the observed relationship between health and marital status, especially among women, and it seems that more work is needed to resolve this debate.

Although married people, particularly men, generally appear to have better health than the unmarried, living with someone other than a spouse does not seem to confer the same advantage. However, it is difficult to assess the impact of living arrangements on health because of the strong association between health, and changes in health, with moves between different types of household. Those who move in with relatives may do so because disability precludes remaining alone (Wolf and Soldo 1988; Crimmins and Ingegneri 1990; Speare, Avery, and Lawton 1991). Living alone in oldest-old age groups may only be a possible, or desirable, option for those in reasonable health with good support systems. Numerous, predominantly cross-sectional, studies of the whole elderly population have found that those living alone are healthier than those living with adults other than a spouse, or even, in some cases, than those living with a spouse (Cafferata 1987; Magaziner *et al.* 1988; Glaser, Murphy, and Grundy 1997; Hébert, Brayne, and Spiegelhalter 1999). However, there are some indications that elderly men may have poorer psychological health if they live alone. Moreover, recent results from longitudinal studies have found that, after controlling for initial health status, elderly people living alone in the USA had a higher risk of functional decline than elderly people living with others (Mor *et al.* 1998; Sarwari *et al.* 1998), although in the latter study this only applied to those who were severely impaired at baseline. A few studies have also reported more cognitive decline in relatively isolated elderly people (Fabrigoule *et al.* 1995; Bassuk *et al.* 1999; Fratiglioni *et al.* 2000).

These studies are important in that they consider several types of social links, not just co-residence, and a wide literature suggests that such wider links may have important implications for health (for reviews see Bowling 1994 and Bowling and Grundy 1998). Fratiglioni's study of Swedes aged 75 or over at baseline took account of marital status, living arrangement, frequency of contact with children, other relatives and friends, and satisfaction with these contacts. After a three-year follow-up it was found that individuals living alone and those without any close social ties both had an adjusted risk for developing dementia of 1.5. The authors concluded that an extensive social network seemed to protect against dementia and noted that groups such as the childless and those living alone could compensate by having other close ties. Unsatisfying contacts with children were also associated with higher risks suggesting that quality of contacts may be as important as quantity.

Unfortunately large, longitudinal data sets of the oldest-old that include information on kin networks and social ties, as well as information on marital status and household composition, are sparse. In Britain, Bowling *et al.*'s longitudinal study of 640 people aged 85 and over in Hackney, a relatively deprived area of London, included information on social networks and a range of health outcomes. Results showed that social networks tended to

shrink in size over time, largely due to falls in the number of close relatives, and that social isolation was associated with a higher mortality risk among men. Among women, attendance at social clubs was associated with lower mortality (Bowling *et al.* 1995; Grundy *et al.* 1996). (These results come from analysis in which health status and disability, and changes in health and disability, were controlled.) Very few of the oldest-old in this survey lacked any social or emotional ties; and a large majority, including the never-married, the childless and those living alone, were well supported by friends and relatives. However, the baseline sample included only those in private households. By follow-up three years later 14% of the sample had no social network. Small social networks were associated with lower life satisfaction at both baseline and follow-up and losses of friends were associated with worsening life satisfaction, again after control for status and disability (Bowling *et al.* 1995).

Marital Status, Household Type, and Perceived Social Support

In the absence of comprehensive nationally representative longitudinal data on the oldest-old in Britain, in the following section we use data from the Health Survey for England (HSfE) to analyse variations in perceived social support by marital status and household type. This annual survey, initiated in 1991, collects detailed information on a range of health indicators and health-related behaviours based both on self-reports and observational methods. There is some slight variation from year to year in topics covered. In our analyses we have combined data from the 1993–1995 surveys, which included a measure of perceived social support, to yield a sample of just over 9,400 persons aged 65 and over, of whom close to 1,900 were aged 80 years or more. The measure of perceived social support used in the HSfE was developed for the earlier health and Lifestyle Survey and was based on responses to seven questions (see Appendix), each of which had three possible responses. The composite social support score derived from these thus ranges from 0 to 21. We followed the developers of the scale in categorising those with a score of less than 18 as having a severe lack of social support and those with scores of 18–20 as having some lack of social support (Blaxter 1990; Colhoun and Prescott-Clarke 1996).

Figures 4 and 5 show mean social support score and the probability of lack of perceived social support by age and sex. Among men, but not women, there are signs of declining perceived social support among the oldest-old; however the numbers on which the figures are based are fairly small at these older ages.

In the sample aged 65–79, men, but not women, who lived alone had significantly increased odds of a perceived lack of social support, as shown in Table 7. This table presents results from logistic regression analyses in which survey year, age, physical complaints, social class, and smoking status were controlled. Even more striking is the increased risk of perceived severe lack of social support among the never-married, again particularly among men. This gender differential is consistent with the results of many studies which suggest that women have stronger social links than do men and are better able to compensate for the loss or absence of a spouse through their other ties. Selection factors, including the differing proportion of very old men and women excluded from the sample because of residence

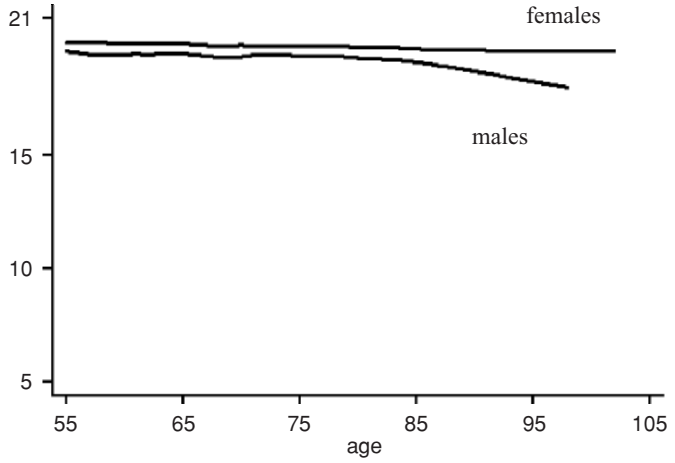

Figure 4. Mean perceived social support score (smoothed) by age. ***Source:*** **Analysis of Health Survey for England data 1993–95.**

in an institution, may also be important. It should also be noted that in the cohorts who now constitute the oldest-old, never marrying was more usual for women than for men. Never married men in very old age groups may include a larger proportion of people with personal characteristics that reduced the chances of marriage and other close relationships. These results lend support to the argument that one of the important mechanisms whereby marital status influences health is through the provision of emotional support.

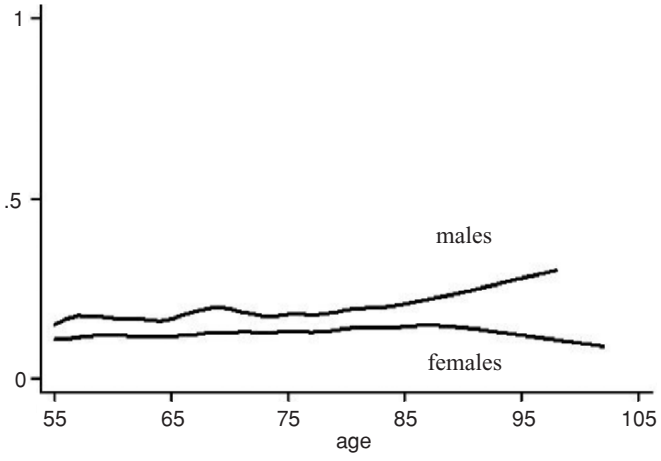

Figure 5. Probability of severe lack of perceived social support by age. ***Source:*** **Analysis of Health Survey for England data 1993–95.**

Table 7. Associations between marital status and perceived severe lack of social support, and living arrangements and perceived severe lack of social support, England 1993–95.

	Men				Women			
	65–79		80+		65–79		80+	
	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
Never-married	2.84***	2.08–3.87	4.30***	1.96–9.45	1.97***	1.41–2.77	1.57	0.85–2.90
Married (Ref)	1.00		1.00		1.00		1.00	
Wid/Div	1.49***	1.19–1.87	1.02	0.67–1.58	1.01	0.83–1.22	0.88	0.56–1.38
N	3288		628		4218		1249	
Lives alone	1.87***	1.53–2.29	1.32	0.87–2.00	1.11	0.91–1.35	0.96	0.61–1.50
Lives with spouse (Ref)	1.00		1.00		1.00		1.00	
Lives with others	1.46	0.97–2.20	1.39	0.56–3.40	1.12	0.78–1.60	0.67	0.33–1.32
N	3287		628		4205		1248	N

*** P<.001; *Source:* Analysis of data from the Health Survey for England, 1993–95.
Controlling for age, survey year, smoking status, physical conditions, and social class.

Implications for the Future

In the short term, demographic influences on the attributes of the oldest-old population appear fairly favourable. The population of never-married women is declining in relative terms and the population of the still married is increasing. In Britain and a number of other European countries, the oldest-old of the next 20 years or so are on an historical cusp: they have the highest levels of partnership and surviving children of generations on either side (Murphy and Grundy 2003). This will tend to ameliorate some of the effects of the (relatively modest) increase in numbers of the oldest-old in the period. Historical variations in childlessness also imply an increasing supply (from a demographic perspective) of family care, particularly when declines in mortality, and consequent increases in the proportion of children surviving to mid life and beyond, are taken into account.

In the longer term prospects appear less favourable. Firstly, those whose marital histories have been disrupted by divorce will feature more strongly in the oldest-old populations of the future. Divorced adults obviously lack the support of a spouse which, as our analyses of transitions to institutions shows, is often a key factor in maintaining residential independence. Additionally studies based on the whole elderly population suggest that divorced elders, particularly men, have weaker ties with children than the married or widowed (Lye *et al.* 1995; Grundy and Shelton 2001). Secondly, as shown in Figure 2, cohorts born after the mid 20th century will include increasing proportions with no or few children. Although some have argued that 'families of choice' based on friendship networks may become increasingly important (Weeks 1999), the current evidence is that such networks do not provide much practical help for those with substantial care needs. Moreover, our analysis of Health Survey for England data shows that never-married elderly people have a significantly higher risk of a severe lack of perceived social support which suggests that, at least in those cohorts who now comprise the old and oldest-old population, friends do not compensate fully for a lack of close family links.

In this paper we have shown that marital status and family/household type exert a strong influence on transitions to institutions and, among men, on perceived social support. These results suggest that changes in the marital status composition of the oldest-old will have major implications for the demand for long term care. However, other parameters not considered here will also be important. These include possible changes in the willingness of younger family members to provide help to the oldest-old and changes in the needs of the oldest-old for assistance. In order to understand and quantify the effect of these influences it is clear that we need better data sets, preferably longitudinal, which include all of the older population, not just those in private households.

Appendix

Questions used in construction of perceived social support scale. Respondents are asked to indicate whether each statement is not true (scored 1), partly true (2) or certainly true (3). This part of the questionnaire is self completed.

There are people I know—amongst my family or friends—who do things to make me happy.

There are people I know—amongst my family or friends—who make me feel loved.

There are people I know—amongst my family or friends—who can be relied on no matter what happens.

There are people I know—amongst my family or friends—who would see that I am taken care of if I needed to be.

There are people I know—amongst my family or friends—who accept me just as I am.

There are people I know—amongst my family or friends—who make me feel an important part of their lives.

There are people I know—amongst my family or friends—who give me support and encouragement.

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References

Arber, S., and Ginn, J. (1990) "The meaning of informal care: Gender and the contribution of older people", *Ageing and Society*, 12:429–454.

Bassuk, S. S., Glass, T. A., and Berkman, L. F. (1999) "Social disengagement and incident cognitive decline in community-dwelling elderly persons", *Annals of Internal Medicine*, 131(3):165–173.

Blaxter, M. (1990) *Health and Lifestyles*. London: Tavistock/Routledge.

Bowling, A. (1994) "Social networks and social support among older people and implications for emotional well-being and psychiatric morbidity", *International Review of Psychiatry*, 6:41–58.

Bowling, A., Farquhar, M., and Grundy, E. (1995) "Changes in network composition among the very old living in Inner London", *Journal of Cross-Cultural Gerontology*, 10:331–347.

Bowling, A., Farquhar, M., Grundy, E., and Formby, S. (1993) "Changes in life satisfaction over a two and a half year period among very elderly people living in London", *Social Science and Medicine*, 36:641–655.

Bowling, A., and Grundy, E. (1998) "The association between social networks and mortality in later life", *Reviews in Clinical Gerontology*, 8:353–361.

Cafferata, G. L. (1987) "Marital status, living arrangements, and the use of health services by elderly persons", *Journal of Gerontology*, 42:613–8.

Carriere, Y., and Pelletier, L. (1995) "Factors underlying the institutionalization of elderly persons in Canada", *The Journals of Gerontology: Social Sciences*, 50B:S164–S172.

Cheung, Y. B. (2000). "Marital status and mortality in British women: A longitudinal study", *International Journal of Epidemiology*, 29:93–99.

Colhoun, H., and Prescott-Clarke, P. (1996). *Health Survey for England 1994*, Vol. 1, Findings. London: Her Majesty's Stationery Office.

Crimmins, E. N., and Ingegneri, D. G. (1990) "Interaction and living arrangements of older parents and their children", *Research on Aging*, 12:3–35.

Dolinsky, A. L., and Rosenwaike, I. (1988) "The role of demographic factors in the institutionalization of the elderly", *Research on Aging*, 10(2):235–257.

Fabrigoule, C., Letenneur, L., Dartigues, J. F., Zarrouk, M., Commenges, D., and Barberger-Gateau, P. (1995) "Social and leisure activities and risk of dementia: A prospective longitudinal study", *Journal of the American Geriatric Society*, 43(5):485–490.

Fratiglioni, L., Wang, H.-X., Ericsson, K., Maytan, M., and Winblad, B. (2000) "Influence of social network on occurrence of dementia: A community-based longitudinal study", *Lancet*, 355(9212):1315.

Glaser, K., Murphy, M., and Grundy, E. (1997) "Limiting long term illness and household structure among people aged 45 and over, Great Britain 1991", *Ageing and Society*, 17:3–20.

Goldman, N., Korenman, S., and Weinstein, R. (1995) "Marital status and health among the elderly", *Social Science and Medicine*, 40(12):1717–1730.

Grundy, E. (1996). "Population review: the population aged 60 and over", *Population Trends*, 84:14–20.

Grundy, E. (1999) "Household and family change in mid and later in England and Wales". In: McRae, S. (ed.), *Changing Britain: Families and Households in the 1990s.* Oxford: Oxford University Press, pp. 201–228.

Grundy, E., Ahlburg, D., Ali, M., Breeze, E., and Sloggett, A. (1999) *Disability in Great Britain: Results from the 1996/97 Disability Survey*. Department of Social Security Research Report. London: The Stationery Office. ISBN 0-11-762571.

Grundy, E., Bowling, A., and Farquhar, M. (1996) "Social support, life satisfaction and survival at older ages". In: Caselli, G., Lopez, A. (eds.), *Health and Mortality Among Elderly Populations*. Oxford: Clarendon Press, pp. 135–156.

Grundy, E., and Glaser, K. (1997) "Trends in, and transitions to, institutional residence among older people in England and Wales, 1971 to 1991", *Journal of Epidemiology and Community Health*, 51:531–540.

Grundy, E., Mayer, D., Young, H., and Sloggett, A. (2004) "Living arrangements and place of death of older people with cancer in England and Wales: A record linkage study", *British Journal of Cancer*, 91:907–912.

Grundy, E., Murphy, M., and Shelton, N. (1999) "Looking beyond the household: Intergenerational perspectives on living kin and contacts with kin in Great Britain", *Population Trends*, 97:19–27.

Grundy, E., and Shelton, N. (2001). "Contact between adult children and their parents in Great Britain 1986–1999", *Environment and Planning A*, 33:685–697.

Grundy, E., and Sloggett, A. (2003) "Health inequalities in the older population: The role of personal capital, social resources and socio economic circumstances", *Social Science and Medicine*, 56:935–947.

Hahn, B. A. (1993) "Marital status and women's health: The effect of economic and marital acquisitions", *Journal of Marriage and the Family*, 55:495–504.

Havens, B. (1997) "Long-term care into the 21st century", *Bold*, 7:2–4.

Hébert, R., Brayne, C., and Spiegelhalter, D. (1999) "Factors associated with functional decline and improvement in a very elderly community-dwelling population", *American Journal of Epidemiology*, 150(5):501–510.

Hu, Y., and Goldman, N. (1990) "Mortality differentials by marital status: An international comparison", *Demography*, 27(2):233–250.

Kramarow, E. A. (1995) "The elderly who live alone in the United States: Historical perspectives on household change", *Demography*, 32:335–352.

Lye, D. N., Klepinger, D. H., Hyle, P. D., and Nelson, A. (1995) "Childhood living arrangements and adult children's relations with their parents", *Demography*, 32:261–280.

Magaziner, J., Cadigan, D. A., Hebel, J. R., and Parry, R. E. (1988) "Health and living arrangements among older women: Does living alone increase the risk of illness?", *Journals of Gerontology*, 43(5):M127–M133.

Martin, J., Meltzer, H., and Elliot, D. (1988) "OPCS surveys of disability in Great Britain, report 1". *The Prevalence of Disability Among Adults*. London: HMSO.

Mor, V., Murphy, J., Masterson-Allen, S., and others. (1989) "Risk of functional decline among well elders". *Journal of Clinical Epidemiology*, 42:895–904.

Murphy, M., Glaser, K., and Grundy, E. (1997) "Marital status and long-term illness in Great Britain", *Journal of Marriage and the Family*, 59:156–164.

Murphy, M., and Grundy, E. (2003) "Mothers with living children and children with living mothers: The role of fertility and mortality in the period 1911–2050", *Population Trends*, 112:36–45.

Murphy, M., and Wang, D. (1999) "Forecasting British families into the 21st century". In: McRae, S. (ed.), *Changing Britain: Families and Households in the 1990s*. Oxford: Oxford University Press, pp. 100–137.

National Statistics. (2005) "Report: 2003-based marital status and cohabitation projections for England and Wales", *Population Trends*, 121:77–84.

Ogawa, N., and Retherford, R. D. (1997) "Shifting the cost of caring for the elderly back to families in Japan: Will it work?", *Population and Development Review*, 23:59–96.

Prioux, F. (1993) "L'infecondite en Europe". In: Blum, A., Rallu, J.-L. (eds.), *European Population Vol. 2*, Demographic Dynamics. Paris: John Libbey Eurotext.

Sarwari, A. R., Fredman, L., Langenberg, P., and Magaziner, J. (1998) "Prospective study on the relation between living arrangement and change in functional health status of elderly women", *American Journal of Epidemiology*, 147(4):370–378.

Saunders, P. A., Copeland, J. R., Dewey, M. E., Gilmore, C., Larkin, B. A., Phaterpekar, H., and Scott, A. (1993) "The prevalence of dementia, depression and neurosis in later life: The liverpool MRC-ALPHA study", *International Journal of Epidemiology*, 22(5):838–847.

Shaw, C. (1999) "1996-based population projections by legal marital status for England and Wales", *Population Trends*, 95:23–31.

Shaw, C., and Haskey, J. (1999) "New estimates and projections of the population cohabiting in England and Wales", *Population Trends*, 95:7–17.

Speare, A., Avery, R., and Lawton, L. (1991) "Disability, residential mobility, and changes in living arrangements", *Journals of Gerontology*, 46:S133–S142.

Sundstrom, G. (1994) "Care by families: An overview of trends", *Caring for Frail Elderly People*. Paris: OECD, pp. 15–55.

Umberson, D. (1992) "Gender, marital status and the social control of health behavior", *Social Science and Medicine*, 34(8):907–917.

Van Imhoff, E., and Keilman, N. W. (1991) *LIPRO 2.0: An Application of a Dynamic Demographic Projection Model to Household Structure in the Netherlands*. Amsterdam: Swets & Zeitlinger.

Verbrugge, L. M. (1979) "Marital status and health", *Journal of Marriage and the Family*, 41:267–285.

Waite, L. J. (1995) "Does marriage matter?", *Demography*, 32:483–507.

Wall, R. (1989) "The residence patterns of the elderly in Europe in the 1980s". In: Grebenik, E., Hohn, C., Mackensen, R. (eds.), *Later Phases of the Family Cycle: Demographic Aspects*. Oxford: Clarendon Press, 222–244.

Weeks, J., Heaphy, B., and Donovan, C. (1999) "Families of choice: Autonomy and mutuality in non-heterosexual relationships". In: McRae, S. (ed.), *Changing Britain: Families and Households in the 1990s*. Oxford: Oxford University Press, pp. 297–315.

Wenger, G. C. (1984) *The Supportive Network: Coping with Old Age*. London: Allen and Unwin.

Wenger, G. C. (1996) "Social networks and gerontology", *Reviews in Clinical Gerontology*, 6:285–293.

Wolf, D., and Soldo, B. (1988) "Household composition choices of older unmarried women", *Demography*, 25:387–403.

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