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ESSENTIALS OF Environmental Epidemiology for Health Protection

A handbook for field professionals



EDITED BY
IRENE A. KREIS, ARACELI BUSBY,
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advice in all cases. The information in this work is intended to be useful to the
general reader, but should not be used as a means of self-diagnosis or for the
prescription of medication.

Preface

The establishment of the United Kingdom Health Protection Agency (HPA) in 2003 created a new focus for skills development and training in environmental public health. At that time, most postgraduate courses in public health were generic in nature, and did not necessarily provide the depth of specialist environmental public health knowledge, skills, and competencies needed for HPA staff to fulfil their roles in advising and supporting local authorities, the UK National Health Service, the emergency services, and other agencies. The HPA will become Public Health England (PHE) in April 2013 where these knowledge, skills, and competencies will continue to be needed.

There is also a continuing need for specialist training in environmental public health for staff in other agencies, including local authority environmental health practitioners and emergency planning officers. This should comprise a comprehensive and structured national approach to education and training, within the framework of continuing professional development and a national scheme of accredited master's level modules and programmes in health protection.

Spiby (2006) developed a model of core competencies required of those working in environmental public health that reflected the need for a 'coming together of the knowledge and skills base of environmental science, public health, clinical toxicology and environmental epidemiology'.

Two main domains of competency were recognized:

1. Specialist environmental public health knowledge and skills, and
2. Generic organizational skills.

The first domain contained five areas of competency:

- A. Toxicology
- B. Environmental Science
- C. Environmental Epidemiology
- D. Risk Assessment and Risk Management
- E. Environmental Public Health.

The second identified the following areas:

- A. Teaching
- B. Research
- C. Management and Leadership.

The need for this book

In developing an ‘Essentials of Environmental Epidemiology for Health Protection’ training module it became clear that there was no single suitable text for students coming from a variety of specialist backgrounds. In particular, no one book covered the epidemiology and investigation of common environmental exposures, such as water contaminants, air particulates, clusters, toxic waste sites, electromagnetic fields, and lead using a problem-orientated approach

Intended audience

This book, a companion to the recently published *Essentials of Toxicology for Health Protection* (Baker, 2012), is aimed at a wide range of professionals working in environmental public health, including health protection consultants, specialists and trainees, public health practitioners, environmental health practitioners, environmental scientists, and staff of the emergency services, the water and waste industries, and other industrial and regulatory bodies.

It is assumed that most readers will be graduates with a good knowledge of public health sciences and an ability to analyse problems. The problem-orientated approach makes the book accessible to field practitioners who require an understanding of the essentials of environmental epidemiology and its uses in a very practical and accessible way.

The scope of the book

Each chapter of the book has been written by an invited expert or experienced practitioner in the specific topic and it covers a broad spectrum of issues in environmental epidemiology.

Section 1 *Identifying the problem* (Chapters 2–6) provides a general introduction to the subject and explains how environmental epidemiological data can be used to evaluate an issue of concern.

Section 2 *Assessing the problems and developing a scoping study* (Chapters 7–13) reviews the environmental epidemiology methods which can be used when developing a protocol for the investigation of a problem.

Section 3 *Environmental epidemiology design and problem analysis* (Chapters 14–18) provides the tools for quantitative analysis of the issue considered to be of most concern.

Section 4 *Special topics* (Chapters 19–26) addresses in detail a selection of important case studies addressing specific issues in environmental epidemiology which illustrate particular investigative approaches.

Many of the chapters were informed by many more sources than could be referenced in the book. Therefore, the authors, editors and the HPA have made a website available with full resources lists. The is available at: <http://www.hpa.org.uk/Publications/ChemicalsPoisons/>

We hope that this book on the *Essentials of Environmental Epidemiology for Health Professionals* will prove useful not only to those who will use these techniques as part of their work but also to all who seek a greater understanding of the impact of the environment on our society.

Irene A. Kreis
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Chapter 19 Clusters: this chapter is based on the Advisory Report of the Health Council of the Netherlands (HCN) (2001). *Local Environmental health concerns; risk communication, exposure assessment and cluster investigation* (<http://www.gr.nl> or <http://www.health-council.nl>), also used as basis for the Dutch Environmental guideline for Municipal Public Health Services about cancer clusters (2012). (<http://www.rivm.nl>).

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List of abbreviations

BSE	bovine spongiform encephalopathy	NO ₂	nitrogen dioxide
CDC	Centers for Disease Control and Prevention	NRES	National Research Ethics Service
CI	confidence interval	O ₃	ozone
CO	carbon monoxide	ONS	Office for National Statistics
COPD	chronic obstructive pulmonary disease	OR	multigroup
CSCI	Commission for Social Care Inspection	PAF	population attributable fraction
DALY	disability-adjusted life year	PAH	polycyclic aromatic hydrocarbon
DH	Department of Health	PCT	Primary Care Trust
dL	decilitre	PDT	passive diffusion tube
DSR	directly standardized rate	PII	personal identifiable data
ED	Emergency Department	PM ₁₀	fine particles with aerodynamic diameter <10 µm
ELF	extremely low-frequency	PM _{2.5}	fine particles with aerodynamic diameter <2.5 µm
EMF	electric and magnetic field	PTSD	post-traumatic stress disorder
EPA	Environmental Protection Agency	QA	quality assurance
EPHT	environmental public health tracking	QC	quality control
GIS	geographical information systems	ReSST	Real-time Syndromic Surveillance Team
GP	general practitioner	RF	radiofrequency
H ₂ S	hydrogen sulphide	RR	relative risk
HCN	Health Council of the Netherlands	RSD	relative standard deviation
HHWS	heat health watch system	SAGE	Stakeholder Advisory Group on ELF EMFs
HPA	Health Protection Agency	SHA	Strategic Health Authority
HPU	Health Protection Unit	SITREPS	situation reports
IARC	International Agency for Research on Cancer	SMR	standardized mortality ratio
IPCC	Intergovernmental Panel on Climate Change	SO ₂	sulphur dioxide
ISEE	International Society for Environmental Epidemiology	SOP	standard operating procedure
km	kilometre	TCDD	2,3,7,8-tetrachloordibenzo-para-dioxin
m	metre	µT	microtesla
NHS	National Health Service	VOC	volatile organic compound
NICOLA	Network for Industrially Contaminated Land in Europe	WHO	World Health Organization
		WMA	World Medical Association

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Section 1

Identifying the problem

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Chapter 1

Introduction to environmental epidemiology for health protection

Irene A. Kreis

Learning objectives

- ◆ Place and value environmental epidemiology among other health disciplines such as other epidemiology branches, toxicology, environmental science, and health protection.
- ◆ Evaluate and apply various prioritization methods that can be used by a local public health practitioner presented with environmental issues.

Epidemiology is the study of the distribution of health and disease in a population, and the determinants of this distribution (Baker and Nieuwenhuijsen, 2008). Environmental epidemiology therefore concerns the environmental determinants of the distribution of health and disease. The environment is a broad concept encompassing the constructed surroundings that provide the setting for human activity, ranging from large-scale geographical spaces to small personal places as well as physical and biological factors that, along with their chemical interactions, can affect an organism. Therefore, environmental epidemiology deals with a very wide range of determinants of health such as air, water, soil, and food.

A consequence of this breadth is that environmental epidemiology has strong relationships with other disciplines such as toxicology and environmental science. In this book, you will see contributions from these and other fields. These inter-relationships strengthen environmental epidemiology, and collaboration across the disciplines is an important aspect of work in public health. Public health practitioners need to become familiar with the terminology and perspectives of these other disciplines to enrich their understanding and response to the environmental problems they encounter. The multidisciplinary environment is one of the main charms of working in environmental epidemiology. These connections can be illustrated by considering a real situation, and describing the contributions each discipline made to our understanding of the problem.

1.1 Lead poisoning: an example of environmental toxicity

Lead has been recognized as dangerous to health for as long as it has been used (Kazantis, 1989). From classical chronicles, we know that the ancient Greeks and Romans were aware of acute lead poisoning, and by the Middle Ages it was called Poitiers colic. By the 1800s, the link had been made between adverse pregnancy outcomes and women being occupationally exposed. In spite of this, lead continued to be used, with production increasing with the spread of industrialization. Throughout most of the 20th century lead was a constituent of paints and petrol and was widely used in water pipes. These products were particularly effective in spreading lead throughout our environment, into our air, soil, food, drinking water, and homes. Such widespread use contributed greatly to the measurable lead body burden of children and adults.

Toxicology is the study of the adverse health effects of chemicals on living organisms. It has contributed to our knowledge of the effects of lead by establishing that, once ingested, it is mainly deposited in the bones. This finding played a major role in helping us to understand how lead is transferred from a pregnant woman to her fetus. Developing babies receive their calcium from their mother's bone store and toxicologists showed that during the mobilization of calcium, any lead in the bones would also become available to the fetus. The amount of lead that is mobilized will increase dramatically if a woman is calcium deficient. This knowledge has allowed us to develop the simple mitigating strategy of giving calcium supplements to women with a high lead burden, thus limiting the mobilization of the lead and reducing exposure of the fetus.

Environmental science is a broad discipline that examines the interaction between human society and the natural environment. The link with environmental epidemiology derives from its examination of environmental pollution and degradation. Studies from environmental science have established the extent and concentration of lead pollutants to which communities have been (or are) exposed. For example, they identified the collection of lead in roof dust as a result of the deposition of air pollutants from leaded petroleum, and they identified lead in soil as a result of both petrol pollutants and degrading paint. This has made it possible to develop effective lead removal programmes ranging from local initiatives to renovate houses safely to national legislation about the use of lead in paint and in petrol.

Environmental epidemiology has contributed substantially to our knowledge of the widespread toxic effects of lead. We have moved from the acute poisonings of the late 1800s to the relatively subtle decreases in intelligence quotient in children, identified through epidemiological studies. These subtle effects were first recognized in the 1960s and 1970s (Lanphaer et al., 2005; Grandjean and Landrigan, 2006), and consequently have led to policy changes on acceptable blood lead concentration, with US guidelines falling from 60 µg/dL surplus and confusing in 1960 to a proposed 2 µg/dL in 2006 (Gilbert and Weiss, 2006).

Policy changes have resulted in a reduction of lead in the environment. This might suggest that, as a public health practitioner, issues due to environmental lead exposure are unlikely to arise. However, there are still many sources of lead exposure. People living in older houses may be exposed to old lead paint and dust, lead water pipes, and other lead

sheet materials (Gilbert and Weiss, 2006). There may be groups in our community who come from areas in the world with poor regulation of lead, leading to exposures in industry and consumer goods. We may also encounter people who are exposed through the use of traditional cosmetics and medicines (Mahmood et al., 2009). In addition, the legacy of our widespread use of lead means that most soils in the developed world contain some lead. It is becoming apparent that there is exposure to lead through the consumption of vegetables, cereals, and nuts, and this may be at a sufficient level to have negative effects on the intelligence of children (European Food Safety Authority, 2010).

1.2 Prioritizing actions for health protection

The focus of this book is on the skills an environmental epidemiologist or a public health practitioner in a local unit might need to deal with environmental health issues. Many chapters describe technical skills relevant to dealing with a recognized health problem. Another important skill is the ability to prioritize between competing environmental health issues and other public health work. It will be necessary for practitioners to decide whether an epidemiological study is justifiable, and in these situations, it is advisable to use a priority setting framework. These frameworks make the relevant benefits and risks explicit, and, consequently, aid discussion and decision-making.

The Health Protection Agency (HPA) in the UK suggests that, in making a submission to the HPA board, a priority setting process should have considered the following topics:

1. Clinical and public health effectiveness (the strength of scientific evidence).
2. Cost-effectiveness of the public health activity/programme. The likely burden of the disease or public health problem on services, including overall population costs.
3. The wider societal benefits and implications.
4. The overall financial costs to the institution, including opportunity costs.
5. A focus on reducing health inequalities, reducing service inequities, and avoiding discrimination.
6. Political, or other, concerns about each disease or health problem.
7. The impact on quality of life on those concerned.
8. The ease of transmission of each disease or public health problem.
9. Public opinion around the disease or health problem (HPA, 2009).

This is a useful framework although not all points are relevant to local environmental investigations. In the context of lead exposure, it can be used to assess the need to investigate the level of lead burden of the local population where there have been indications that environmental lead exposures are above acceptable levels. The framework can help demonstrate the pros and cons of undertaking the assessment, and provide support for a funding application. There would be benefits because:

(Re: 1) the strength of the evidence is great.

(Re: 3) the social benefits of having unaffected people in the population is clear (and quantifiable).

(Re: 4) the cost of dealing with larger numbers of children and adults with impaired IQ levels is considerable (and quantifiable).

(Re: 5) lead exposure is usually higher in more deprived areas and thus associated with health inequalities.

Additional benefits include well-established techniques for environmental sampling of lead and relatively straightforward biological sampling techniques.

These benefits would need to be balanced against the cost-effectiveness of remedial action. Remediation could require substantial resources because it may involve removing lead pipes or contaminated soils (for example, in playgrounds/fields). Who would legally be responsible for paying for such remediation work needs to be known at the outset, and a good understanding of applicable policies and regulations is important. It would also be worth considering the intrusiveness of the investigation (such as taking lead blood samples in the case of lead) and the implications of the study design for the interpretation of the results.

Another barrier to getting agreement for action is the perception that issues like lead poisoning are no longer relevant. It is therefore important in environmental epidemiology to be able to communicate about risk effectively to both professionals and the public. The priority setting framework is useful for communication with experts and public officials but this approach is unlikely to be adequate for public communication. Research suggests that the public evaluate risks differently to experts. The reaction of the public tends to reflect issues such as familiarity, vulnerability, acceptability, fear, voluntariness, controllability by others, benefits, what is known by science, and how quickly the health effect will occur (Visschers et al., 2007). For example, for a problem of lead burden in children, the public typically see the exposure as involuntary, controlled by others, affecting a vulnerable population, and with a serious, long-lasting health effect.

1.3 Conclusion

The practice of environmental epidemiology in health protection involves dealing with a wide range of potential determinants of ill health such as pollutants in air, water, soil, and food as well as other substances. It is necessary to set priorities about what to investigate, and this requires a balancing act between what is amenable to investigation, what the funders think is important and what the public finds relevant. Practitioners need to be aware of the lessons from past experiences and be ready to collaborate with other disciplines. It is important not to be restricted to the standard approach but to choose between all the options available. Doing this is likely to result in powerful, well-planned epidemiological studies. This book aims to help you to do this.

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Epidemiology of environmental hazards

Giovanni S. Leonardi

Learning objectives

- ◆ Justify prioritizing environmental hazards for health protection.
- ◆ Evaluate the key environmental hazards in Europe.
- ◆ Judge the role of relative, absolute, and attributable risks in assessing hazards.
- ◆ Evaluate the advantages and limitations of carrying out multinational environmental epidemiology studies.

2.1 Introduction

An epidemiologist strives to study and control the factors that influence the occurrence of disease or other health-related conditions and events in defined populations, has expertise in population thinking and epidemiological methods, and is knowledgeable about public health and causal inferences in health. If the health of the public is to be protected against environmental hazards, epidemiology needs to be applied to these. However the application of epidemiology within a public service requires considerations beyond those needed to produce scientifically valid results. In addition to striving for methodological competence, practitioners of environmental epidemiology within a public health service need to:

- ◆ apply their skills to setting the priorities for epidemiology work most likely to improve health in the community by review of many environmental hazards to health
- ◆ commission investigations by appropriately skilled investigators
- ◆ organize appropriate research in response to an emergency or as a proactive activity when no academic unit is available to address a topic of public interest, and
- ◆ based on available epidemiological and other information, design appropriate public health interventions effective at reducing the hazard to health.

This chapter will review key results of environmental epidemiology focusing on their relevance to the application of environmental epidemiology as a component of a public health service.

2.2 Environmental epidemiology in practice

Public health protection operates in a health service dominated by tight budgets and concern for the care of patients with chronic disease. The environment is often only considered as a public health problem when a big bang occurs, either physically in the form of an explosion or other incident causing serious harm to those present, or perceived threat to health whether or not there is any real effect. Therefore, epidemiology may only be thought of as useful when applied to acute environmental hazards, and these are indeed familiar if not common scenarios within the service. However, nothing could be further from the truth because most of the preventable disease burden of environmental hazards is attributable to ongoing, if not recognized or visible, exposure to factors that can be traced back to common everyday activities such as breathing, eating, walking. This is illustrated in Fig. 2.1.

Based on this evidence, it is crucial that epidemiology within a public health agency considers chronic exposures, both of single chemicals and mixtures, as will be illustrated by the following scenarios.

2.2.1 Case study 1: A landfill concern

A group of residents complained to their local authority about the smell coming from a waste landfill in the vicinity of their dwellings. Apart from the unpleasantness of the odour, many were concerned about possible impacts on their health as well as on the value of their property. Therefore the local director of public health would consult with

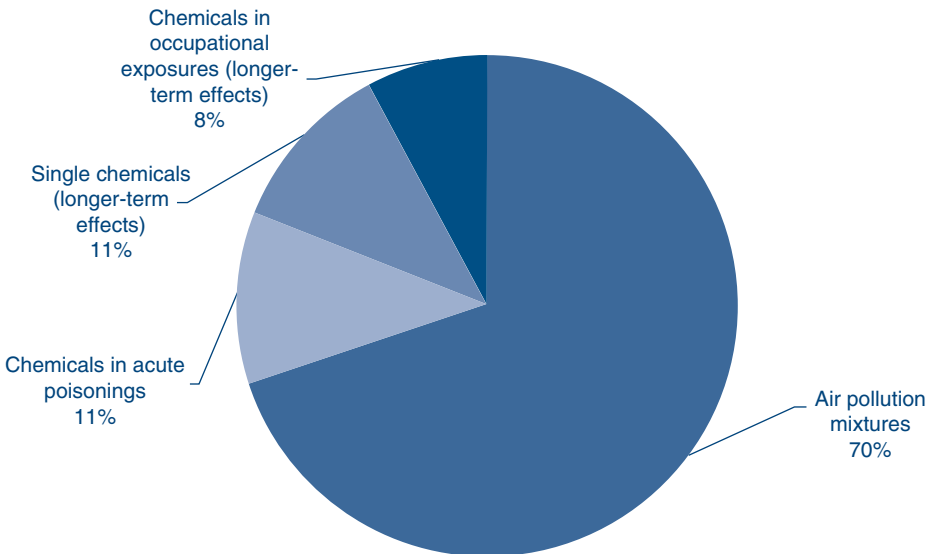


Fig. 2.1 Distribution of known burden of disease from chemicals.

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the local specialist in health protection to consider: Which of these concerns should be followed-up? What criteria could be used to decide? What design and analytical issues may be involved in a population study? What communication issues? A study on population exposure was conducted in this example (Mohan et al., 2009).

2.2.2 Case study 2: water (acute and chronic issues)

A national public health institute was tasked to examine the potential consequences of a report on arsenic concentrations in drinking water supplies across several local authorities, which indicated that a substantial proportion were above the current water guideline value recommended by the World Health Organization. The national parliament had agreed an initial intervention to bring all water supplies into compliance with the guideline but this reduction of population exposure would be very costly. The public health institute was asked to examine the possibility that water supplies containing arsenic at concentrations a little above the guideline value could still be regarded as safe. As a member of the public health team, what information would you wish to examine for an initial assessment of the potential value of environmental epidemiology in these circumstances?

What is the role of routine data in establishing the need to conduct an in-depth investigation? What is the role of attributable fraction in establishing such need? What is the balance between innovative measurement techniques and the use of well-established ones? What is the balance between planning, execution, and analysis of such studies? A study on arsenic risk assessment and molecular epidemiology (ASHRAM) was conducted to address this (Leonardi, 2012).

2.3 Evidence on health effects of environmental hazards

2.3.1 Definitions

Mostly, disease from environmental causes cannot be distinguished from disease from other causes. At present, cardiovascular deaths attributable to air pollution cannot be identified by examination of the body, for example. It might take much effort to gain the detailed biological and pathological knowledge that allows us to characterize the environmentally-caused features in specific diseases. This has not stopped scientists reaching sufficient consensus on the causation, for example, of cardiorespiratory disease by air pollution to lead to effective interventions. The demonstration that a certain environmental factor is a cause has been derived by analysing differences in disease incidences by geography and over time, and by studying disease rates in migrant populations. Epidemiologists have identified many environmental causes of disease with sufficient certainty to justify interventions. These achievements have been the result of population-level thinking and careful group comparisons.

Population thinking comprises considering information relevant to population health in space and time (Chapters 19 and 21), as well as measurement issues, such as validity and accuracy of exposure information (Chapters 7 and 8). It is typical of environmental epidemiology that an initial exploration of the problem starts from definition of the exposure and its population prevalence, rather than case definition. For example, when

designing the ASHRAM study, a key first activity was establishing the proportion of population potentially exposed at different arsenic concentrations.

Group comparison comprises application of principles of study design (Chapter 14), statistics (Chapter 17), and causation.

Measure of effect in epidemiology refers to measures which describe the effect of a certain exposure on the occurrence of disease. The most common measures of effect are the difference in disease occurrence between exposed and unexposed and the ratio of disease occurrence between exposed and unexposed. The latter is usually called the relative risk (RR).

The contribution of a risk factor to a disease or a death is quantified using the *population attributable fraction* (PAF). PAF is the proportional reduction in population disease or mortality that would occur if exposure to a risk factor were reduced to an alternative ideal exposure scenario (e.g. no tobacco use). Many diseases are caused by multiple risk factors, and individual risk factors may interact in their impact on overall risk of disease. As a result, PAFs for individual risk factors often add up to more than 100%.

When estimating *burden of disease* based on epidemiological evidence, summary measures are required that integrate information from several studies. The disability-adjusted life year (DALY), is a time-based measure that combines years of life lost due to premature mortality and years of life lost due to time lived in states of less than full health.

2.3.2 Disease-based overview

Several cancers have been associated with exposures to occupational and environmental risk factors (International Agency for Research on Cancer (IARC), 2004). The effects of carcinogens have been particularly well documented in the occupational setting, with 28 agents considered to be definite, 27 agents probable, and 113 agents as possible occupational carcinogens. This information is relevant to the general population when the occupational carcinogen is present outside the workplace and the distribution of its exposure is known. Lung cancer causes the largest disease burden of all cancers globally, about 15% of the total cancer burden. By far the largest risk factor for lung cancer is smoking (PAF = 86% in the UK). About 9% of the disease burden of lung cancer has been attributed to occupation, about 5% to outdoor air pollution, and 1% to exposure to indoor smoke from solid fuels. Other exposures that pose a risk include exposure to environmental tobacco smoke, radon and occupational exposure to ionizing radiation, asbestos, and other chemicals (e.g. chromium, nickel, cadmium, arsenic). It was estimated that environmental factors account for 31% of the global disease burden of lung cancer and 30% (6–55%) of the disease burden in developed countries, for both men and women.

For cancer sites other than lung, there is strong epidemiological evidence for the following environmental factors as causes as assessed by the IARC (1990):

- ◆ bladder: aromatic amines, arsenic, coal tars, metalworking fluids, and mineral oils
- ◆ brain: ionizing radiation
- ◆ breast: ionizing radiation
- ◆ larynx: asbestos, metal working fluids, mineral oils, sulphuric acid
- ◆ leukaemia: benzene, ionizing radiation

- ◆ liver and biliary: ionizing radiation, trichloroethylene, polychlorinated biphenyls (PCBs), vinyl chloride
- ◆ mesothelioma: asbestos
- ◆ multiple myeloma: benzene, ionizing radiation
- ◆ nasal and nasopharynx: chromium, formaldehyde, mineral oils, nickel, wood dust
- ◆ non-Hodgkin's lymphoma: benzene, dioxin
- ◆ pancreatic: acrylamide, metal working fluids, mineral oils
- ◆ rectal: metal working fluids, mineral oils
- ◆ skin: arsenic, coal tars, creosotes, ionizing radiation, metalworking fluids
- ◆ soft tissue sarcoma: dioxin, ionizing radiation, vinyl chloride
- ◆ stomach: asbestos, metal working fluids, mineral oils
- ◆ thyroid: ionizing radiation.

For non-cancer health effects, the world lacks an authoritative international agency that can coordinate the systematic evaluation of the available evidence on environmental hazards. However, the development of disease registries in several countries represents a resource toward this goal. Another element of progress will be integration of toxicological principles in the design and interpretation of population studies.

There is consensus that cardiovascular diseases can be caused by, amongst other factors, outdoor air pollution, risks in the workplace, exposure to chemicals such as lead, and exposure to indoor air pollution such carbon monoxide.

The most important risk factor for total respiratory disease burden is active smoking, estimated to contribute to 36% of the global disease burden of chronic obstructive pulmonary disease (COPD). Most other risk factors are occupational or environmental, including dusts and chemicals in the workplace, air pollution, and environmental (second-hand) tobacco. Asthma development and exacerbation can be triggered by a variety of indoor and outdoor environmental exposures.

Injuries are one of the largest disease groups with recognized preventable environmental factors. Epidemiology of injuries is complex but often directly applicable to evaluation of interventions for prevention of:

- ◆ road traffic injuries
- ◆ falls
- ◆ unintentional poisonings
- ◆ fires
- ◆ drowning
- ◆ natural hazards (e.g. floods, storms, periods of excessively hot or cold weather, earthquakes).

A summary of other confirmed or strongly suspected causes for other diseases is provided in Table 2.1

Table 2.1 Main disease groups with confirmed or strongly suspected linkage to chemicals

Diseases/disease groups	Examples of exposures	Examples of associated outcomes
Respiratory infections and chronic respiratory diseases	Occupational exposures to dusts, gases, irritant chemicals, fumes	Chronic obstructive pulmonary disease (COPD)
	Second-hand smoke; occupational exposures to cleaning-agents, pesticides, hairdressing chemicals etc.	Asthma onset and exacerbation
	Second-hand smoke	Acute lower respiratory infections
	Occupational exposure to asbestos, metal dusts, particulate matter	Asbestosis bronchitis, pneumoconiosis, silicosis
Perinatal conditions	Maternal exposure to pesticides or other chemicals	Low-birth-weight and preterm infants
Congenital anomalies	Maternal exposure to pesticides, polychlorinated biphenyls (PCBs), polychlorinated dibenzofurans (PCDFs), lead, mercury, other endocrine disruptors	Various birth defects
Diseases of the blood	Lead, arsine, naphthalene, benzene	Anaemia, methaemoglobinaemia
Neuropsychiatric and developmental disorders	Lead, methylmercury, PCBs, arsenic, toluene etc.	Cognitive development, mental retardation, Parkinson disease, attention-deficit disorder, Minamata disease
Sense organ diseases	Carbon disulfide, mercury, lead	Hearing loss
Cardiovascular diseases	Ultrafine particles in polluted air, lead, arsenic, cadmium, mercury, pollutant gases, solvents, pesticides, second-hand smoke	Ischaemic heart disease, cerebrovascular disease
Diabetes mellitus	Arsenic, N-3-pyridylmethyl-N'-p-nitrophenyl urea (rodenticide), 2,3,7,8-Tetrachlorodibenzo-p-dioxin.	Diabetes type II
Systemic autoimmune diseases	Crystalline silica dust	Systemic sclerosis, systemic lupus erythematosus, rheumatoid arthritis, systemic small-vessel vasculitis
Endocrine diseases	Ethanol, hexachlorobenzene	Porphyria
Genitourinary diseases	Beryllium, cadmium, lead	Calculus of kidney, chronic renal disease

(continued)

Table 2.1 (continued) Main disease groups with confirmed or strongly suspected linkage to chemicals

Diseases/disease groups	Examples of exposures	Examples of associated outcomes
Digestive diseases	Ethanol, chloroform, carbon tetrachloride, manganese	Hepatitis, cholestasis, pancreatitis
Skin diseases	Antiseptics, aromatic amines, cement, dyes, formaldehyde, artificial fertilizers, cutting oils, fragrances, glues, lanolins, latex, metals, pesticides, potassium dichromate, preservatives	Atopic dermatitis, allergic and irritant contact dermatitis, chloracne, hyperkeratosis
Musculoskeletal diseases	Cadmium, lead	Osteoporosis, gout
Oral conditions	Fluoride	Dental fluorosis
Poisonings	Accidental ingestion of household products, occupational exposures and accidents, intentional self-harm by ingestion of pesticides	Unintentional poisonings, self-inflicted injuries

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2.3.3 Environment-based overview

Instead of starting from a disease group and ascertaining all known preventable environmental causes, another approach is to consider several health impacts of a single exposure such as ‘noise’ or of several exposures pertaining to a single setting, such as transport or housing. An advantage of such an ‘environment-based’ approach is that it might be easier to interpret its results in terms of possible interventions at local or national level. An example of this approach is the recent review of housing related hazards prepared by the World Health Organization (WHO), summarized in Table 2.2 (WHO, 2011). Other available burden of disease overviews from WHO are available for outdoor air pollution, water, sanitation and hygiene, lead, mercury, second-hand smoke, smoke from solid fuel use, noise, occupational carcinogens, solar ultraviolet radiation, and climate change.

2.4 Disease burden of environment and related uncertainties

2.4.1 Overall burden of disease of environmental hazards

When experts review the burden of human disease attributable to preventable factors, they tend to focus on quantifiable direct effects, and this is true also for estimates concerning effects of environmental factors on human disease. WHO have estimated that 24% of the global disease burden (healthy life years lost) and 23% of all deaths (premature mortality) can be attributed to preventable environmental factors (Prüss-Üstün and Corvalán, 2006). This figure varies across the globe from 14% in Western Europe to over 30% in Africa. In many cases, disease burden was not quantifiable even though the health impacts are readily apparent. For instance, the disease burden associated with changed, damaged, or depleted ecosystems in general was not quantified. Therefore, the quantified burden, although based on specific assumptions that have a degree of uncertainty almost certainly underestimate of the true environmental burden of disease.

This quantified evidence is a key component of the knowledge required to motivate public health workers, but it has proven insufficient as a basis for developing effective environmental health services. Burden of disease estimates need to be supplemented by other approaches, highlighting and estimating expected future impacts on health of current environmental trends. Mathematical modelling and its application to development of decision support tools in the environmental health field, is an example of a tool for environmental health that deserves increased attention. Other approaches are provided by social sciences such as anthropology.

2.4.2 Uncertainties in estimating health effects of environmental hazards

Several considerations can be taken into account when judging the validity of a measured health effect caused by an environmental hazard, and the related estimate of burden.

2.4.2.1 Population thinking

Here we must consider if the authors evaluated a region in space or period of time as being most relevant to the question and whether they developed a valid measurement of

Table 2.2 Housing related hazards, their effects on health and burden of disease

Exposure	Health outcome	Exposure/ risk relationship	Population attributable fraction	Environmental burden from housing per year
Mould	Asthma deaths and DALYs in children (0–14 years)	RR = 2.4	12.3%	45 countries of WHO European Region: 83 deaths (0.06/100,000) 55,842 DALYs (40/100,000)
Dampness	Asthma deaths and DALYs in children (0–14 years)	RR = 2.2	15.3%	45 countries of WHO European Region: 103 deaths (0.07/100,000) 69,462 DALYs (50/100,000)
Lack window guards	Injury deaths and DALYs (0–14 years)	RR = 2.0	33–47%	WHO European Region: ~10 deaths (0.007/100,000) ~3310 DALYs (2.0/100,000)
Lack smoke detectors	Injury deaths and DALYs (all ages)	RR = 2.0	2–50%	WHO European Region: 7523 deaths (0.9/100,000) 197,565 DALYs (22.4/100,000)
Crowding	Tuberculosis	RR = 1.5	4.8%	WHO Euro B and C subregions: 15,351 TB cases (3.3/100,000) 3518 deaths (0.8/100,000) 81,210 DALYs (17.6/100,000)
Indoor cold	Excess winter mortality	0.15% increased mortality/ ^o	30%	11 European countries: 38,203 excess winter deaths (12.8/100,000)
Traffic noise	Ischaemic heart disease including myocardial infarction	RR = 1.17/10 dB(A)	2.9%	Germany only: 3900 myocardial infarcts (4.8/100,000) 24,700 ischaemic heart disease cases (30.1/100,000) 25,300 DALYs (30.8/100,000)

Radon	Lung cancer	RR = 1.08/ 100 Bq/m ³	2–12%	Three western European countries: France: 1234 deaths (2.1/100,000) Germany: 1896 deaths (2.3/100,000) Switzerland: 231 deaths (3.2/100,000)
Residential second-hand smoke	Lower respiratory infections, asthma, heart disease and lung cancer	Risk estimates range from 1.2–2.0	PAF estimates range from 0.6–23%	WHO European Region: 64,700 deaths (7.3/100,000) 713,000 DALYs (80.7/100,000)
Lead	Mental retardation, cardiovascular disease, behavioural problems	OR = 4.4	66%	WHO European Region: 694,980 DALYs (79.2/100,000)
Indoor carbon monoxide	Headache, nausea, cardiovascular ischaemia/insufficiency, seizures, coma, loss of consciousness, death	Case-fatality rate 3%; DNS/PNS incidence 3–40%	50–64%	WHO Euro A subregion: 114–1545 persons with DNS/PNS (0.03–0.4/100,000) 114 ± 97 deaths (0.03 ± 0.02/100,000)
Formaldehyde	Lower respiratory symptoms in children	OR = 1.4	3.7%	WHO Euro A subregion: 0.3–0.6% of wheezing in children
Indoor solid fuel use	COPD, ALRI, lung cancer	RR = 1.5–3.2	6–15%	WHO European Region: 8490 ALRI deaths in children <5 years (16.7/100,000) 293,600 ALRI DALYs in children <5 years (577/100,000) 5800 COPD deaths in adults ≥30 years (1.1/100,000) 100,700 COPD DALYs in adults ≥30 years (19.3/100,000)

ALRI = acute lower respiratory infections; COPD = chronic obstructive pulmonary disease; DALYs = disability-adjusted life years; DNS/PNS = delayed or persistent neurologic sequelae; OR = odds ratio; N/A = not available; RR = relative risk.

Reproduced with permission from WHO (2011). *Environmental burden of disease associated with inadequate housing: Methods for quantifying health impacts of selected housing risks in the WHO European Region* (Braubach, M., Jacobs, D.E., and Ormandy, D. Eds.). Available at: http://www.euro.who.int/_data/assets/pdf_file/0003/142077/e95004.pdf © World Health Organization 2011.

population exposure. For example, in case study 1 (section 2.2.1), measurement of exposed residents near a landfill might benefit from integration of information from monitoring, modelling, and responses from individuals. Self-reported information might be affected by participants' expected gain from a certain type of result, but integration of more objective methods would reassure about the validity of any later health assessment (Mohan, 2009). Effective study of exposures over long time periods requires measurements taken at multiple time points. Because repeated direct measurements can be prohibitively burdensome, it may be necessary to develop alternative strategies that rely on external indicators of exposure. In case study 2 (section 2.2.2), exposure of participants could include historic information or measured concentrations only, and although the former is based on older data as well as being less precise from the point of view of laboratory analysis, it might provide a valid proxy for exposure at a crucial period in life not otherwise directly assessable (Hough, 2010). The choice of exposure indicator would have practical consequences as it may lead to different estimated health effects and this could affect the ranking of the importance of the health issue in terms of the need for intervention (Fletcher, 2011).

2.4.2.2 Group comparison

Here we must consider if the health effect could be an artefact of the way the comparison group was selected. In case study 1 (section 2.2.1), any population study could consider whether participants might be more anxious about their health compared to non-participants, and more inclined to report ill health depending on the degree of anxiety. If participants are recruited more easily to the study from geographical areas where the environmental factor of interest is less frequently found, this could lead to an error in the health effect estimation. In case study 2 (section 2.2.2), this problem was minimized in the study design by including all hospitals in the study area and not just those where cases were diagnosed, although at considerable cost in terms of logistics and finance (Leonardi, 2012). We should also consider if the epidemiologist paid sufficient attention to exposures that can induce acquired susceptibility to disease; considered the importance of multiple exposures and their sequence in the determination of chronic diseases; and appreciated and allowed for the fact that interaction is not only a statistical concept, but is deeply rooted in our models of biological causation. Ignoring these aspects can often lead to errors in the estimation of the environmental effect. In case study 1, dispersion modelling of a 'tracer' pollutant informed about the pattern of possible exposure to multiple pollutants (Mohan, 2009). In case study 2, the estimated effect of arsenic on cancer was stronger in participants with urinary markers indicating incomplete metabolism of arsenic, and the statistical analysis of interaction was motivated by prior knowledge of the biological mechanisms involved in modification of arsenic metabolism and its effect on cancer (Leonardi, 2012).

2.4.2.3 Burden of disease attributable to environment

There are also several uncertainties in the calculation of the PAF for a hazard. Often the extent of population exposure is not well known; the estimation does not take into account widespread low exposures to a recognized harmful agent; exposures to suspected

hazards are not documented in good human studies; the analysis does not take into account that most chronic diseases arise from a complicated collection of multiple exposures, not exposure to single agents. As a result, the PAF estimates often underestimate the true disease burden.

2.5 Concluding remarks

All the considerations summarized in this chapter need to be taken into account when reviewing the evidence underlying a summary measure such as a PAF, therefore such summary measures should not be seen as stable over time but need to be revised as frequently as possible to reflect the constantly changing evidence base.

The complexity of information on the biological, toxicological, genetic, ecological, physical, and chemical aspects of the relationship between an environmental hazard and health is such that the combination of optimally exposed population, multidisciplinary scientific team, and practical means for doing the investigation is often difficult to identify within a single country. International collaborations are therefore key to the development of the evidence base. The additional advantage of international collaboration is in the identification and evaluation of appropriate control measures for common problems such as cross border movement of waste/chemical/goods etc, historical contamination issues, and sometimes also agreement on guidance and principles for implementation of exposure reduction activities. The disadvantages of international studies are related to the increased logistical and organizational complexity compared to more local studies; but these may well be a false economy when their costs and contribution are added up.

Having discussed the limitations of many currently available epidemiological measures of environmental effects on health, it is worth considering the future scope of research in this field combining analysis of genetic and environmental factors. Historically, studies of twins have been helpful to examine environmental and heritable factors in the causation of disease. For example, analyses of cohorts of twins from Sweden, Denmark, and Finland have shown that inherited genetic factors are significant in only a small number of cancers (such as prostate and colorectal cancer) and are of only a minor significance in most types of neoplasms. It follows that the environment has the principal role in causing sporadic cancer. Although this result refers to ‘environment’ in the broadest sense, comprising nutrition and social factors as well as physical and chemical agents, the importance of this should not be underestimated. It confirms the impression that the uncertainties in the estimation of accurate measures of effect and PAF for environmental hazards lead to underestimating the importance of such factors in causing disease. Given the social and economic benefits that have already been achieved even with the current shamefully incomplete knowledge of the situation, this information from twin studies should encourage renewed efforts to carefully design, implement, and interpret further environmental epidemiology studies of disease.

Identification, confirmation, and quantitative estimation of the importance of environmental hazards for health and disease are helped by the application of epidemiological methods to these issues. The relative importance of hazards is often difficult to establish,

due to the incomplete nature of the available information. Based on current evidence it seems reasonable to assume that for most disease there exists a set of environmental causes (including physical, chemical, nutritional, and social factors), that in principle account for the majority of the disease variation in space and time. Like for other public health problems, it is most efficient to address environmental factors at population level. Epidemiological findings confirmed in several populations and using a variety of methods and validation approaches to each of the relevant measurements are a solid foundation for planning interventions aimed at reducing exposures and thus reducing the burden of disease at population level.

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Literature reviews—systematic, but how and why?

Irene A. Kreis and David A. Cromwell

Learning objectives

- ◆ Synthesize the principles of systematic reviews and their role in the scoping of a problem.
- ◆ Critically evaluate possible data sources for systematic reviews.
- ◆ Design and conduct a systematic review on a defined topic and be able to present the methods and results correctly.

3.1 Introduction

There are many situations when a public health practitioner or an environmental epidemiologist is asked to write a summary of what is known about a particular topic. Two possible scenarios are:

1. needing to write about the specific health effects arising from the contamination of soil with persistent organic pollutants such as dioxin, particularly the hypothesis of a link with childhood leukaemia.
2. needing to contribute to a health risk assessment on the local development of a new waste incinerator for which the main pollutant of concern could be dioxin.

These scenarios will both require the collection and critique of scientific evidence from the environmental health literature. However, slightly different approaches are needed. In the first scenario, the aim will be to trace and summarize *all evidence* about the health effects of a particular exposure. The review will have a narrow focus and may be limited to the strongest pieces of evidence. In the second scenario, the aim will be to trace and summarize evidence about *all possible health effects* of the environmental source. The review will have a broad focus and may draw on varied sources of information.

While the aims of individual reviews may differ, the process should always have the same key feature: it should be systematic. This means that the strategy used to identify the literature is chosen so as to identify all relevant literature, and that the critique and

synthesis of the literature is performed in a transparent and unbiased manner. In addition, the process should be documented clearly enough to be reproducible. The challenge is balancing the need for rigour with the limitations imposed by the available time and resources.

3.2 Case study

The scenarios in this chapter both concern persistent organic pollutants, of which the most problematic is generally dioxin or 2,3,7,8-tetrachloordibenzo-para-dioxin (or TCDD) and related compounds. The mass media have labelled dioxins as ‘the most toxic materials in the world’ which has caused high levels of concern about dioxin exposure among the public. As a public (environmental) health practitioner, there will be various situations where you might encounter concern about these compounds. For example, dioxins can arise when organic material or matter containing chlorine (such as cables) burns at relatively high temperatures. So, a cable factory fire could trigger the need for a briefing paper that reviews the evidence on the effects of acute dioxin exposure. Alternatively, a dioxin problem might emerge when an established, illegal dumpsite containing pesticides or industrial waste is identified. In this situation, as the exposure may have existed for a long period, the aim of a review is likely to be broad, like scenario 2, and look at all possible health effects (World Health Organization (WHO), 2010).

3.3 The review

The methods for conducting systematic reviews of health care evidence are well developed, particularly in relation to evaluating health care interventions. In this area, the Cochrane Collaboration has taken a leading role in publishing methodological advice on how to identify clinical trials and combine their results in a meta-analysis to produce a more precise estimate of treatment effects.

Many systematic review methods proposed for the evaluation of health care interventions can be applied to reviews of environmental health issues (Bambra, 2011). There is most overlap when the systematic review aims to answer a precise question which is associated with a limited set of health effects. In this situation, following the Cochrane guide (Higgins, 2011) can help to formulate a precise topic/question and then to search for the relevant primary research studies that looked at the same set of outcomes. The methods may be less applicable when the review has a broader aim (such as to describe the causes of childhood leukaemia or scenario 2). In this situation, it may be impractical to examine and critique primary studies, and the principal approach will be to undertake a review of systematic reviews.

Nonetheless, both narrow and broad reviews can be separated into a number of steps. These steps will be described sequentially but it is important to remember that the process is iterative and it may be necessary to repeat earlier steps.

The key steps of a systematic review are:

1. Identifying experts and key literature to formulate/check the objective of the review.

2. Identifying a comprehensive set of literature by:
 - a. Searching abstracting databases using relevant terms
 - b. Snowballing from identified literature
 - c. Searching alternative information sources
 - d. Applying eligibility criteria.
3. Extracting relevant information from selected literature, and evaluating the scientific value of the publications.
4. (If necessary), performing a meta-analysis to produce a combined effect estimate.
5. Reporting your findings.

3.4 Review objectives, experts, and key literature

It is essential that the review objective is formulated as clearly as possible. This not only ensures the review answers the correct question, it also helps ensure that the subsequent steps are performed effectively and efficiently. For questions about the effectiveness of health care interventions, it is common to think of the review question as having four components, referred to as *PICO*:

1. the *population* or patient group
2. the *intervention* (or exposure)
3. the *comparison* or control, and
4. the *outcome(s)*.

Conceptualizing the aim into these four components is not always easy for environmental health problems. However, it can be used in scenario 1—the population would be children of a specific age range (the range may vary depending upon the context), the exposure would be dioxin, the comparison or control would be no exposure (although it can be debated whether this is relevant here), and the outcome would be childhood leukaemia.

Before starting a systematic search, it is necessary to understand the environmental issue in order to clarify the question. This is where experts in the area can help to focus on the right aspects of the problem, explain the levels of uncertainty that exist in specific areas, and highlight controversial issues. They are also likely to know the key pieces of literature and thus facilitate further searches.

A useful first step to finding appropriate experts is to contact a national body (such as the Health Protection Agency in England and Wales or the National Institute for Public Health and the Environment (RIVM) in the Netherlands). However, it is also good practice to identify people who the public may see as experts, even if not recognized as such by national bodies. This is good practice for two reasons. Firstly, if public engagement is an important part of the work it is helpful to have involved experts that the public recognize. Second, it can ensure all issues are recognized at the start. Even if everyone does not agree with an ‘expert’, it can ensure that their opinions are not ignored and, if necessary, challenged.

While a national health (protection) body can also be a useful source of documents on the problem of interest, it is now common to search the Internet with a search engine such as Google. If we consider the question posed in the second scenario, in Google:

- ◆ ‘Waste incinerator’ identifies a European Union directive which indicates possible health effects but also indicates guidelines for emissions. Dioxin is mentioned in the summary.
- ◆ ‘Dioxin’ gives a lot of country/language specific information and, by using your ISP address, Google will direct you to the local health authorities dealing with these problems (if you did not already know who they are).

Web searches can generate widely different results depending upon the search terms used so it is important to record what was done and what it produced. A range of search terms should also be used to achieve a broad coverage of the topic.

Once sufficient insight is achieved to clarify the aim of the review, a more systematic search can be done. The precise question should lead to a set of eligibility criteria for including and excluding studies from the review. These will generally incorporate information about the population, the intervention/exposure, and (if relevant) the comparison as well as the types of studies that should be considered. It may not be necessary to specify the outcome as part of the eligibility criteria, although the primary outcome would be pre-defined for scenario 1 type reviews. The aim is to find all relevant studies regardless of the outcomes an individual study might report.

3.5 Identify a comprehensive set of literature

3.5.1 Searching abstracting databases

The abstracts of peer-reviewed journal articles are collected together on a number of databases, such as Medline and Web of Science. As no abstracting databases will cover all potentially relevant journals, it is good practice for a systematic review to search a minimum number of databases. Medline and Embase are often used for the Cochrane Collaboration systematic reviews. However, these databases are oriented more towards clinical evidence and will not necessarily cover public health and environmental health science literature.

Access to abstracting databases can be an issue for some public health practitioners. Fortunately, the National Library of Medicine (USA) provides an Internet version of MEDLINE called PubMed. As well as providing journal abstracts, PubMed (via PubMed Central) also includes access to open-access full-text articles.

Each database has a slightly different terminology for building search algorithms. Consequently, identifying the search terms and combining them into an algorithm is a process of trial and error. A workable approach is to try out a number of options and see how many hits they give you and whether they identify the key literature that you have already identified. The PICO components (see section 3.4) can help to guide this process.

The search teams can be formulated in terms of standard phrases. However, many databases have indexed terms that can help find related topics. For example, Medline and PubMed use an indexing system called medical sub-headings (MeSH). These indexed

terms are typically organized in a hierarchical structure that allows the search to be as broad or narrow as required. Selecting the appropriate index terms can help improve a search strategy. It can give it a high sensitivity (i.e. it will find a high proportion of the articles relevant for the topic) and a high specificity (i.e. it will find a low proportion of articles not relevant to the topic). It is advisable to aim for a strategy with a high sensitivity, even at the cost of a low specificity, because it is better to discard irrelevant articles later than miss those that are important.

A variety of search terms are usually needed to retrieve all articles relevant to the same issue (e.g. the type of exposure). In this situation, it is necessary to combine the results of the searches using these terms. This is achieved using the ‘OR’ Boolean operator (e.g. dioxin OR TCDD OR 2,3,7,8-tetrachloordibenzo-p-dioxin). The other principal ways to combine search terms are to use the AND operator to include only articles containing both terms such as ‘childhood leukaemia’ AND ‘dioxin’, and the NOT operator to exclude particular articles, such as studies that involved animals if your study is only interested in humans. The combination of search terms with Boolean operators works like a mathematical formula and you may need to use brackets for the Boolean operators to be performed in the correct order. If you are unfamiliar with this phase of the process, get advice from a librarian.

3.5.2 Searching alternative information sources

In environmental health, a lot of the research gets published in reports, conference proceedings, theses, and other documents that are not peer-reviewed journals. It is therefore necessary to search this ‘grey’ literature.

In the past, identifying the grey literature was difficult. With the creation of the World Wide Web, it is now much easier. Organizations will typically place reports on their websites. Websites are set up to help find grey literature (e.g. OpenGrey, 2011). Nonetheless, searching for grey literature remains a challenge because there are so many potential websites and resources. The best approach when searching for grey literature is to use a number of different sources: online databases, topic-based websites, and different search engines. Options to consider include:

1. identifying websites of national bodies that might commission or conduct the required research
2. using conference abstracts to identify organizations involved in such research
3. checking whether non-governmental organizations such as environmental lobby groups have commissioned research.

For reviews like scenario 1, this part of the process is important because it is necessary to identify all research on the topic, including studies that did not make it to peer-reviewed publications. This is a standard part of the Cochrane Collaboration process as clinical trials that do not find a treatment effect are often unpublished, and their omission from a meta-analysis would distort the findings. This can occur in environmental health as well, although the opposite publication bias may also occur. Cases exist where studies which find an effect go unpublished because the results are considered too ‘sensitive’.

For scenario 2 style reviews, a particularly useful type of grey literature can be reports from working parties of official bodies. These reports often list the topics the experts jointly believe to be important. Such lists make useful checklists to ensure all suggested outcomes have been identified. An example of this is the WHO briefing reflecting several Expert Committee meetings which listed all relevant effects (WHO, 2010). This list could be checked against the literature you have identified to ensure all topics are covered. Often, there will be a review for each important topic. However, where there is not a review, you may need to do the kind of in-depth work required for scenario 1 reviews.

3.5.3 Snowballing from identified literature

It is unlikely that the search strategy used for the abstracting databases will identify all relevant publications (Greenhalgh et al., 2005). Some databases may not contain all issues of a journal for a given year or the most recent publications. The aim of a systematic review is to identify all relevant evidence.

One way to overcome this limitation is to look through the reference lists of the identified literature. This process of ‘snowballing’ can be a good way to find publications by the same authors. Reference lists may also cite research that challenge the authors’ conclusions. Of course, judgement is required about how long to devote to this task. An average of (say) 30 references per publication yields a lot of references to check. However, in practice, it becomes obvious when the process is no longer productive and can be terminated. It is important to keep track of the number of new references generated through this process.

3.5.4 Applying eligibility criteria

The search for literature will have identified many studies. If more than one source of information was used, it will first be necessary to remove any duplicates (this can be easily achieved in common literature management software such as Endnote). It will then be necessary to remove those studies that do not meet the eligibility criteria. Whether an article meets the criteria is first assessed by screening the title and abstract. If it is unclear from the abstract, the full article should be examined.

To improve the objectivity of the selection process, it is common for several researchers to read through the titles and abstracts, and compare their selections. Any disagreements are discussed and resolved.

The search and selection process needs to be transparent and reproducible. It is necessary to describe the search strategies used to find the literature, and the results of the selection process. It is possible, for a scenario 2 type review, that you will not have identified any literature on one or more of the possible health effects. When stating this in the report, it is important to demonstrate that your search strategy was sufficiently comprehensive to have found relevant literature.

The results of the selection process are often best summarized as a flow diagram. This typically shows the number of articles found from the different sources (databases, Internet, snowballing, expert nominated), the number of duplicates, and the number of articles that did not meet the inclusion criteria. Producing this type of flow diagram and having the list of articles available are among the criteria that define a high-quality systematic review.

3.6 Data extraction and evaluating scientific value

After the eligible publications have been compiled, it is necessary to extract the study details in summary tables, and to evaluate the scientific quality of the results. Summary tables will typically cover three types of information. The first is the basic study characteristics—who were the authors, when was it performed, where was it published? The second type of information relates to the study methodology. It is common for some or all of the following to be extracted (even if individual studies do not report it): the setting, the population group, the sample size, the definition of the exposure, the outcome measures, and (for observational studies) key confounders. The final type of information will cover the results. When deciding on what data to extract, it is worth referring to an appropriate checklist for publications which will help to avoid overlooking (say) an important aspect of methodology (Vandenbroucke, 2009).

There are also checklists for assessing the quality of studies (Deeks et al., 2003; Katrak et al., 2004). Care needs to be taken when selecting a checklist because many are designed for research on the effectiveness of health care interventions or for disease-centred research. These checklists tend to be very weak on the evaluation of exposure assessment, which is challenging because it is often the most important problematic methodological issue in environmental epidemiology. Vlaanderen et al. (2008) covers this aspect well and is also useful because it uses ‘gatekeeper checks’ to eliminate publications from a review. Gatekeeper criteria are a good way of reducing the workload without loss of important information.

The aim of the review needs to be kept in mind when using gatekeeper questions:

- ◆ For scenario 1: is the study able to contribute to the knowledge about this particular health effect? Does it have sufficient detail on exposure and outcome?
- ◆ For scenario 2: is this the most recent and/or the most complete review on this outcome?

Some critical appraisal tools produce an overall score for the quality of a publication (Deeks et al., 2003; Katrak et al., 2004) although there are arguments against this practice, particularly when the scores get used as weights in a meta-analysis (Greenland et al., 2001). Finally, it is worth noting that most of the critical appraisal tools are designed for the assessment of individual research studies, and would be appropriate for scenario 1 type reviews. Appraisal tools for systematic reviews (required for scenario 2 reviews) are less common. One example is AMSTAR (Shea et al., 2007) which has a 37-item checklist that focuses on the completeness of the review and the quality of its assessment of the papers it reviewed.

3.7 Perform a meta-analysis to produce a combined effect estimate

The main purpose of a systematic review in clinical research is to create an overall estimate of the effect of treatment (Elwood, 2007). This requires the combination of the quantitative results from the various identified studies using, for example, meta-analysis techniques. This is a relatively simple statistical task; the harder aspect of the process is

interpreting the results and considering all the possible assumptions involved in the pooling process. In environmental epidemiology, the evidence is likely to come from observational study designs such as cohort and case–control studies. This poses problems in terms of pooling estimated effect sizes, and a review may only be able to list the evidence identified. The impact of potential confounders is also more likely to be a problem than in clinical research where meta-analyses can be restricted to randomized clinical trials. A meta-analysis could be appropriate if sufficient evidence is available from similar types of study. However, the technical process goes beyond the scope of this chapter and statistical support will be needed. A meta-analysis might be feasible for scenario 1 type reviews, but it is highly unlikely for scenario 2 reviews because the extensive variety of outcomes being considered.

3.8 Reporting the findings

There are several guidelines for the reporting of systematic reviews (Vandenbroucke, 2009). These are useful for ensuring a review publication contains sufficient details about its aim and methods to allow it to be reproduced, as well as evaluated, by readers. These guidelines typically emphasize the need to keep track of how publications were found (much easier said than done) and to have a clear strategy for critique of the evidence and presenting the results.

3.9 Conclusion

Reviewing the literature is an essential part of the work of public health practitioners and environmental epidemiologists. There are many books and publications on how to conduct systematic reviews but a common weakness is that they focus on the evaluation of health care interventions and may be less applicable to environmental health studies. It is important to keep the aim of the review at the forefront of your mind to ensure that the decisions about how it is conducted are appropriate. Focusing on the aim will help to produce a review that is informative and whose methods are transparent and rigorous.

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Communication in epidemiological studies

Fred Woudenberg

Learning objectives

- ◆ Justify the importance of communication for environmental epidemiology.
- ◆ Assess and apply the basic rules for the use of media in communication.
- ◆ Plan for the use of appropriate communication with communities under investigation.
- ◆ Identify and evaluate the differences in structure and language in various communication settings

4.1 Introduction

Contaminated land risk assessment and remediation can either be driven by the need to protect the public and the environment or by brownfield redevelopment. Epidemiologists are the primary, but certainly not the only people with an active interest in these data; others include patients looking for causes of ailments, members of the public concerned that an exposure may be harmful, politicians responsible for protecting or promoting people's health, and the media who are interested in newsworthy issues. Epidemiologists should be good communicators but may find that people they are trying to communicate with are only interested in the final study conclusions. In addition these conclusions may be accepted or rejected using non-scientific criteria or 'beliefs'.

This chapter uses a case study to demonstrate communication issues for epidemiologists; it does not offer solutions but demonstrates who needed to know, what they needed to know, and the failures that occurred. Whilst brownfield redevelopment brings tangible benefits that are clear to all, different stakeholder groups will perceive a different balance of 'costs' (in their broadest sense) and benefits. It might be assumed that all stakeholders would welcome remediation if it is used to protect public health and the environment. However, experience has shown that responses can range from concern to outright opposition to any action. Effective communication can lead to a better quality and more widely accepted solution for all parties.

4.2 Case study: remediation of a former gas works factory, Kralingen, the Netherlands

The former Kralingen gas factory in Rotterdam operated between 1854 and 1928 in a densely populated area. The gas production resulted in soil pollution with a range of chemicals, including polycyclic aromatic hydrocarbons, benzene and hydrochloric acid. Local residents discovered the pollution during building activities in 1980. A local community group campaigned for many years on health-based concerns to get ‘the poison out of the soil’. A risk assessment showed that health risks from the contamination were minimal (Rotterdam Council, 1993). Some local people did not believe this risk assessment and pressed for a review. The official decision to clean up (remediate and decontaminate) the site was not based on immediate health risks to the community from the contaminated soil but was based on the longer-term risk of chemical contamination into ground water (Rotterdam Council, 1993).

Once the decision had been made to clean up the site, the local community lost interest in the health risks identified by epidemiological data. Interest rapidly shifted to information supporting the community coping with the decontamination. The remediation process had an enormous impact on the community. It led to a 100 million Euro clean-up/remediation operation with 110 houses demolished and about 2500 people had to leave their homes, temporarily or permanently. Many of these were elderly people who had lived a large part of or even their whole lives in the neighbourhood and many did not want to leave. Significant distress amongst the elderly was reported with some crying in despair; a man refusing to leave the house he was born in 72 years ago, said he would await his eviction behind his door with a shotgun (which he didn’t); and most worryingly a terminally ill man deciding to end his life on the day he had to leave his house, writing that he did not want to face the burden of moving.

The social impact of their removal was enormous and had large health consequences in its own right. Those staying in their homes during the decontamination had to live in houses surrounded by a pool of mud, with years of stench, noise, and traffic problems and children having few outdoor play areas. Most of the local shops were hard to reach or even closed. The elderly who had to move had concerns about their new homes and maintaining contact with their Kralingen social environment. People who didn’t have to move were more concerned about the risks and annoyance they would have to endure for many years.

The local community were involved in the remediation operation as much as possible. They were informed about the recovery activities in detail. Excursions to the site were organized; with special sessions for children, who could smell the ‘poisonous’ chemicals, dress up in white overalls and become ‘inspectors’ watching for ‘intruders’ (thus teaching them that climbing over the fence was prohibited and dangerous). Special measures were taken to reduce the local impacts of the remediation: for example, no noise was allowed before 07.00 hours, which was enforced with the help of the community.

The land contamination and remediation resulted in a stigma on the area and deterioration of the neighbourhood. Those who stayed behind during the remediation did not

take proper care of their houses. Abandoned houses were used by homeless people and by drug addicts. As a result, rent and tax revenues decreased.

The clean up lasted 6 years and caused significant disruption but on completion in 2000, new houses had been built, people returned, rents and taxes returned to economic levels, and daily life has been resumed on what is now one of the cleanest soils in Rotterdam (Network for Industrially Contaminated Land in Europe (NICOLE), 2004). Strikingly, the residents who campaigned for the remediation in the beginning, at the end had serious doubts whether it was worth all the trouble and sorrow (Hilbrands, 2000).

4.3 Summary of some of the communication issues

The local community were involuntarily exposed to contamination and felt powerless, leading to indignation and anger. The only action that the local community could take was to fight their cause. The local people lost their trust in the local environment or health authorities because of the delay in sharing knowledge and suspected that they were withholding information. Most of the information given to the local community came from the media who focused on headline-grabbing information, alleged cover-ups and the identification of ‘guilty’ parties. Therefore the public was seldom convinced by information given by experts or authorities. The impact of perceptions and anxieties was as real as any health risks. These perceptions led to significant societal and economical impacts and in some extreme cases led to stress-related effects. The expert consultant of the citizens kept a diary which reflects this process (Vusse, 2009).

NICOLE (2004), on review of the Kralingen land contamination incident and others, recommended that to improve communication:

- ◆ Denial does not work.
- ◆ Risk communication needs to address community concerns.
- ◆ Be open, honest and prepared to go the extra mile.
- ◆ Give people the information and let them choose what is right for them.
- ◆ Allow people to evaluate the risks within their own life plan.

For any environmental epidemiological issue, a proactive approach to the dissemination of key messages can provide communication benefits—these key messages are summarized in Box 4.1.

Trust: in Kralingen, although the local and national government were paying for the decontamination, the community held a general view that the government valued money over health and had a vested interest in keeping clean-up costs low. Problems with trust and reliability can be mitigated by being open about intentions and affiliations. A solution to improving trust, which was adopted in Kralingen, was to involve independent experts. The only expectation of the project team was that the expert had to have appropriate credentials but the budget was made available for citizens to hire their own consultant. In addition, in Kralingen, the health experts needed unbiased knowledge of the public concerns so a public stakeholder committee was set up which supported a newsletter distributed to the local community. The value of trust and credibility is summarized in Box 4.2.

Box 4.1 Proactive approach: key messages

- ◆ Risk communication should not be considered in isolation. It should be part of a proactive approach to community stakeholder working.
- ◆ The success of environmental management often depends on the interrelationship between communication and technical flexibility.
- ◆ Do not wait for problems to surface; be proactive on working with local stakeholders—pro-activeness is beneficial.
- ◆ Talk to local communities, get their views; you do not necessarily know what they want.
- ◆ Take responsibility for environmental concerns where possible and resolve as quickly as possible—show how you intend to work by making the ‘start’ visible.

Adapted with permission from NICOLE, *Communication on contaminated land*, 2004.

Box 4.2 Trust and credibility: key messages

- ◆ Build-up trust before it is needed ... Stakeholder participation offers possibilities to build trust.
- ◆ Public participation and working together can be beneficial.
- ◆ Trust should be based on mutual respect.
- ◆ Develop positive relationships with stakeholders and work together for a better environment.
- ◆ If the epidemiological messenger is not considered trustworthy then the message will never be: work with credible sources and spokespeople.

Adapted with permission from NICOLE, *Communication on contaminated land*, 2004.

Public perception: one of the most difficult aspects of risk perception for the health professional is the mismatch between ‘lay’ and ‘expert’ evaluation. The expert may be bewildered by the fear exhibited by citizens who live on a (mildly) polluted soil when at the end of the meeting the majority quickly goes outside to light a cigarette. The alleged difference between the risk perception of experts and the public was central to the public concerns about remediation. This difference was especially controversial if numerical risk data were considered to be the most effective way of sharing risk. Quantitative information is a measure preferred by experts. Being aware of the many qualitative aspects that influence people’s perceptions helps in being more compassionate with the ‘irrational’ public. All stakeholders needed to be explicit, open, and honest about their own perceptions. The communication issues relating to public risk perception are summarized in Box 4.3.

Box 4.3 Public and (risk) perception: key messages

- ◆ Perceptions may change over time.
- ◆ There may be discrepancies between the risks perceived by experts and the way in which these risks are perceived by the local communities.
- ◆ Denial does not work; the impact of perceptions is as real as any health risks are.
- ◆ Vague threats are more frightening than having a clear picture of the situation.
- ◆ Take the fears of people seriously and as an epidemiologist be willing to take steps to address these even if they are not necessary from a technical perspective.

Adapted with permission from NICOLE, *Communication on contaminated land*, 2004.

Emotions and control: informing and involving people at an early stage offers a valuable opportunity to manage people's expectations and allows them to feel in control. In Kralingen, most of the concerned community considered that their 'fate' had been decided by a local government with more interest in their financial balance sheet than community well-being. During the decontamination, public participation was used as a means to hand 'ownership of their community' back to the locals. Members of the community were involved in planning of activities and were personally informed about changes (e.g. the need to work over the weekend) or particular activities (e.g. pile-driving close to their house). When agreements made in the public participation process were flouted the community reacted angrily as they felt the decision had not been respected. This happened the day after the decision that there would be no noise before 07.00 hours, when workers started their engines at 06.30 due to a misunderstanding. Box 4.4 summarizes some of the key messages relating to emotions and control.

Timing of media coverage: the situation in Kralingen was brightly illuminated by the local press which as well as reporting factual information, described and sometimes

Box 4.4 Emotions and control: key messages

- ◆ Communication is not just a technical issue; it encompasses emotions.
- ◆ Merely providing scientific data and ignoring the emotional aspects may cause local community outrage.
- ◆ Listen to concerns and respond appropriately.
- ◆ Ensure the well-being of those affected: if appropriate consider having programmes in place.
- ◆ Accept that there are not always immediate answers or clear-cut solutions; be flexible.

Adapted with permission from NICOLE, *Communication on contaminated land*, 2004.

promoted the opinions of the concerned citizens. The concern about the contaminated soil, which at first was restricted to a small group of ‘activists’, spread to the community after the media picked up the story. More people got involved and became angry or afraid. Therefore the media reports had significant influence. Most risk perception researchers doubt that the media alone can cause serious concerns but the media can amplify concerns and the worries of local community if they are not well informed beforehand. The key messages about timing are summarized in Box 4.5.

Openness and transparency: openness and transparency were very important when a large number of people were forced to leave their homes during the decontamination process. However, they were all offered the opportunity to return to the same neighbourhood in a new house after decontamination and rebuilding. People who were not required to leave were nonetheless offered the opportunity to do so, as well as being offered considerable assistance including compensation for the costs of moving and refurbishing a new house. Of these, very few decided to leave because they were strongly attached to their homes and neighbourhood. Once the decontamination was complete very few of those who had been relocated chose to return. It is likely that many of those who chose to stay might have objected if they had not been given the chance to leave. Some key messages around issues relating to openness and transparency are summarized in Box 4.6.

Clear language: an example of issues around clear language occurred when the public, administrators, journalists, and even scientific colleague had high expectations of toxicological and epidemiological analysis, believing it is possible to obtain an exact answer on a very vague question within a very short time. In Kratingen, for instance, people wanted to know the exact location and the border of chemical contamination. However, ongoing investigations often changed or sometimes even contradicted earlier results leading people to doubt the expertise and trustworthiness of investigators and their sponsors. A summary of key messages for clear language is given in Box 4.7.

Box 4.5 Planning and timing: key messages

- ◆ Planning and timing of information release is important. Make sure stakeholders get the information first hand and not from an external party or the media.
- ◆ The alarm caused by early information will be less than the alarm caused by holding onto information.
- ◆ Communication should be structured and regular with a clear communication strategy in place and preferably agreed by all stakeholders.
- ◆ Plan information meetings carefully and well in advance.
- ◆ Start an open communication as early as possible—preferably build on existing relationships.

Adapted with permission from NICOLE, *Communication on contaminated land*, 2004.

Box 4.6 Openness and transparency: key messages

- ◆ Provide open and honest communication; listen to the local community concerns and encourage feedback.
- ◆ Openness creates trust and acceptance.
- ◆ Unscheduled variations of a remediation plan need to be explained ahead of time as far as possible and documented.
- ◆ Open communication prevents delays caused by opposition and legal procedures.
- ◆ Open communication creates a more positive working environment, resulting in fewer complaints.

Adapted with permission from NICOLE, *Communication on contaminated land*, 2004.

Box 4.7 Clear language: key messages

- ◆ Be as specific as possible.
- ◆ If you say the contamination has gone, it better had be; if you tell people you are removing to safe levels ensure they understand that some material will remain.
- ◆ Meaningful communication is based on a willingness to understand.
- ◆ Communication is a two-way process—listening is essential.
- ◆ Use understandable language; hire communication expertise if necessary for public and/or media meetings.
- ◆ Say what you do and do what you say.

Adapted with permission from NICOLE, *Communication on contaminated land*, 2004.

4.4 Learning points

Risk communication is not the transmission of outcomes of risk assessments calculated by experts in order to change the perceptions of threatened people to be in line with the ‘objective’, ‘real’ risk levels. Risk communication is about taking the fears of people seriously, interacting, and being willing in some cases to take more protective measures than are needed from a technical perspective. It involves being open, transparent, honest, able to listen, and share scientific and epidemiological data appropriately.

The communication of risks associated with remediation of contaminated land to local people is complicated because soil and groundwater contamination tends to be invisible and may therefore be perceived as a ‘hidden danger’ caused by others, with exposure being largely involuntary. Remediation is often disruptive and with no perceived direct benefits to many of those inconvenienced.

4.5 Further reading

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Identifying and dealing with high-risk groups systematically and transparently

Harrie van Dijk and Wilfried Notten

Learning objectives

- ◆ Synthesize the evidence for the existence of high-risk groups.
- ◆ Specify the high-risk groups which must be considered in decision-making.

5.1 Introduction

In many countries, it is the government's responsibility to protect and promote public health. Instead of relying on the curative care alone, governments actively promote prevention approaches with the aim of providing health protection for all. A complicating factor is that people differ considerably in terms of their risk of disease and health impairment. How can such variations in the population be dealt with consistently, across a broad range of issues? Identification of high-risk groups requires a standard, well-documented approach. This chapter describes a systematic approach to identify high-risk groups for specific issues. It is based on a recent advisory report of the Health Council of the Netherlands (HCN) (2011a). The approach is illustrated with a case study on Q fever in the Netherlands, also based on Health Council advisory reports (HCN, 2010a, 2010b, 2011b).

5.2 Case study: Q fever in the Netherlands

Q fever is a highly infectious zoonosis caused by the bacterium *Coxiella burnetii*. It is a small obligate, intracellular, Gram-negative bacterium living in the phagosomes of monocytes and macrophages. Many animal species including livestock and pets can host the bacterium. Humans can also host the bacterium. Resistant spore-like forms enable the bacterium to survive outside its hosts for a long period of time.

In the Netherlands, aerosols appear to be the major route of transmission to humans. Dairy goats and sheep are held in dedicated farms on an almost industrial scale and are the most frequent sources of human infection. Particularly high concentrations of bacteria are found in the mammary glands, placental tissue, and milk of *C. burnetii*

infected animals. In ruminants, infection can cause abortions and stillbirths. During parturition, large numbers of bacteria are released and can spread considerable distances. Additionally, contaminated blood products and body materials may form a person-to-person transmission route.

The majority of people infected with *C. burnetii* remain asymptomatic. Those who fall ill may develop acute or chronic forms of the disease. The typical manifestation of acute Q fever is influenza-like illness, sometimes accompanied by pneumonia and hepatitis. This form is usually self-limiting, although patients may suffer from fatigue for a long period of time. The chronic form is rare (approximately 2% of Q fever cases). It manifests as endocarditis (inflammation of the tissue lining the inner layer of the heart chambers and valves). This is a serious condition which, untreated, may result in death. Patients may develop the chronic form without having shown noticeable symptoms of the acute form. It is not known whether Q fever during pregnancy can result in spontaneous abortions or preterm birth in humans.

Q fever used to be a rare disease in the Netherlands with approximately 20 new cases per year. In 2007 the number of cases rose dramatically to 168. In the next 2 years this trend continued with 1000 cases in 2008 and 2354 cases in 2009. The cause of this sudden increase is unknown and it is unclear whether a new, more virulent strain had emerged. In 2010 and 2011, the number of new cases dropped again: 504 in 2010 and 82 in 2011.

5.3 Assessment framework for identifying high-risk groups

The term ‘high-risk group’ is commonly used to designate those groups within the population who are at increased risk of health impairment. ‘High-risk group’ is a relative term. It refers to a subpopulation that is at greater risk of exposure to a given agent, or that is more susceptible to a given disease, than the rest of the population. In absolute terms, however, the risk involved may be quite small. In general there are two approaches to defining high-risk groups: those associated with exposure to an agent with properties that are hazardous to health, or those associated with a disease or disorder (see Fig. 5.1). Accordingly, a high-risk group can consist of:

- ◆ individuals with a particular trait that can adversely affect exposure to the agent, sensitivity to it, or both
- ◆ individuals with a particular trait that increases their risk of acquiring the disease or disorder in question.

Many factors can influence the risk of disease and health impairment, such as:

- ◆ personal traits, including gender, age, genetic characteristics, and health status (i.e. fitness, pre-existing disease)
- ◆ lifestyle-related traits such as dietary pattern, exercise, and smoking
- ◆ aspects of the physical and social environment, including environmental quality in residential areas and workplaces and food safety.

The essence of the assessment framework consists of a systematic analysis of the impact (actual or potential) of personal, lifestyle, and environmental traits on the risk of health

impairment or disease (see Fig. 5.1). This analysis is based on all of the available knowledge about an agent or disease (or both), depending on the approach selected. Groups can be identified within the population at risk whose increased risk results from one or more traits that adversely affect exposure, sensitivity, or both at the same time. In addition, a given disease may exhibit clear links to one or more traits, even if the underlying mechanisms are not understood. Associations themselves are not proof of causality.

This approach is used in many fields to assess the risk of disease or health impairment. There may be a large degree of uncertainty and the framework may need to be used again whenever new information becomes available that might alter the potential high-risk groups. This becomes an iterative process as a growing understanding of high-risk groups for certain diseases can help to identify causes (agents) and mechanisms of action. Conversely, an understanding of causes can shed light on new high-risk groups.

Assessment frameworks are tools primarily intended for use by experts with the relevant expertise. These experts should work closely with policymakers and stakeholders, as the identification of high-risk groups always involves normative choices. Such choices

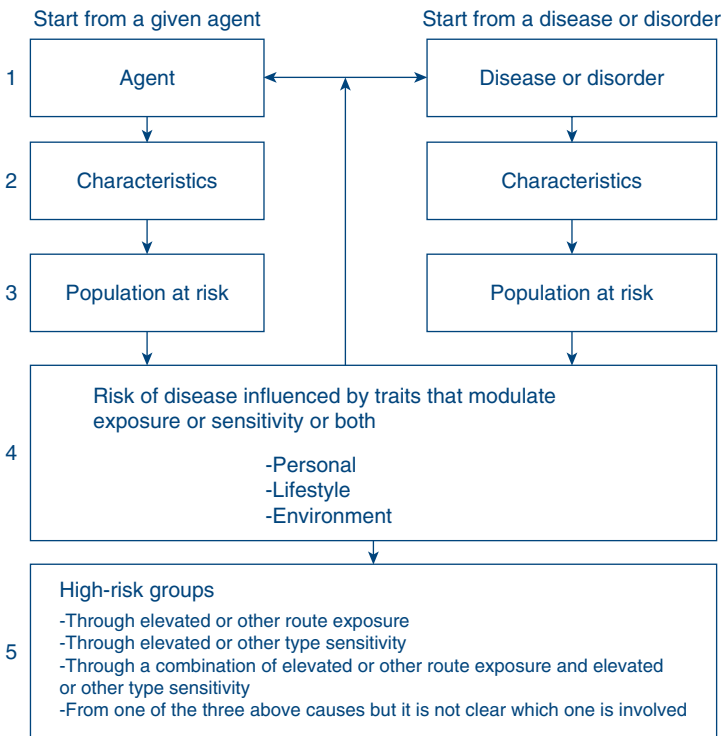


Fig. 5.1 Assessment framework for identifying high-risk groups.

Adapted from Health Council of the Netherlands (2011). *Guideline for the identification and protection of high-risk groups*. The Hague: Health Council of the Netherlands; publication no. 2011/39 with permission from the HCN.

include the risk threshold for designating a high-risk group, the effort required in identifying specific groups, and the degree of refinement of the analysis involved. The more precisely the analysis reflects the information needs of policymakers and stakeholders, the more relevant it will be for decision-making.

5.4 Decision framework for decision-making with regard to high-risk groups

The analysis of possible courses of action is a necessary prerequisite to decision-making on health issues. This includes an analysis of the possible courses of action with respect to the identified high-risk groups. A decision framework (see Box 5.1) illustrates the options available to decision-makers.

Before a choice can be made, the anticipated impacts of various courses of action on high-risk groups and on society as a whole must be identified. This requires a range of analyses, in the areas of health, finance, economics, law, and ethics. All the analyses will involve a degree of uncertainty. Decision-making is not just about balancing costs and benefits, it also involves the allocation of responsibilities between government bodies, business, and individuals, as well as an equitable distribution of advantages and drawbacks across population subgroups.

Two general considerations for the protection of high-risk groups can be identified:

1. The protection of high-risk groups is sometimes the most efficient way of improving public health.
2. Sometimes, justice dictates that special consideration is given to reducing (unfair) socioeconomic health differences or to protecting people from risks caused by others.

Assigning weighting factors to the various values at stake will enable policymakers to decide after consultation with stakeholders which measure or combination of measures are preferable, and thus to determine the extent to which policy can be geared to high-risk groups.

This decision-making process is also dynamic in nature. New knowledge can cast fresh light on high-risk groups. In a dynamic society, normative views about balancing costs and benefits, the distribution of advantages and drawbacks across population subgroups, and the allocation of responsibilities to government bodies, businesses, and individuals are all likely to change.

5.5 Application of both frameworks to the Q fever case study

The application of the frameworks requires the identification of traits influencing the risk of disease by modulating exposure, sensitivity, or both.

5.5.1 Population at risk

Probably the whole human population is at risk.

Box 5.1 Decision framework for decision-making with regard to high-risk groups

Optional courses of action with regard to high-risk groups

- ◆ Deliberately make allowance for some or all high-risk groups:
 - through the implementation of generic measures that are geared to such groups
 - through measures (which may be supplementary in nature) specifically targeting some or all high-risk groups.
- ◆ Consciously take no account of some or all high-risk groups; generic measures that deliberately offer suboptimal protection (or none at all) to some or all high-risk groups.

Criteria

Efficiency (all related to cost-effectiveness)

- ◆ Severity of health impairment.
- ◆ Effectiveness of measures.
- ◆ Added benefits of measures.
- ◆ Costs of measures in broadest sense.

Justice and responsibility

- ◆ Allocation of responsibilities between government bodies, business, and individuals.
- ◆ Cause of disease or health impairment.
- ◆ Mental competence; risk awareness.
- ◆ Distribution of costs and benefits between population subgroups.
- ◆ Accumulation of risks.
- ◆ Feelings within society including those in high-risk groups.

Adapted from Health Council of the Netherlands (2011). *Guideline for the identification and protection of high-risk groups*. The Hague: Health Council of the Netherlands; publication no. 2011/39 with permission from the HCN.

5.5.2 Traits influencing the risk of disease by modulating exposure, sensitivity or both

5.5.2.1 Environmental traits

In the Netherlands, cases of Q fever predominantly occur in areas of intensive goat farming in the provinces of Noord-Brabant and Limburg. A study of one contaminated farm revealed that people living within 2 km of the farm had a 30 times higher risk of contracting the disease than people living more than 5 km away. The increased risk was probably the result of a higher exposure of the local population to the bacterium.

People who occupationally come into contact with goats and sheep are exposed to the bacterium at a higher level too. This group includes dairy goat and dairy sheep farmers, their family members living on the farms, sheepshearers, contract workers, and veterinarians. Serological research in the Netherlands has shown that 80% of dairy goat farmers and veterinarians are (or had been) infected with *C. burnetii*. Nevertheless, the burden of disease within this group is very limited in terms of both number and seriousness of cases.

5.5.2.2 Personal traits

Chronic Q fever occurs more frequently in individuals with underlying medical conditions, such as (hidden) heart valve defects. Their risk of complications, in particular endocarditis, is increased. Based on a retrospective study, French researchers estimated that Q fever in patients with heart valve defects results in endocarditis in approximately 40% of the cases. In the University Medical Centre in Nijmegen in the Netherlands, 10–20% of all patients with endocarditis have been diagnosed with Q fever since 2008. This percentage was practically zero in the years before.

It is less clear whether other groups such as pregnant women and those who have received blood or human transplants are at high risk of Q fever. Transplant patients may be at a higher risk if they receive contaminated material due to their underlying condition or the use of immunosuppressive medication. The bacterium causes reproductive loss in animals and thus needs to be investigated in humans too.

In spite of the higher exposure to the bacterium, Q fever is no more prevalent among agricultural professionals (including farmers and veterinarians) than the general population. The reason for this remains elusive. One possible explanation is that prolonged contact with less virulent strains in the past has resulted in an increased immunity both to existing and newly emerged and potentially more virulent strains. If that is the case, new cohorts of occupational exposed people, for example, student veterinarians, might be at an increased risk.

In summary, this outbreak has identified the following high-risk groups for developing illness associated with *C. burnetii*:

- ◆ As a result of increased exposure:
 - people living in the neighbourhood of contaminated farms
 - possibly professionals (under instruction) who have not yet build up immunity
- ◆ As a result of increased sensitivity:
 - patients with cardiac and vascular diseases
 - possibly pregnant women
- ◆ And as a result of a combination of both:
 - patients who receive contaminated blood or human transplants.

5.5.3 Decision-making in the Netherlands

On the basis of the ‘harm principle’, the Dutch government imposed several measures against Q fever in 2010 and 2011. This required consideration of both public health and

economic (e.g. agricultural and touristic) interests as well as ethical issues (e.g. animal welfare).

First, measures were taken at the source. A duty to report was imposed on dairy goat and dairy sheep farmers and veterinarians whenever they suspected animals were infected by Q fever. Pregnant animals on contaminated farms were culled. Under certain conditions breeding was prohibited. Many sheep and goats were subject to compulsory vaccination. Periodic testing of samples from milk tanks for the presence of the bacterium was made mandatory for all farms with more than 50 animals.

Secondly, in addition to these measures directed at the source, vaccination of humans against Q fever was considered. Decisions about to whom to offer the comparatively little-researched vaccine involved consideration of the advantages and disadvantages: in particular how do complications of Q fever compare with the potential side effects of the vaccine? In 2010 the Health Council of the Netherlands recommended to the Minister of Health not to vaccinate the whole population, but to offer the vaccine as part of extended patient care to medically well-defined groups of patients suffering from cardiac and vascular diseases. The complications of Q fever outweigh the potential vaccine side effects for these individuals. The final vaccination decision would be delegated to the treating doctor in consultation with the patient. The Council recommended vaccination of this group in the high-risk areas of Noord-Brabant and Southern Limburg. However, outside these areas any decisions to vaccinate cardiac patients were left at the discretion of the treating doctor. As the vaccine is relatively little-tested, the council did not recommend the vaccination of pregnant women, young children, and people living in the contaminated farming areas. The Council did not consider vaccination of occupationally exposed persons indicated, because of the limited burden of disease in this group. The Dutch Minister of Health has endorsed the Council's advice.

In follow-up reports, the Health Council of the Netherlands advised against the vaccination of farming and veterinary students. They considered that the burden of disease in this group would remain low, as the number of new Q fever cases in the Netherlands had dropped substantially over the last 2 years, probably as a result of measures taken at source. They also noted that other options could be considered from an occupational health perspective. Finally, the Council deemed measures necessary to prevent person-to-person transmission through organ donation. The Council also recommended addressing the advantages and disadvantages of testing blood donors for Q fever. Recently, the government has endorsed some of these recommendations, while entering into consultation with stakeholders about the others.

5.6 Benefits of a systematic approach

The frameworks presented here provide a structured approach to the identification of high-risk groups and to dealing with such groups in the decision-making process. The assessment framework triggers a systematic check of personal, lifestyle, and environmental traits that, separately or in combination, can affect the level of risk in terms of health impairment or disease. This reduces the likelihood of relevant factors being overlooked,

thereby facilitating a more precise characterization of high-risk groups. An added advantage of this systematic approach is that it helps to uncover gaps in knowledge, which in turn can influence future research. The decision framework highlights the available courses of action with regard to high-risk groups, and helps those involved to make clear-cut choices.

These frameworks provide a generic approach that is potentially applicable to all health protection policy. They could address the lack of clarity about how much allowance is made for high-risk groups in a number of policy areas (environment, working conditions, consumers, and health) and about whether decisions represent deliberate choices. Usually, consideration is focused on obvious gender and age-based high-risk groups. Only occasionally does decision-making appear to take account of other personal factors such as genetic background, physical condition, lifestyle, and environmental factors.

At present, choices about whether or not to make allowance for high-risk groups are often implicit. For example, under the terms of REACH (legislation regulating the authorization of chemicals within the European Union), requirements concerning the scope of the toxicological studies to be carried out depend on the production or import volumes. This criterion involves the implicit choice not to take possible high-risk groups into account when production and import volumes are low.

In the authorization policy for plant protection products, e.g. insecticides, acceptable intake levels of residues in food are implicitly geared to the resilience of healthy individuals. Are the same levels suitable for individuals with severe metabolic diseases, liver, or kidney disorders?

The same focus is seen in the policy on exposure to harmful substances in the workplace, which is traditionally geared to healthy young and middle-aged workers. This approach may need adjustment, now that everyone in the Netherlands (including those with chronic disorders) is expected to continue working until they are older.

The frameworks presented here can be used to make the choices more explicitly. They allow interdisciplinary collaboration about how to deal with high-risk groups.

The frameworks can assist in gathering and organizing any available information and in clarifying the pros and cons. The question of how to weigh up the factors involved remains as thorny as ever.

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Health registers as a tool for disaster epidemiology

Oliver Morgan and Sue Odams

Learning objectives

- ◆ Synthesize the main issues in person registration in incidents.
- ◆ Discuss common methods in creating a person register in acute situations.
- ◆ Appraise in lay terms the legal, political, and ethical issues in creating or not creating a person register.

6.1 Introduction

Many countries invest considerable resources in disaster preparedness. In the health sector this often includes resilience of acute hospital services, the provision of prehospital emergency medical care, and mass fatality management. Increasingly, epidemiology is also integrated into disaster response planning. Recent examples where public health surveillance has played a prominent role include the South Asian tsunami disaster in 2004 and Hurricane Katrina in 2005.

While methods for ‘disaster epidemiology’ such as early warning surveillance systems, retrospective mortality surveys, and syndromic surveillance (Chapter 11) are becoming well established, methods to integrate acute-phase epidemiological investigation with longer-term epidemiological follow-up have received less attention. In this chapter we describe how health registers can be used to generate both acute-phase epidemiological intelligence and long-term follow-up cohorts. We consider the challenges of establishing health registers and their strengths and limitations as a tool for epidemiology.

6.2 Case study: the Enschede fireworks disaster

On a sunny Saturday afternoon (15 May 2000) in the middle of the spring holidays with many people outdoors, a fireworks factory located in the centre of Enschede, a medium-sized town in the Netherlands, exploded (Roorda et al., 2004). An estimated 2000 houses were destroyed (leaving 1250 people homeless), 23 people were killed (including four firefighters), and 947 people were injured. After the immediate care of the wounded and

dead, one of the key actions of the Ministry of Health was to commission an affected population health register: the Enschede Firework Disaster Health Monitoring Project.

6.3 What is a health register?

Gathering basic epidemiological information about exposed or potentially affected individuals after a disaster should be considered good public health practice. However, this apparently simple task has a number of hidden complexities that require careful consideration.

For epidemiological purposes, a health register is a database of individuals from a defined population who share similar health outcomes or relevant exposures. In essence there are two types of register: population-based and case-based registers. Population-based registers have the distinct epidemiological characteristic that the population at risk is known and thus it is possible to calculate population incidence rates. Examples of population-based registers include congenital anomalies (British Isles Network of Congenital Anomaly Registers (BINOCAR website)), cancer (United Kingdom Association of Cancer Registries (UKACR website)), and mesothelioma (Health and Safety Executive (HSE), 2005). Case-based registers are often used in hospitals to collect information about patients with specific diseases or undergoing certain treatments. Case-based registers are epidemiologically limited because little is known about the underlying population at risk from which the cases are drawn.

Recently, health registers have been adapted for disaster settings where health outcomes and/or exposures are uncertain or long latency periods for disease are expected. Scenarios where post-disaster health registers have been used include industrial/transport accidents such as the Bhopal gas disaster and terrorist incidents like the attack on the World Trade Center in New York.

In the context of disaster epidemiology, health registers can be used in the acute phase to record individuals who are affected, exposed, or at risk, conduct early surveillance, and, if required, form the basis for longer-term health follow-up. Types of incident in which health registers can be useful are summarized in Box 6.1. A list of disasters where health registers have been used is in Table 6.1.

Box 6.1 Situations in which health registries can be particularly useful

- ◆ Outcomes are anticipated but the extent or timing may be uncertain
- ◆ There is a long period between exposure and health outcome
- ◆ Health and/or social care need to be provided to the affected population:
- ◆ Public reassurance about the absence of disease is needed
- ◆ Exposures and health outcomes are uncertain
- ◆ Exposures have been identified but health outcomes are unknown.

Table 6.1 Examples of health registers established following a disaster

Register	Year	Type of disaster	Enrolment	Registry members
National Exposure Registry—Trichloroethylene Subregistry (Davis et al., 2005)	1988	Environmental Contamination	Residents of homes with TCE contaminated water	4986 individuals (4652 living, 334 deceased)
Three Mile Island (Talbot et al., 2000)	1979	Nuclear power plant accident	Persons resident within a 5 mile radius	36,000 individuals
Bhopal Gas Disaster Research Centre	1984	Industrial accident	A sample of individuals living within the exposed area	80,000 exposed individuals and 16,000 unexposed individuals
Amsterdam airplane crash (Slottje et al., 2005)	1992	Cargo aircraft crashed into two apartment buildings	Telephone call centre for concerned residents	900 individuals
Oklahoma City bombing (Mallonee et al., 1996)	1995	Bomb outside federal building	Individuals seen by health services, surveys of building occupants, and newspaper advertising	841 injured people
Fireworks depot (Roorda et al., 2004)	2000	Explosion	Residents from affected area, rescue workers, victims/survivors	11,000 individuals
World Trade Centre Health Registry (WHCHR) (New York City Department and Mental Hygiene, 2004)	2001	Airplane crash and collapse of World Trade Centre buildings	Individuals in the vicinity of the disaster and rescue/clean-up workers	71,437 individuals
7/7 Register	2005	Terrorist bombing in London	Individuals in the vicinity of the disaster and rescue/clean-up workers	900 individuals
Explosion at an oil storage depot	2005	Industrial accident	All individuals occupationally deployed to the site	1000 individuals

6.4 Establishing a health register following a disaster

6.4.1 Administrative arrangements

First and foremost, sufficient administrative arrangements need to be available. While this will depend on the size of disaster even small health registers require dedicated time, funding, and effort. A register needs to be set up as soon as possible after a disaster, and pre-agreed arrangements facilitate a clear and quick decision on the establishment of a register. An example of a decision-framework to assess the need for establishing a health register for major incidents is available (Paranthaman, in press). Successful registers need clear institutional and political support from the relevant public health bodies. While this is typically negotiated in the post-disaster phase, pre-agreed arrangements, especially

about data sharing, are beneficial. Any research use of the register, once established, would require further consultation and a decision on the ethical and practical aspects of such use of the register, but this could be agreed and implemented at a later stage.

6.4.2 Identifying populations

The single biggest challenge following a disaster is to identify the affected population. The first decision which has to be made is whether to attempt a complete census of exposed individuals, or whether a selective sample from the affected may suffice. There are usually three main sampling groups for a health register: (1) emergency responders and occupational groups; (2) members of the public who seek medical attention or advice; and (3) members of the public affected but who do not seek formal medical attention or advice. Suggested sources of information are given in Box 6.2.

A key consideration is how to classify people as affected or unaffected. For Enschede this was not straightforward. In the end the register used a broad definition to classify ‘persons affected’ which included both those whose exposure to the disaster had manifested acute effects such as physical harm and those whose exposure was less close (Roorda et al., 2004). Initial estimates were that the register population would comprise approximately 9000 individuals, of whom approximately 3500 would be rescue workers (van Camp et al., 2006).

6.4.2.1 Emergency responders and occupational groups

Occupationally-exposed persons can usually be traced from work records. Emergency responders will primarily be members of the fire, police, and ambulance services. However, a large number of other organizations may also have deployed staff to an incident including local authorities, utility companies, private industry, military, civil

Box 6.2 Sources of information that can be used to identified individuals affected by a disaster

- ◆ Primary data collect at the disaster scene
- ◆ Hospital or Emergency Department information systems
- ◆ Ambulance services
- ◆ Police
- ◆ Occupational health departments
- ◆ Special Incident telephone helplines for the public
- ◆ Websites
- ◆ Notification by family doctors or other primary health care worker
- ◆ General public announcements via media
- ◆ Via the emergency services
- ◆ Poisons Information or Control Centres.

defence, and voluntary organizations. Additionally, some individuals affected by the incident may have been working at the time, such as train drivers or security guards. Follow-up of individuals from this group can be done in collaboration with occupational health departments.

6.4.2.2 People who seek medical attention or advice

Individuals who receive hospital care may be identified through hospital computer systems, by reviewing medical case notes, or by collecting patient details on arrival at the Emergency Department. For large incidents, especially in urban areas, many different hospitals may be involved. In the days following a disaster, some affected people may seek medical attention from their family doctor or from hospitals outside the disaster area. Therefore all medical facilities in the local area should be alerted to the need to notify affected individuals. If telephone help-lines have been set-up to provide medical advice, or existing telephone services such as NHS Direct in England or poisons information services have been accessed, callers to these services can also be included in a health register. Individuals who receive medical attention at the scene of an incident but do not go to hospital need to have their details recorded on-site or traced later through appeals to the general public.

6.4.2.3 Affected people who do not seek medical attention or advice

This group may be the most difficult to identify and contact and depending on the type of incident this may be the largest group. In some cases people may be identifiable through routine records such as time-cards for office or factory workers, immigration records, hotel guest registers, and so on. Advertising through the local or national media and via the Internet may encourage individuals to self-report. Collecting details of individuals at the scene of the incident may be possible if teams of public health professionals, with sufficient training and preparation, can be mobilized quickly enough.

The Enschede fireworks register initially established an Information and Advice Centre for victims of the disaster. Letters were sent to residents and broadcasts about the project were made by local media, requesting that they register. Persons affected were also notified by their general practitioner (GP) and, in the case of rescue workers, by the regional occupational health service. The youth health care services department was also used to identify child victims. Further information was obtained by the setting up of an aftercare centre exclusively for persons affected by the disaster (Roorda et al., 2004).

6.4.3 When to begin data collection

Once it has been decided to establish a register the investigators must decide whether to start data collection immediately or to defer data collection until protocols are agreed and defined. Data collection which is undertaken in the immediate post-disaster period is useful for short-term public health follow-up. For example, the Agency for Toxic Substances and Disease Registry (ATSDR) Rapid Response Registry (ATSDR, 2011) has been established to develop a registry of affected persons during the immediate aftermath of an event and aims to be set up in 8 hours. If a pre-prepared minimum dataset is used

in the initial stage of implementing a register, containing little more than name, contact details, and permission to be contacted later, a register could be begun more promptly. In this way, the affected population could be identified early, before decisions are needed on more detailed follow-up of their exposure, health status, and care. This would allow for further follow-up studies by gathering detailed information on exposure and health outcomes once a protocol and measurement instruments are available and justified on public health grounds.

In Enschede, due to disorganization at the commencement of the study, research questions were devised by the researchers using prior experience rather than including the relevant ‘health care professionals and policymakers’. The questionnaires were later evaluated as not being broad enough for the purposes of the follow-up research (Roorda et al., 2004). The researchers at Enschede used this rapid method because it was feared that vital information would be lost with delay.

Alternatively, data collection can be postponed until the details of the incident have been fully clarified and the type of information to be collected can be properly specified. Despite the obvious advantages from a scientific point of view, retrospective identification of individuals is difficult and developing agreed protocols can take a considerable amount of time. For example, the World Trade Center Health Registry (WTCHR), which was designed for research purposes, began data collection 2 years after the incident (New York City Department for Health and Mental Hygiene, 2004).

6.4.4 Minimum datasets

The initial data obtained from those registered in the Enschede fireworks disaster were demographics and lifestyle, self-reported mental and physical health prior to and following the disaster, and the individual’s whereabouts and experiences during and in the immediate aftermath of the disaster. Many of the residents were immigrants, so the questionnaire was available in four different languages (van Camp et al., 2006). A proposed minimum dataset is given in Box 6.3. In the later questionnaires, additional information was gleaned regarding effects on employment and social life.

6.4.5 Managing the data collection process

At the heart of any register is a list of individuals and their contact details. Generating such a list is the first step in developing a health register and it involves the reconciliation of data gathered prospectively and retrospectively from several different sources. The need for manual processing may be reduced by use of semi-automated data entry facilities or web-based data entry forms, accompanied by manual correction of data entry and other errors. This is needed because data often contain small variations such as misspelling of names and transposition of first and second names that can not easily be dealt with by a computer. Building a health register is an ongoing task involving identification and tracing of new members and the verification of existing members.

The main challenges to registry completeness are loss of continuity (two or more unlinked registrations of the same person) and loss to follow-up (misinformation or

Box 6.3 Minimum dataset to collect during the acute phase of an incident

- ◆ Demographic
- ◆ Contact details
- ◆ Age
- ◆ Sex
- ◆ Date of birth
- ◆ Name
- ◆ Home address
- ◆ Telephone numbers (including mobile telephone)
- ◆ Email address
- ◆ Family doctor
- ◆ Location during the incident (free text)
- ◆ Brief description of 'exposure' (free text)
- ◆ Consent to follow-up in future studies (yes/no).

misidentification leading to non-traceable individuals, subjects withdrawing from the register, and subjects who die).

6.5 Uses and limitations of health registers

As a minimum, case-based health registers are used to gather descriptive information about who was affected by a disaster, the acute health impacts, and health care service needs. In other circumstances analytical epidemiology may be able to measure health effects related to exposure. This is best done using population-based health registers that contain details of all individuals exposed to a disaster. The type of disasters most amenable to population-based registers are those that are geographically constrained, with a clearly defined exposure and a readily identifiable population. However, in many situations, the nature or extent of exposure and/or the population may be uncertain and complete enumeration of the population at risk will not be possible. Nevertheless, case-based data can still be used for epidemiological investigation, although analysis will be limited by the lack of a denominator and will rely on case-control and case-case study designs.

Bias can be reduced by early definition of the affected population, based on type and distribution of the exposure considered relevant, and institution of arrangements to systematically recruit individuals from the whole of the affected population. Those with the highest exposures and/or most significant health effects are more likely to be recorded because they are the easiest to identify. Typically this would include emergency responders, occupational groups and members of the public who sought medical attention. Recruiting via the

media is likely to capture individuals who are concerned about their health or differ in other ways to individuals who do not self-report. The Enschede cohort study had a problem of non-response (35.2% at 3 weeks; van der Berg et al., 2005) leading to follow-up bias. Bias may lead to either an overestimate or underestimate of health effects.

Health registers are particularly suited to longitudinal cohort studies. In Enschede, a longitudinal cohort of individuals affected by the disaster was followed-up using questionnaires disseminated over a 4-year period: at 3 weeks, 18 months, and 4 years after the disaster. A control group (derived from a sample of the residents of Tilburg, a comparable town, in the Netherlands) also completed the questionnaires (van der Berg et al., 2005). Samples of blood and urine were taken at the 3-week point and stored for possible future analysis (Roorda et al., 2004). Such cohorts are especially useful for the epidemiological investigation of long-term health outcomes. Their analysis, strengths, and weaknesses have been well described. Although longitudinal studies of health registry members are an attractive prospect, maintaining up-to-date records of individuals is costly. Funds for follow-up may be hard to secure where little is known about what health effects might follow.

In such instances alternative strategies could be explored, such as follow-up of a ‘sentinel’ subgroup, such as those with the highest exposures, which may alert public health authorities of potential problems among the total exposed population. Additionally, follow-up may be integrated into individuals’ routine health check-ups or as part of routine follow-up by their occupational health department. In some countries and for some types of disaster it may be possible to use record linkage between a health register and vital statistics, cancer registers, or even healthcare computer systems. In Enschede a secondary follow-up method used data provided by GPs, local mental health, occupational health, and youth health services to follow-up those identified as having been affected or involved in the disaster. An advantage was the availability of individual pre-disaster data such as sick leave and health service utilization, although the issue of diagnosis bias and diagnosis suspicion bias must be addressed. A disadvantage was the lack of information on the extent of the individual’s involvement in the disaster compared with the follow-up questionnaire methodology. Den Ouden et al. (2007) overcame both these problems by combining the two methods in their study.

6.6 Ethical issues and potential misuses of health registry data

Developing a health register following a disaster should be considered part of the public health response and ethical committee approval is therefore not required. Initial baseline exposure and health data collection is part of the public health response and can be implemented without ethical approval. However, further follow-up and longer-term storage of patient identifiable data will require consent from register members and would probably require full ethical approval.

A steering committee of reputable individuals may be needed from the early stages to ensure the ethical management of a health registry. The steering committee should

regulate access to the register by researchers and others and consider the validity of any research proposals. The steering committee must also protect against the misuse of health register data, such as access by insurance companies or special interest groups. There may also be circumstances when criminal investigators may want to use a health register to identify individuals potentially involved in the disaster or its consequences.

A steering group was set up to oversee the Enschede Health Monitoring Project which was highly resource intensive, requiring approximately 27 full-time workers (Roorda et al., 2004). The key ethical issues identified during the follow-up of affected individuals from Enschede were patient privacy, blood sample acquisition, usage and storage, and informed consent (Chapter 18). However, for person registries in particular a crucial ethical issue is that there is no time to formally consult an ethics committee before beginning data collection and registry construction; although it is possible to consult an ethics committee for the generic case. Another important issue is that the participants cannot be fully informed, when giving their initial consent, of the actions that will be taken in the future investigation (for example, which samples will be analysed and what for, which health effects will be evaluated). Participants can only give an agreement that they will allow later contact and informed consent will be a requirement of any later investigations. It is therefore paramount to build into the framework the capacity for individuals to freely withdraw from the registry at any stage, without any consequences for their medical care.

6.7 Conclusions

The use of health registers following disasters is an evolving method in the disaster epidemiology toolbox. Collecting information about individuals exposed to a disaster sounds simple. However, considerable resources are needed to collect information in a timely manner, from many different sources and manage it appropriately. In addition to providing essential descriptive epidemiology about the affected population, health registers can be used for analytical epidemiology, including follow-up studies that may provide insights into the health effects of exposures and disasters. In the case of the Enschede fireworks disaster, studies have been conducted on the health of rescue workers using sick leave data, post-traumatic stress disorder among ambulance personnel, and, for the wider population, whether gender and age were disaster-related risk factors. These have helped to improve the understanding of people's physical and mental reactions to disasters and thus improve provision of health care in disaster situations.

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Section 2

Assessing the problems and developing a scoping study

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Environmental measurements

Sotiris Vardoulakis

Learning objectives

- ◆ Critique different approaches to environmental monitoring.
- ◆ Contrast the applicability of different sampling techniques.
- ◆ Appraise the advantages and limitations of these techniques.
- ◆ Identify and choose appropriate environmental data analysis methods.
- ◆ Assess environmental data requirements in epidemiological and risk assessment studies.

7.1 Introduction

Environmental measurements are used in wide range of epidemiological and risk assessment studies. For example, if you are faced with complaints from local residents about air pollution and related health effects around a heavily-trafficked road in a densely populated area, you will need to use a range of environmental measurement techniques to assess the levels of pollution and characterize population exposure in that area.

The case study used in this chapter is traffic-related air pollution in an urban area. However, most of the principles and issues discussed here are also relevant to other environmental media (e.g. water and soil), pollution sources (e.g. manufacturing industry, waste management, and energy generation), and locations (rural, home, and working environments).

7.2 Traffic-related air pollution: a case study

The case here is air pollution levels around a road axis linking two major urban areas in a typical city centre location within the UK. This is a very busy road passing through residential and shopping areas, with three- to four-storey buildings almost continuously lining both sides of the street. The total width of the street is approximately 25 m and the average building height 12–14 m. The annual average daily traffic flow is around 30,000 vehicles per day, while the average vehicle speed is only 10–25 km/h with many stop-starts near street junctions due to congested traffic. An automatic air quality monitoring station is

permanently located in the street (at less than 5 m from the kerb and around 60 m from the nearest intersection). This monitoring station has recorded some of the highest nitrogen dioxide (NO₂) and particulate matter (PM₁₀: fine particles with aerodynamic diameter <10 µm) concentrations in recent times, often exceeding national air quality limit values for the protection of human health. This has caused concern among local residents and council representatives, who are pressed to investigate related health risks and, in particular, any associations with the prevalence of childhood asthma in the area.

To address these concerns, a study can use a hospital based case–control design, relating air pollution levels at residential addresses to cases (e.g. children admitted with asthma or other respiratory illness) and controls (e.g. all other children with an emergency admission during the study period) living within the area of interest. For this chapter, we focus on the environmental measurements applicable in such a study.

7.3 Background

7.3.1 Environmental monitoring and exposure assessment

Environmental monitoring evaluates the concentration of a contaminant or multiple contaminants in an environmental medium (or *compartment*), i.e. in air, water, sediment, dust, or soil (Fig. 7.1). Methods usually involve collection of a *sample* (a small but representative quantity of air, water, or soil) and further chemical analysis in a laboratory to establish the quantity of the contaminant within the sample, which represents the contaminant *concentration* in the environment. To characterize exposure relevant to a human population, environmental measurements can be combined with:

- ◆ Personal monitoring, aiming to establish contaminant concentrations in personal air, drinking water, food, or dust.
- ◆ Questionnaires and time-activity diaries, which aim to infer personal exposure to contaminants from lifestyles, dietary habits, residence location, and other characteristics.
- ◆ Biological monitoring, which estimates directly the total uptake (i.e. via all exposure pathways) of a contaminant into the human body using a biomarker (e.g. urine, blood, etc.).
- ◆ Environmental modelling techniques that calculate pollutant concentration by mathematically simulating environmental processes usually with the help of computers.
- ◆ Geographical information systems (GISs), which are computer-assisted mapping systems that allow visualization and analysis of multiple datasets, including pollutant concentrations, land use, and population data (see Chapter 13).

7.3.2 Measurements in different environmental media

Traffic pollution, such as in our case study, mainly affects the lower atmosphere. This is a dynamic medium in which pollutants are quickly diluted and dispersed. These dilution and dispersion processes depend on several factors, such as local weather conditions, land cover, and nature of emission sources (e.g. industrial stacks, motorways, etc.).

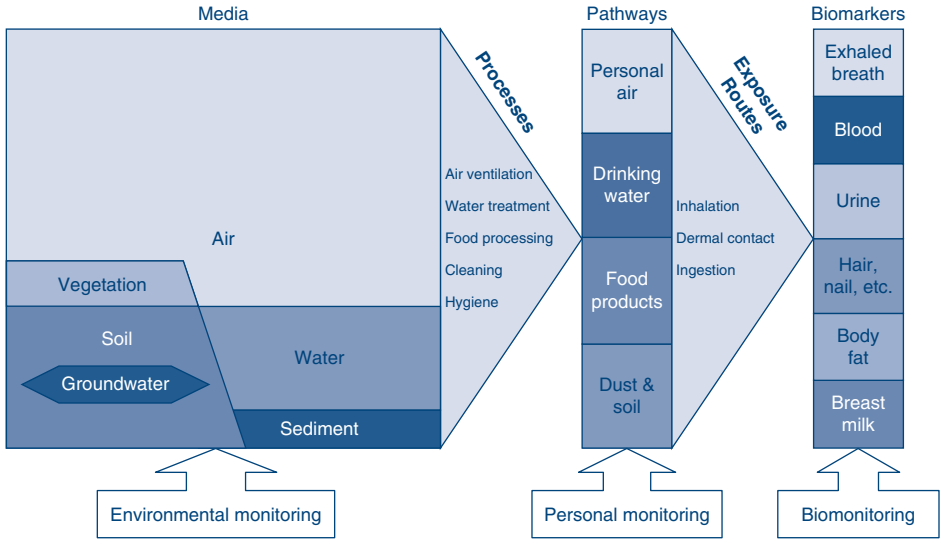


Fig. 7.1 Environmental media (or compartments), processes, and exposure routes.

Similarly, contaminants released in the water (drinking water, sea, lake, river, or groundwater) or soil (top or deep soil) can be diluted and dispersed, but at generally lower rates.

For example, contamination with aromatic hydrocarbons, such as benzene, can occur in any environmental medium. Depending on soil type and air temperature, aromatic hydrocarbons from petroleum products spilled on the ground can migrate to other environmental compartments: to ambient air through evaporation, and to deeper soil and potentially groundwater through infiltration. Some of these hydrocarbons may penetrate into the personal air and/or drinking water of subjects through different exposure pathways, and eventually cross human absorption barriers via inhalation and/or ingestion and accumulate in the body (Fig. 7.1). Therefore, depending on the type of contamination, environmental measurements may need to be taken in several media (air, water, and soil) to estimate aggregate exposure levels to a chemical or group of chemicals.

7.4 Sampling strategy

Taking reliable and representative measurements in any environmental medium, air, water, or soil, is a challenging job. Environmental and public health practitioners need to ensure that environmental measurements are representative of exposure levels of the studied population over a relevant time period. This can be achieved by determining the optimum layout and spatial density of a monitoring network, and taking related costs and other practical constraints into account.

Before collecting any environmental measurements, we need to make sure that an appropriate sampling strategy is in place. First, it is important to clearly define the objective of the study, e.g. in this study the aim was to characterize traffic-related air pollution at postcode address level within an urban area. One or several indicators of traffic-related

air pollution, and corresponding sampling and analysis techniques need to be selected, as well as locations, duration, and frequency of sampling.

In general, sampling design should not be solely guided by where pollutant concentrations are likely to be higher, but also by where most people (including sensitive subgroups such as young children and elderly) live, study, and work. This is particularly important in spatial epidemiology studies, as they aim to associate spatially-disaggregated population exposures with health outcomes.

Several *markers* (or *indicators*) of environmental pollution can be used in epidemiological studies depending on the pollution sources and health effects of interest (Nieuwenhuijsen, 2003). Proximity to motorways, road traffic density, and measured or modelled ambient concentrations of NO₂, PM₁₀, PM_{2.5}, carbon monoxide (CO), volatile organic compounds (VOCs; e.g. benzene), and polycyclic aromatic hydrocarbons (PAHs; e.g. benzo[a]pyrene) have been used as indicators of exposure to traffic-related air pollution (Krzyzanowski et al., 2005).

In our study, the exposure of cases and controls to traffic-related air pollution can be characterized using the distance of residence from nearest main road or the traffic volume within certain distance of residence as surrogates (Wilkinson et al., 1999). Alternatively, NO₂ can be used as a marker of traffic-related air pollution, because of its relative specificity (road transport is the largest source of NO₂ in the UK), low cost and practicality of available measurement techniques (e.g. passive diffusion tubes). NO₂ is a respiratory irritant which has been associated with daily mortality and hospital admissions in several studies, although its independent effect on mortality and morbidity may be confounded by other vehicle-derived pollutants (Touloumi et al., 1997; Chiusolo et al., 2011).

Therefore, we have decided to obtain repeated monthly measurements outside residences of study participants over a representative time period (1 year). This will also allow a direct comparison of NO₂ levels at various locations within the study area with the NO₂ levels recorded at the automatic air quality monitoring station operating in the main street, as well as with the annual NO₂ limit value (40 µg/m³) for the protection of human health in the European Union.

7.5 Air quality monitoring networks and instruments

In air pollution epidemiology studies, available air quality datasets from existing monitoring networks are often used. Most large and medium size cities in high income countries are covered to some extent with automatic air quality monitoring networks providing continuous, real time measurements of key pollutants, such as NO₂, fine particles (PM₁₀ and PM_{2.5}), sulphur dioxide (SO₂), CO, and ozone (O₃). In addition, non-automatic monitoring networks mainly involving passive diffusion tubes (PDTs) for measuring NO₂ and VOCs such as benzene, as well as gravimetric instruments for collecting fine particles on filters for laboratory analysis, are implemented in many urban areas (Vardoulakis, 2009).

Automatic monitoring stations are usually air conditioned units equipped with gas analysers and particle monitors which involve active (i.e. pumped) sampling. They need

therefore quite a lot of space and are expensive to set up, operate, and maintain. For this reason, their number within a city is limited.

Passive sampling provides a low-cost, alternative air quality monitoring technique. PDTs are based on the principle of molecular diffusion for drawing molecules of the pollutant onto a chemical adsorbent material. PDTs are generally easy to deploy, but their measurements tend to be less accurate and of much lower temporal resolution (e.g. monthly) than those obtained with automatic gas analysers. PDTs do not involve pumped sampling, therefore they do not need a power supply.

The main advantage of automatic air quality monitoring networks is that they provide continuous measurements of key pollutants at a high temporal resolution (e.g. hourly), which can capture peak exposures. Data obtained with automatic monitoring techniques can be used in time-series epidemiological studies aiming to establish associations between short-term exposures to air pollution (e.g. daily mean concentrations) and health outcomes, such as daily counts of deaths or hospital admissions. On the other hand, passive sampling can be used to characterize the spatial variability of air pollution (e.g. identifying pollution hotspots and establishing discrete exposure zones) in spatial epidemiology studies.

Some of these monitoring techniques (both active and passive) involve collection of gaseous pollutants or particles on an appropriate adsorbent bed (passive diffusion sampling) or filter (gravimetric sampling), respectively, which can be then analysed or weighted in a laboratory. This is called *integrating* (or *pre-concentration*) monitoring and is usually labour intensive as it requires manual collection of samples and laboratory work. On the other hand, automatic fast-response instruments usually rely on optical or electrochemical techniques to record pollutant concentrations continuously and transmit them electronically with a modem. Therefore they require less frequent attendance for instrumental calibration and maintenance.

In our case study, we need to characterize exposure of subjects (cases and controls) to NO₂ at their residential addresses over a relatively long period of time. Using data from the nearest permanent monitoring stations could introduce an exposure misclassification bias to the study, as these stations are limited in number and likely to be located at some distance from the residential addresses of interest. PDT sampling can provide NO₂ concentrations at higher spatial resolution, while measurements from the existing automatic monitoring network can be used for data validation.

It should also be mentioned that personal monitoring has been used in targeted, traffic-related air pollution health effect studies. This can be done by using passive diffusion or active (i.e. pumped) monitoring instruments carried by specific groups of volunteers, such as cyclists, commuters, or industry workers. In the case study we focus on here, this technique was not used as it is impractical for measuring longer-term exposure especially in children.

7.6 Air pollution modelling

In the traffic-related air pollution case, passive sampling can be used to a certain extent to characterize experimentally the exposure of cases and controls. If the number of

participants is very large, then we may need to characterize population exposure indirectly using a mathematical model. A model is a simplified representation of an environmental system involving one or multiple environmental compartments (air, water, soil, groundwater, etc.).

Modelling is particularly useful for estimating population exposure in places where measurements are not fully available, as well as for predicting future or reconstructing past exposures. It can also be used to understand the behaviour of different components of an environmental system, and to test different “what if” scenarios related, for example, to different environmental policies (Vardoulakis et al., 2008).

Depending on their complexity, models require a range of input data and some independent environmental measurements for verification (i.e. comparison of model results against monitoring data). Input data requirements can vary from distance from the sources in very simple *proximity* (or *buffer zone*) models to very large meteorological, land use, and emission datasets in highly complex *fate and transport* or *geostatistical* models. It should be remembered that although complex models can be physically more realistic, they are not necessarily more accurate than simpler models as they involve a large number of input parameters that can be highly uncertain.

Apart from the level of model complexity, and associated user expertise and computation costs, we also need to determine the right spatial scale for our application. Environmental modelling domains can vary from global, to continental, regional, urban, street, and single-building scale. In our case, an operational street-scale pollution model (Vardoulakis et al., 2003) can be used to estimate NO₂ levels in a city. The results of the model can be verified against the automatic monitoring and passive sampling measurements obtained as part of the study (Vardoulakis et al., 2007, 2011).

7.7 Quality assurance and quality control

Obtaining environmental measurements for epidemiology can be expensive, labour intensive and time consuming. Therefore, we want to make sure that they are worth the effort in terms of accuracy and precision. The quality of environmental measurements can be ensured by adherence to carefully designed standard operating procedures including robust quality assurance and quality control (QA/QC) procedures.

PDT measurements (NO₂) should be tested for accuracy against data obtained with the reference technique (chemiluminescence gas analyser) at the same location and averaged over the same time period (e.g. 1 month) (Vardoulakis et al., 2009). If there is a significant difference between the two techniques, the PDT measurements will need to be adjusted using an empirical correction factor. Similarly, NO₂ modelling results need to be tested for accuracy using automatic monitoring and passive sampling measurements at number of locations.

The precision (or repeatability) of measurements also needs to be evaluated using multiple sets of samplers exposed at the same location. In our case study, we have used co-located triplicate PDT to calculate the relative standard deviation (RSD) of NO₂ measurements (RSD <10% is usually considered satisfactory).

We have also collected *blank* (i.e. unexposed) PDTs to ensure that there has not been contamination of samples during handling, transportation, storage, and laboratory analysis. If contaminant levels above the limit of detection are found in the blanks, the average blank concentration should be subtracted from the contaminant concentration observed with the exposed samples.

7.8 Data analysis and interpretation

In our example, we have used NO_2 as a marker of traffic-related air pollution because of the well-established and relatively inexpensive monitoring and modelling techniques available for this pollutant. It is, however, recommended that a correlation analysis be conducted between the chosen marker (NO_2) and other key pollutants. A strong correlation between NO_2 and PM_{10} , for example, would reflect the common, mainly vehicular origin of these pollutants in the study area.

The monthly NO_2 data obtained with PDTs need to be averaged over the entire sampling period. This should ideally cover all four seasons, including holiday periods, as NO_2 concentrations can vary substantially from winter to summer. The monitoring and modelling data obtained in our study can be presented as air pollution maps using standard GIS interpolation techniques (see Box 7.1).

Box 7.1 Averaging of environmental data in air pollution epidemiology studies

In epidemiological studies, the statistical analysis of environmental measurements is largely dictated by the nature of the health outcomes, data availability, and study design. Air pollutant concentrations need to be averaged over exposure periods relevant to specific health outcomes. Consider the following examples from the scientific literature:

- ◆ Exposures of mothers to several air pollutants for different gestation trimesters and for the entire pregnancy period were estimated in a case-control study focusing on adverse pregnancy outcomes (Wu et al., 2011).
- ◆ Exposures of mothers to benzene and NO_2 during pregnancy and of children under 15 years of age to the same pollutants during childhood (until the time of diagnosis) were estimated in a childhood cancer case-control study (Raaschou-Nielsen et al., 2001).
- ◆ Exposures of children to several air pollutants (including NO_2 and $\text{PM}_{2.5}$) averaged over 24-hour periods were used in panel study investigating the short-term effects of air pollution on wheeze in asthmatic children (Mann et al., 2010).

7.9 Findings of the case study

Using the environmental measurements obtained in this study and routine hospital admission data, odds ratios of hospital admission for asthma and respiratory illness for children living within the area of interest were calculated. These odds ratios are used to assess the association between the risk of hospital admission for childhood asthma and respiratory illness and local traffic-related air pollution levels. Odd ratios (and confidence intervals) above unity would indicate a significant positive association.

In our study, participants living at addresses with the same postcode are assumed to be exposed to the same air pollution levels. If sufficient resources are available, we could refine our analysis by using full residential addresses to monitor and model air pollution at individual address level. We have also assumed that ambient air pollution levels at postcode addresses are representative of total personal exposure, which is not strictly the case as children spend substantial time at school. Ideally, typical time-activity patterns need to be combined with pollutant concentrations measured in a range of micro-environments (street, home, school, car, etc.) in order to establish more realistic exposure levels for the study population. However, most epidemiological studies use residential postcode addresses only, like in our example, due to practical and cost constraints. In future studies, confounding factors such as socioeconomic deprivation and smoking in the household, as well as statistical power issues arising from possible small numbers of households involved in the study will need to be addressed.

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Exposure assessment for epidemiology

Ariana Zeka

Learning objectives

- ◆ Synthesize the key concepts in exposure assessment.
- ◆ Understand the use and limitations of exposure assessment in epidemiology.
- ◆ Discuss different approaches to exposure assessment for epidemiology.
- ◆ Critically review the underlying assumptions of exposure assessment and its applicability to health protection.

8.1 Introduction

Exposure is the quantity of a substance in the environment that may adversely or beneficially affect human health, usually by direct contact with the human body through mediums such as water, air, soil, or food. The uptake of external exposure into the body is referred as dose (Nieuwenhuijsen, 2003). For example, air pollution is an environmental exposure that has consistently shown adverse health effects; conversely, certain medications and nutrients in our diets produce beneficial effects on individual health. This chapter focuses on adverse environmental exposure and the methodological issues associated with its evaluation.

Exposure measurement determines the levels or concentrations of exposure factors in different media. Exposure measurements are done for environmental monitoring or compliance purposes (e.g. industrial). Exposure assessment is the study of the distribution and determinants of exposure factors that affect human health (Nieuwenhuijsen, 2003), and it comprises both the measurement of exposure and of other factors determining the distribution and exposure levels relevant to human health.

In order to quantify adverse health effects of environmental exposures it is necessary to first be able to characterize and quantify the exposure. In contrast to, for example, clinical studies where the exact exposure (e.g. medication dose) is known, the majority of studies in environmental epidemiology are observational (see Chapter 14). The environmental exposures and their determinants are not known to researchers; hence the need for an exposure assessment.

Accurate characterization and quantification of exposure is important in epidemiological studies for several reasons: (1) it allows for stronger evidence of causality in observational studies, by strengthening the validity of the exposure–response assessment; (2) it supports setting of environmental standards by estimating the health effects of specific levels of exposure; and (3) it allows quantitative risk assessment.

8.2 Case study: indoor and outdoor air pollution in schools

Current evidence suggests that exposure to common air pollutants is associated with acute adverse health effects in children (Brunekreef et al., 1997; Schwartz, 2004; Annesi-Maesano, 2007). The main pollutants of concern are particulates less than 10 µm in aerodiameter (PM₁₀), nitrogen dioxide (NO₂), and carbon monoxide (CO) which may be found in both outdoor and indoor sources. Children spend an important proportion of their day in home or residential environments (50–60%) or in schools (30–40%) with relatively little time in outdoor activities (10–20%). Because residential exposures are difficult to measure and characterize, costly, and may raise ethical concerns, schools provide a more accessible common environment to examine potential environmental exposure to air pollutants. This discussion of exposure assessment therefore considers how the evaluation of air quality in schools could be done to investigate potentially related acute, or short time-lag health effects. The timescale from exposure to health effect is not considered further here, though it would need to be in a study.

8.3 Fundamentals of exposure assessment

Exposure is characterized by three dimensions: (1) intensity/concentration level; (2) duration; and (3) frequency. *Intensity* is determined by the level and source of air pollutants. In the school study, during busy traffic times outdoor pollution concentrations are high at levels potentially adverse for health. Outdoor PM₁₀ and CO and NO₂ levels sourced from vehicle emissions contribute to outdoor and indoor air pollutant concentrations in schools. Other factors contribute to varying indoor air pollutant levels including use of paints, glues, ventilation patterns (e.g. opening of the windows), and proximity to school kitchens. *Duration* of exposure to air pollutants will depend on the length of the school day (typically between 6.5 and 8 hours) and children’s activity patterns (whether they are playing outside or are in lessons in classrooms). During a school day, traffic will usually increase in the morning and in the late afternoon. Therefore the likely *frequency* of the increased concentrations as result of ambient air pollutant level contribution from traffic is twice during the school day.

Fig. 8.1 shows that higher levels of air pollutants in the classroom (in this case count per liter of particles of size 0.5–5.0 µm in aerodiameter: PM_{0.5–5.0}) are only experienced during short periods. In classroom 2, the *frequency* of these high level events is three times per day: between 9.30am and 9.45am, 12.10pm and 12.30pm, and home time (15.00pm to 15.20pm). The *intensity*, (PM_{0.5–5.0} concentration) during these time periods, is about 2–4 times higher than the background concentration during the rest of the day. In the hall, two episodes of higher intensity of PM_{0.5–5.0} occur, corresponding to high activity pupil times: lunch and physical education.

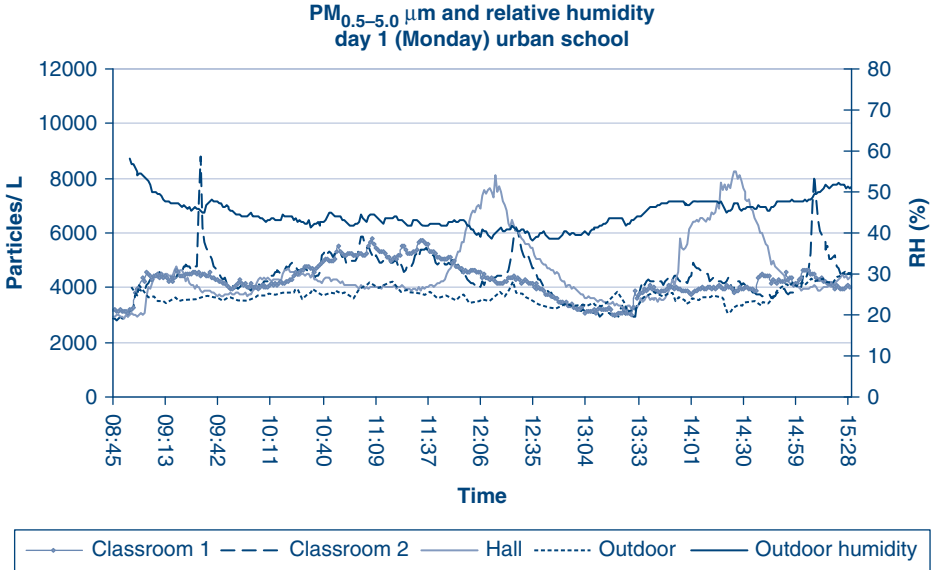


Fig. 8.1 Daily variability of particle count (0.5–5.0 μm in diameter) and relative humidity during usual school hours in an urban school.

Epidemiological studies of air pollutant health effects require the evaluation of representative environmental pollutant levels for each child taking part in the study. The biological processes involved in the exposure–response pathway may be of acute or longer-term duration. This will depend on the nature, level, and duration of the relevant exposure(s). There are two biological internal measures of actual exposure which include level and duration: *body burden*, the quantity of toxic substance in the body or a target organ at a moment in time (typical unit of measurement: mg or mg/kg); and *dose*, which represents the burden–time profile, and it is the measure of the total quantity of substance effectively taken up by the target tissue over time (typical unit of measurement: mg-years or mg/kg-years).

Fig. 8.2, shows that because *biological dose* and related mechanisms of the exposure–response pathway are generally unknown in observational epidemiology studies, the

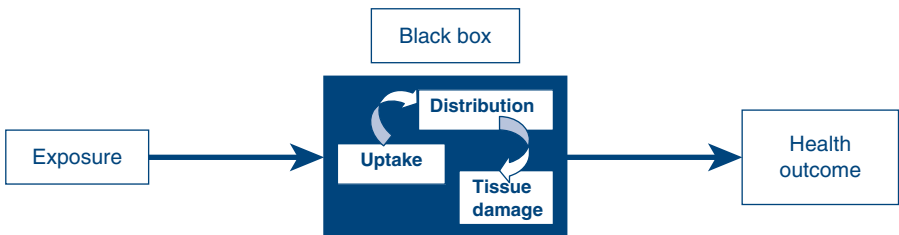


Fig. 8.2 The epidemiologist's black-box.

best approximation of internal dose may be made using the summary measurement of external personal exposure, with or without biomonitoring data.

There are two exposure assessment methods, direct and indirect. Direct methods use *biological* and *personal exposure monitoring*. They are considered the best methods to approximate biological dose in epidemiology studies. Biological monitoring requires identification of valid biological exposure markers (e.g. levels in a biological medium such as blood). In air pollution, there are several biological markers of exposure–response such as changes in inflammatory markers, coagulation factors, and oxidative stress markers. However, these are usually difficult to measure in children in particular due to their intrusiveness, ethical issues, and costs. Additionally, their specificity (correlation with actual exposure) is not sufficiently clear; hence the interpretation of these markers is complex. Personal pollutant monitoring is less intrusive than biological measurement, but would nevertheless require specially designed personal monitors attached to each child. Additionally one monitor cannot usually measure several pollutants and given the concern about multiple air pollutants, this would require more than one personal monitor per child. This may not be feasible for the schools and children involved in the study, as well as being very expensive.

Indirect methods for measuring exposure involve the development of *exposure models*. One method integrates observed activity-patterns of the children in combination with representative location-specific routine air pollution monitoring to develop personal exposure patterns for groups of children. This integrated method was used in the school study and is described in section 8.4. Another indirect, method uses *questionnaires* or *diaries* to assess exposure. However, the disadvantage of this method is the lack of an objective and quantitative measure of actual exposure.

Table 8.1 illustrates best to worst exposure measures in relation to their representation of actual exposure and biological dose. An accurate estimate of external exposure contributes to a closer approximation of actual biological dose. The table shows the types of exposure measure proxies used in environmental epidemiology and their levels of accuracy and precision for assessment of individual exposure.

Table 8.1 Types of exposure data obtained in environmental epidemiology studies

Type of data	Approximation to actual exposure and dose
Quantified personal measurements	Best
Quantified location-specific measurements	
Semi-quantified based on specific location and duration of exposure	
Classified based on small-scale location (school, for example)	
Classified based on a geographic area (neighbourhood, for example)	Worst

8.4 Exposure assessment methodology

There are a number of important elements that determine how exposure assessment is carried out:

- ◆ time of exposure
- ◆ location of exposure
- ◆ route of entry
- ◆ study population
- ◆ magnitude of expected risk
- ◆ the relation between external exposure and biological response
- ◆ other contributing and modifying factors (e.g. exposures, socioeconomic status).

These elements need to be considered in relation to the methodology, feasibility, and validity of exposure assessment.

8.4.1 Time of exposure

Exposures may be concurrent, retrospective, or prospective. In our case study, exposures are measured at the time of the study and are thus *concurrent*. If there is no exposure-to-health-effect lag, direct measurements of concurrent air pollutant concentrations provide valid exposure assessment for investigating the association with concurrent acute health effects. If, however, we want to evaluate whether recent changes to the school environment or children's behaviour have affected pollutant levels, a *retrospective* exposure assessment would be necessary. For example, replaced windows may affect the contribution of outdoor concentrations to indoor levels of air pollutants; internal building changes may affect the air flow and generation and/or spread of air pollutants indoors. Air pollutant levels would have to be estimated using appropriate assumptions about the effects of the change on the current pollutant levels. Exposure to air pollutants can also be measured *prospectively* using longitudinal exposure assessment, though this method is not always feasible. It involves placing measuring equipment in the school environments for long periods of time and may require ongoing presence of researchers. Alternatively, intermittent longitudinal measurements using shorter periods of continuous measurements, for example, over 1 week, repeated across long periods such as 1 or 2 years can be adopted.

8.4.2 Location of exposure

Exposure location is an essential component of environmental studies. During a school day, air pollutants concentrations will vary considerably between classrooms, halls, canteens, and outdoors. These levels will also differ in each location at different times of day, on different days, and according to the season, ventilation practices, and children's daily activities.

In this case study the best approach for exposure assessment would be to measure children's personal exposure to air pollutants directly and continuously. However, personal exposure measurement is not always feasible as explained earlier. Continuous environmental monitoring is the next best option to capture the variation in pollutant concentrations across

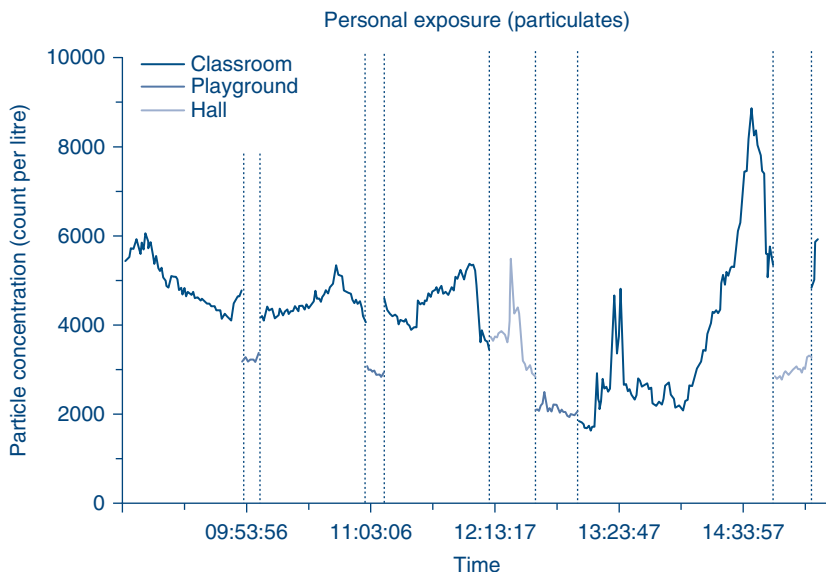


Fig. 8.3 Variation of personal exposure concentrations of air pollutants during a school day.

a usual school day and take into account seasonal variations. However, as already described, this may be resource intensive.

An alternative way is to develop personal exposure profiles to air pollutants for individuals or groups of school children, as discussed in section 8.3, using a combination of time-activity patterns and environmental measurements. These integrated models create a representative personal exposure profile for each child according to time spent in different environments and the measured concentrations of air pollutants in each of these environments. The concentration of air pollutants in school is measured during hours of occupancy, in several representative locations, including classrooms, halls, corridors, libraries, and outdoor areas in order to capture concentrations of relevant pollutants. Fig. 8.3 is an example of one such exposure profile for one child (or group of children) based on their time-activity spent in each school environment and representative measured pollutant concentrations during a usual school day. In order to validate these exposure profiles, it may be necessary to carry out a subset ‘standard study’ which involves personal monitoring of study subjects doing representative activities for longer periods of time.

8.4.3 Exposure route of entry

For common air pollutants, the most likely route of entry is by inhalation. Other routes such as ingestion or dermal absorption are likely to be insignificant by comparison and are not considered here. To reflect inhalation as the likely exposure route in the school study, representative locations for exposure monitoring are placed at the breathing height of children.

8.4.4 Study population

This investigation studied children of primary school age: 6–11 years old. This age group needs particular consideration with regard to the method of exposure assessment.

Children are smaller, less tolerant, and more active therefore it is less easy for them to wear multiple monitors than adults.

8.4.5 Magnitude of expected risk

In this study, small to medium health effects were expected because of the relatively modest levels of exposure (compared to industrial or extreme weather settings). Also, exposures will not differ much between subgroups in one school, and there may be several measurable or un-measurable potential confounding factors (see section 8.4.7). Accurate and precise individual exposure estimates strengthen the exposure–health risk assessment. In our case study, personal exposure to air pollutants in schools would be considered the best measure of exposure. However, the study is constrained by practical considerations to use a combination of location-based and continuous air pollution monitoring and time-activity patterns of groups of children. Sources of potential error and loss of power need to be considered carefully when evaluating study outcome.

8.4.6 Relation between the external exposure and biological response

Every person has an exposure intensity profile that changes over time. An epidemiological model needs a way of integrating this profile for each person. The choice of an exposure summary measure (dose metric) and a representative duration of this exposure (or exposures) is a key part of assessing the individual’s overall exposure. An accurate and precise metric of exposure chosen for epidemiological assessment will represent biological dose, thus strengthening the power of epidemiological studies to find exposure–response associations.

8.4.7 Consideration of other relevant exposures and factors

Children do not only spend time at school. Each environment they visit has different air quality and pollution from different sources. The contribution of other environments to the total environmental exposure burden and thus to observed health effects in children needs to be considered.

- ◆ Home/residential exposures include exposures from cooking, heating, crowdedness, smoking at home, residential environment (proximity to traffic, industry, green space).
- ◆ Extracurricular activities in other indoor or outdoor environments (e.g. swimming).
- ◆ Family and neighbourhood socioeconomic status. A child’s health will also depend on the socioeconomic background of her/his parents, and that of the neighbourhood. Socioeconomic factors are strong determinants of the distribution of environmental exposures, thus they can act as strong confounders in the study.

Assessment of other concurrent non-school exposures for multiple varying residential and extracurricular environments for each child is complex. Issues include the ethics and costs and validity of measuring different environments for different children

need consideration. Information on non-school exposures and socioeconomic factors can be collected using questionnaires and (or) diaries.

8.5 Limitations of exposure assessment in environmental epidemiology

Exposure assessment in environmental epidemiology has limitations. It is rarely possible to obtain direct exposure measurements and indirect exposure measures are only an approximation of the biological dose of the relevant pollutant. However, using the best approaches, measurement of external exposure can directly relate to the biological dose profile. In the school study, the best approach for approximating internal dose was estimated by integrating continuous exposure measurements of representative periods of time and locations and children time-activity patterns to capture short and long term variability in exposures. The potential limitations of this approach should be carefully considered when interpreting results.

8.5.1 Reproducibility and validity of assessed exposures

Reproducibility in exposure assessment takes account of whether by use of different methods (e.g. proxy, integrated, or a ‘gold standard’-‘true exposure’ assessment method) we obtain similar exposure estimates. *Validity* of exposure assessment defines whether the assessed exposure is representative of personal external exposure and internal biological dose. For example, even if the measurements of certain environments are valid instrumentally, they may not be valid epidemiologically if they show poor correlation to biologically relevant markers of exposure or dose.

The integrated approach combined the use of environmental measurements of relevant air pollutants in children-representative locations and children time-activity patterns used in this study tries to address both reproducibility and validity in exposure assessment. Time-activity patterns captured variability of exposure, for example, times of high pupil activity in classrooms. These were reproduced by measured classroom elevated levels for $PM_{0.5-5.0}$ during the same periods. It also allows the assessment of multiple pollutants with reproducibility, as the same pupil time-activity patterns and environmental monitoring locations are used. The approach aimed to model ‘true’ personal exposure, therefore ensuring validity of exposure assessment for epidemiological assessment. Further, validation of this approach against a ‘gold standard’ would reassure about its validity. This can be achieved by use of personal sampling in a subset of the study population. The integrated approach for exposure assessment of air quality in schools is less costly and easier to use across groups of people.

8.5.2 Issues of bias and misclassification in exposure assessment

Misclassification in exposure assessment can be defined as a difference between what is measured and the truth (actual exposure). Misclassification can be either random (chance) or systematic (bias) (the effects of chance and bias on health outcomes are

discussed in more detail in Chapter 14). Bias cannot be controlled or measured directly, so it must be avoided or minimized in the design of the study.

There are two opportunities to misclassify in exposure assessment. One is by misclassification of measurements of exposure intensity or duration. In the school study, three representative weeks were chosen to measure: one each during the autumn, winter, and summer terms. However, these weeks may not have been truly representative of the whole exposure profile of children in schools. High exposure events may have been excluded by chance and thus not counted in the health assessment. In the event of acute health responses this may lead to the underestimation of the exposure–health association. If an exposure–health response lag is likely, it is possible that the effects observed may be overestimated.

The second opportunity to misclassify is by the choice of the summary measures of the assessed exposure for health risk investigation. To represent intensity, duration, and frequency, the three dimensions of exposure pattern over time, several summary measures are used. In the school study, a weekly average exposure for each location can represent intensity. Frequency and duration of higher exposure concentrations can also be used. A combination of duration and intensity will result in a measure of cumulative exposure over time. All these summary measures should be valid in terms of the health effect of interest and the likely mechanisms for this health effect to occur. If acute respiratory health is of concern amongst the school pupils, then a measure of exposure intensity (weekly mean concentration) is relevant. If allergic symptoms are of concern, the role of sensitization must be considered, thus duration of exposure should be also taken into account.

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Toxicology and its practical use in chemical incident response

Virginia Murray and Rachel MacLehose

Learning objectives

- ◆ Describe, assess, and apply basic toxicological concepts.
- ◆ Using a case study, integrate the application of toxicology in environmental epidemiology.

9.1 What was the initial problem?

In the north-west of England, one Sunday night in October 1997, between 5 and 10 litres of elemental mercury stored in glass jars (weighing approximately 70–100 kg), were allegedly stolen by several youths from a locked cupboard on an industrial site which had formerly been a scrap yard (MacLehose et al., 2001). In the process, elemental mercury was spilt on adjacent paths and roadways and the youths played with the mercury by throwing it and spitting it at one another. The youths took much of the material back to their homes (MacLehose et al., 2001).

The following morning the Fire Brigade was called about the ‘silver like’ material on the roads, paths, and along a nearby canal, and they alerted the local authority environmental health department. The incident occurred on the borders of two local authorities and also two health authorities. Mercury was found in all these coterminous authorities’ areas (MacLehose et al., 2001).

At 12.30 hours the local Children’s Hospital (now closed) was alerted by police and advised that they could receive children with possible, or even probable, mercury poisoning. The hospital sought toxicological advice and contacted the Guy’s and St Thomas’ Poisons Unit (now closed) and their Chemical Incident Response Service (CIRS) for advice. Toxicological data were dispatched from CIRS to the hospital. CIRS, with the consent of the hospital, contacted the local health authorities and, through them, the local general practitioners were also informed. In total, 76 children attended the Emergency Department on the Monday, placing great pressure on resources leading to requests for help from the police and other local responders by the local health authorities. A press statement released

on the same day informed the public of the incident and people were advised to attend hospital if they considered they had been exposed (MacLehose et al., 2001).

9.2 Sources and uses of mercury

Mercury occurs widely in the environment, due to natural and anthropogenic processes. Most of the mercury released from man-made activities is elemental mercury released into the air due to mining ore containing mercury, burning fossil fuels, and incinerating waste (Bull, 2011). Mercury also enters the soil from fertilizers, fungicides, and waste from thermometers or electrical switches. It has three forms, namely elemental (metallic) mercury, inorganic, or organic mercury (Bull, 2011):

- ◆ Elemental mercury, which was involved in this incident, is a shiny, silver white metal, liquid at room temperature. It evaporates to form mercury vapour, which is the predominant form of mercury in the atmosphere.
- ◆ Inorganic mercury compounds contain mercury combined with other elements such as sulphur, oxygen, or chlorine. They are mostly white powders or crystals.
- ◆ Organic mercury exposure, particularly methyl mercury, can occur via diet, largely due to ingestion of contaminated fish. It can cause ataxia, visual disturbances, hearing loss, muscle weakness, and mental retardation with *in utero* exposure risks since it readily crosses the placenta to the fetus (Bull, 2006).

9.3 Source–pathway–receptor framework for investigating an environmental exposure incident

The application of the concepts of chemical toxicity and the risks from environmental exposures can be most simply expressed via the source–pathway–receptor concept which is very useful in investigating chemical incidents (Fig. 9.1). For a hazardous substance to pose a risk to human health there has to be a source of that substance, viable exposure pathway(s), and receptors (people) who can be exposed. If a source, pathway(s), and receptors are present, a ‘pollution linkage’ will be complete. Illness may be identified in the receptor and concerns raised about possible chemical causes if there is a pathway back to a source. Conversely, if there is no pathway, then a source cannot cause illness in a receptor.



Fig. 9.1 Source–pathway–receptor concept for toxic exposures.

Adapted from Saikat, S. and Wilson, J. (2012). Public health risk assessment of contaminated land. In Baker, D. et al. (Eds.) *Essentials of Toxicology for Health Protection—a handbook for field professionals* (2nd edn.), pp. 125–35. Oxford: Oxford University Press, Copyright © 2012 with permission from Oxford University Press.

In the mercury incident identification of the source (the elemental mercury alleged to have been stolen from an industrial site), the relevant pathway (dermal, inhalation, ingestion), and the initial receptors (the children involved in removing the mercury from the site) allowed comprehensive investigation of this chemical incident to be made.

9.4 Key concepts in toxicology

Toxicology is essentially the science of toxins (commonly known as poisons). It studies the manner in which toxins cause harmful effects to living organisms, the amounts (doses) that cause such harm, the consequences of harm (e.g. disordered function, disease, death), how harmful effects can be treated, and how to prevent such harm. Toxins or toxic substances vary in their origin, chemical structure, and physical properties and these variations affect how they cause toxicity.

9.4.1 Dose response

Paracelsus, in the 16th century as the father of toxicology stated ‘No substance is a poison by itself. It is the dose that makes a substance a poison’. It is also important to know whether the dose was received in one event, repeated events, or slowly over a long time. The dose and the nature of the exposure are critical factors in determining the potential toxicity of a substance:

$$\text{Dose} \times \text{Exposure (single or repeated)} = \text{Toxic effect}$$

The dose/amount may be expressed as weights or volumes: milligrams, micrograms, litres, or millilitres or as concentrations in air with units such as milligrams per cubic metre (mg/m^3).

9.4.2 Routes of exposure to toxic substances

The following are the main routes by which a chemical may enter a living organism:

- ◆ *Inhalation*: a common route of exposure, particularly in occupational settings. Toxins inhaled via the nose and breathing tubes (bronchi and bronchioles) enter the lung and pass into the thinly lined air cells (alveoli), which are surrounded by blood vessels. The harmful substances diffuse across the thin lining of the alveoli into the blood stream, albeit to varying degrees.
- ◆ *Dermal (across the skin)*: a common route of exposure is absorption through the layers of the skin. The rate of absorption often depends on the substance in which the toxin is dissolved.
- ◆ *Ingestion (orally)*: if the toxin is swallowed absorption of the administered dose usually occurs in the gastrointestinal tract (especially stomach, intestines).
- ◆ *Through mucous membrane*: substances may enter the body by absorption through the mucous membrane in the mouth, around the eyes, or via the rectum or vagina.

- ◆ *Injection:* toxins can be administered directly into the bloodstream into a vein (intravenous injection), or less commonly into an artery. Injections given into muscle (intramuscular) produce slower absorption into the bloodstream.

Exposure to mercury may occur from breathing contaminated air, eating contaminated food or water, or by skin contact (Bull, 2011). Spillages of elemental mercury from broken thermometers or barometers may result in exposure to mercury vapour and skin contact during clean up.

In the case study on mercury exposure most of the index cases were found to have had acute exposure and a few developed acute poisoning. Elemental mercury was rapidly spread by the children involved in the incident (Maclehose et al., 2001). As the children were playing with it, they were exposed via all routes described with the exception of injection. Games with the mercury involved ‘blowing’ the substance from their upper lips, playing with it in their hands and storing in their clothes. The mercury was also transported into their homes via clothing and thus contaminated washing machines, vacuum cleaners, and furniture. Contamination of vacuum cleaners led to the mercury being re-vaporized leading to further inhalation of mercury. Precise estimates of doses received are unknown due to the variety of routes and unknown duration of exposure.

9.4.3 Fate of toxins in the body

Fig. 9.2 summarizes the possible routes of exposure and pathways of absorption, distribution, and excretion of toxic chemicals in humans.

The harmful effects of mercury depend on the way people are exposed and the type of mercury they are exposed to. After ingestion of elemental mercury, very little enters the body, whereas after breathing elemental mercury vapour, about 80% enters the blood from the lungs (Bull, 2011). Toxic effects of inhaled mercury vapour include acute nervous system and respiratory effects including tremors, walking difficulties, chest pains, breathlessness, and damage to the lining of the mouth and lungs. Kidney damage may also occur as well as stomach irritation, nausea, vomiting, and diarrhoea. The thresholds for toxicity and clinical features of mercury exposure are shown in Tables 9.1 and 9.2.

The *toxic effect* or the harmful effect of a potentially toxic substance on the body is determined primarily by the dose of the toxic substance that reaches *target organs* (such as the lungs, liver, kidneys, heart, or brain). This is known as the *target dose* and it depends not only on the dose entering the body but also on the metabolic processes that take place within the body once the potentially toxic substance has entered the body.

Once inside the human body, a toxin is subjected to metabolism, excretion, or binding to tissues, cells, or blood components such as proteins, and this is referred to as *toxicokinetics*. The key processes involved in toxicokinetics are shown in Box 9.1. These can result in the total elimination of the chemical substance with no ill health or ill effects from altered function of biological systems, neurotransmitters, enzyme systems, or cell death.

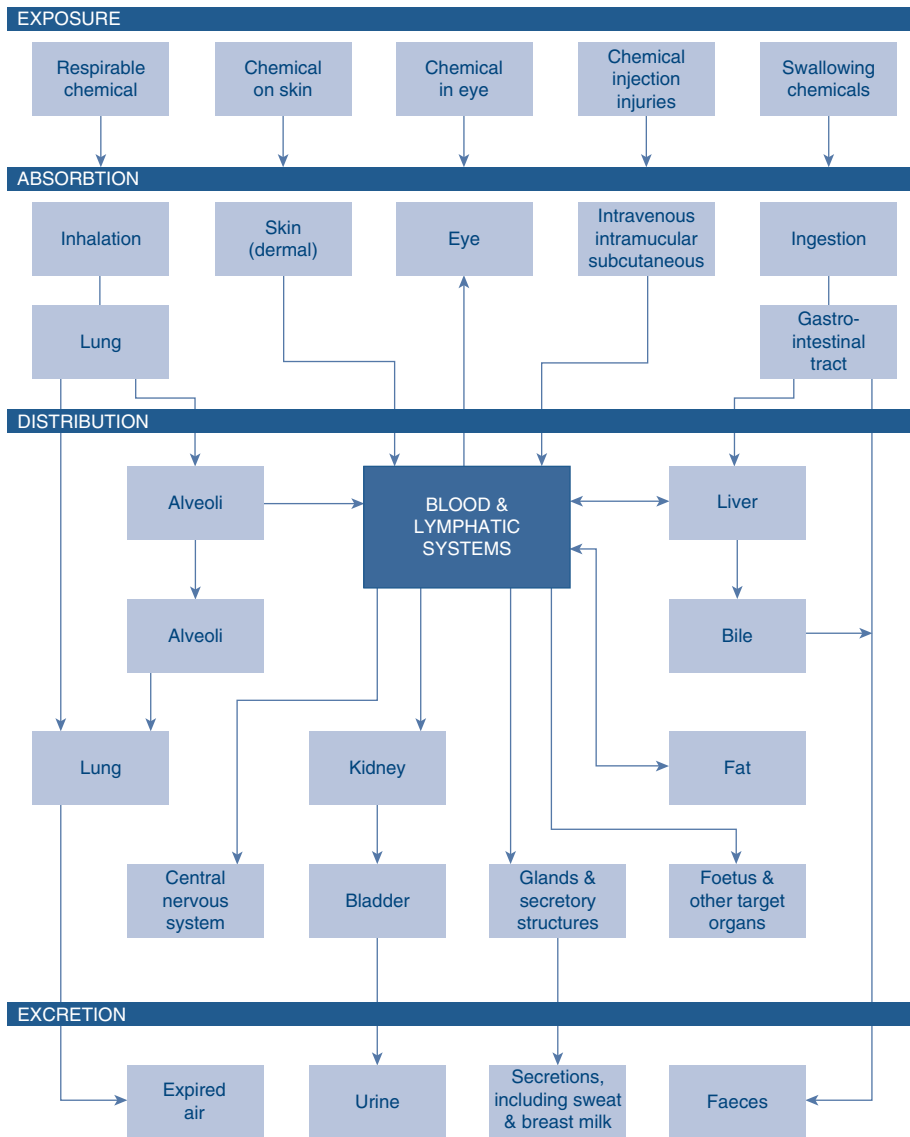


Fig. 9.2 Summary of routes of exposure, absorption, distribution, and excretion of toxins in the body.

Reproduced from Karalliedde, L., Baker, D., and Murray, V. (2012). Introduction to toxicology. In Baker, D. et al. (Eds.) *Essentials of Toxicology for Health Protection—a handbook for field professionals* (2nd edn.), pp. 1–17. Oxford: Oxford University Press, Copyright © 2012 with permission from Oxford University Press.

Table 9.1 Mercury threshold toxicity values in air leading to health effects

Exposure via inhalation		
Parts per million (ppm)	Milligrams per cubic metre (mg/m)	Signs and symptoms
0.006	0.05	Non-specific symptoms
0.012–0.024	0.1–0.2	Tremor
0.12–4.83	1–40	Chest pain, haemoptysis, dyspnoea, cough, impairment of lung function, metallic taste, and excessive salivation

Reproduced with permission from Bull, S. (2011). *Inorganic mercury/elemental mercury*. HPA Compendium of Chemical Hazards. © Health Protection Agency 2011.

Table 9.2 Toxicity of elemental mercury

Blood concentration (µg/L)	Urine concentration (µg/L)	Clinical features
<10	<10	Normal concentrations
50	100	Some renal function impairment
100	200	Serious neurological dysfunction and some renal impairment
200	400	Renal shutdown possible and very serious neurological effects
400	800	Renal shutdown certain
1000	2000	Immediate shutdown
5000	10,000	General organ failure

Data from House, I., Guy's and St Thomas' Poisons Unit (1997) personal communication.

Box 9.1 Key concepts in toxicokinetics

- ◆ *Rate of absorption*: from the gut if the toxin is ingested, the rate of breathing if intake is inhalational, blood flow if intake is by intramuscular injection or intravascular injection.
- ◆ *Metabolism*: the process by which a substance is made less harmful (although the opposite may occur) usually in the liver, kidney, or intestine.
- ◆ *Binding*: the extent to which the toxin may bind to proteins, fat and other tissues.
- ◆ *Distribution*: toxins are distributed around the body, usually in the blood for excretion via the kidneys, lungs, intestine, sweat, or breast milk or for storage in fat or other tissues.
- ◆ *Excretion*: the removal of the potentially toxic substance from the body in the urine, faeces, bile, breath, or sweat.

9.5 Incident management

Assessing the scale of the mercury incident was challenging given that it originated from an alleged theft. Once a press release had been issued, children started to attend hospital and could then be followed-up. The first set of elevated blood and mercury levels were returned for two individuals within 5 days of the start of the incident. As further blood and urine tests were taken the wide scale of the incident became apparent.

An Incident Control Team was set up early on in the incident to ensure effective, coordinated incident management. This Incident Control Team was led by the local Directors of Public Health with approximately 30 organizations involved including local health care staff, environmental health, police, fire and ambulance services, and CIRS. Questionnaires were drawn up by the Incident Control Team and these were used by health care and environmental health staff to identify individuals at risk and identify premises that might be sources of ongoing exposure. The questionnaires were informed by knowledge of the source–pathway–receptor model for mercury.

The case definitions for the investigation were:

- ◆ An exposed individual was one who had been in contact with the elemental mercury following the theft of the mercury.
- ◆ A case of poisoning was defined as a person at risk of toxic effects due to blood mercury levels greater than 15ug/g (normal <10 µg/L) and urine mercury to creatinine ratios greater than 15ug/g (normal <10 µg/L).

The toxicological results, both environmental and clinical, combined with the questionnaire data enabled the appropriate follow-up of affected individuals and contacts. In addition to demographic information, details such as school attended and numbers and ages of others living at the same address were collected. All the children involved in the initial exposure were followed-up, and through them contacts were identified and assessed to see if they had been exposed to the mercury using the incident-specific questionnaires. Identifying cases (and exposure routes) was problematic given the nature of the incident and original source of exposure. A number of children in the incident were of no fixed abode or living in temporary accommodation and some became adults during the follow-up phase. The accuracy of the questionnaire data (for addresses and exposure routes) was variable but the factual analytical toxicological data was vital in clarifying individual risks and identifying other potentially contaminated people and premises.

Susceptible groups can be classified into three main types based on biological, sociocultural, or ethnic characteristics that may affect their vulnerability to adverse effects resulting from environmental exposure to elemental mercury and other toxins (Chapter 5). However, it is important to remember that susceptibility is not the same for all chemicals. The range of an individual's risk factors should be considered when making any assessment of toxic harm.

In the mercury incident the main exposure route was inhalation. The vulnerable exposure group was mainly children. One hundred and sixty-two children aged 0–16 years were exposed, with 27 deemed to be at risk of toxic effects due to blood mercury

Table 9.3 Age distribution of patients involved in the incident

Age at time of incident	Not at risk of toxicity ^a	At risk of toxicity ^b		Total
		Total	Symptomatic Hg poisoning	
0–5	9	2	1	11
6–16	126	25	10	151
17–25	17	1	1	18
26–35	9	2	0	11
36–55	26	6	1	32
>56	1	1	0	2
Totals	188	37	13	225

^a Blood mercury, <15 µg/L and urine mercury creatinine ratios <15 µg/g.

^b Blood mercury, >15 µg/L and urine mercury creatinine ratios >15 µg/g.

Reproduced with permission from MacLehose, R., *et al.* (2001). Mercury contamination incident. *J Public Health* 23(1):18–22, © Oxford University Press 2001, doi:10.1093/pubmed/23.1.18.

levels greater than 15µg/g (normal <10 µg/L) and urine mercury to creatinine ratios greater than 15µg/g (normal <10 µg/L). A small number of children were involved in the alleged theft of the mercury and they subsequently transported it to schools and domestic premises resulting in further exposure to adults and other children. The age distribution of those exposed to mercury and their levels of blood mercury is summarized in Table 9.3.

The toxicological information also provided the basis for environmental assessments by the environmental health departments. Toxicological data in particular indicated where follow-up might be necessary for individuals who were not showing any clinical signs of mercury poisoning at the time. Identification of individuals at risk of toxicity was done by environmental sampling using a Shaw City Vapour Monitor and biological sampling (urine and blood samples). Clinical and environmental health data, combined with information from the questionnaires was used by the Incident Control Team to assess locations for possible contamination from the mercury.

Once individuals had been identified as potentially being exposed to the mercury, they were asked to attend for blood and urine tests. The results of these tests, combined with information from the questionnaires, allowed more detailed environmental monitoring to occur. Individuals with elevated blood or urine levels, who were considered at risk of toxic effects, were followed-up with monthly tests until two consecutive samples showed levels less than 15µg/L for blood mercury concentrations or less than 15µg/g for urine mercury creatinine levels.

Mercury was found to have contaminated 21 houses (78 were assessed for contamination) and schools. As a result of this contamination and continued exposure route, 1.5 tonnes of property, including a sofa, carpets, curtains, vacuum cleaners, and washing machines, was removed from these premises.

Exposure to mercury continued over the next few months through the use of contaminated domestic machines (primarily vacuum cleaners and washing machines) leading to continuing exposure. Because of the environmental hazards it was agreed that follow-up was not completed until those classified as at risk of toxicity provided two clear samples with mercury levels below the required limit, or it was considered that the risk to individuals was either eliminated or reduced as far as possible.

By the end of the investigation 188 individuals were classified as exposed, with 37 identified as being at risk of mercury poisoning. The Incident Control Team finally declared that the mercury contamination incident was officially closed after 15 months.

9.6 Toxicology and environmental epidemiology

Toxicology is the study of the nature and mechanism(s) of toxic effects of substances on living organisms and other biological systems. This chapter summarizes a chemical incident where the source–pathway–receptor concept facilitated the investigation and remediation using environmental epidemiology tools.

Toxicology is one of the key disciplines informing environmental epidemiology as it identifies harmful toxins and the precise nature of the potential harm. One of the main criteria for inferring causality proposed by Bradford Hill (1965) is biological plausibility, and toxicology is fundamental to understanding the way in which a given toxin enters the body and acts on specific biological systems. The source–pathway–receptor model is a crucial part of our understanding of how environmental toxins can reach humans (and the susceptibility of particular population groups). This is particularly important in environmental epidemiology where exposures are often to complex mixtures of chemicals (waste sites, industrial effluent, smoke plumes, etc.) with multiple routes of exposure (air, water, soil) and levels of exposure are often relatively low. Toxicological information is vital in identifying which chemicals are most likely to cause toxic effects and in which form, so that any investigation of health effects correctly classifies individuals as exposed or unexposed. An understanding of chemical behaviour in the body informs the correct evaluation of environmental exposure and gives an indication of which media to sample in order to determine the relevant environmental exposure levels.

9.7 Further reading

Baker, D., Fielder, R., Karalliedde, L., Murray, V.S.G., and Parkinson, N. (Eds.) (2012). *Essentials of Toxicology for Health Protection—a handbook for field professionals* (2nd edn.). Oxford: Oxford University Press.

This book summarizes toxicology found to be of value for frontline professionals and is organized into four sections and an appendix covering:

- ◆ *Fundamentals of toxicology* provides a general introduction to the subject and explains how toxicological information is derived.
- ◆ *Applications of toxicology* addresses exposure assessment, susceptible populations, and the medical management of chemical incidents. It also provides valuable pointers to sources of toxicological data.

- ◆ *Environmental toxicology* considers pollutants in air, water, and land, and food contaminants and additives. In ‘Occupational toxicology’ it considers exposures to toxic agents in the workplace.
- ◆ *A review of some toxic agents* addresses in detail a selection of important toxic agents: carbon monoxide, pesticides, heavy metals and trace elements, as well as the emerging issues of traditional medicines and the deliberate release of toxic agents in warfare.
- ◆ An appendix on basic concepts of human science, and a glossary are included as appendices for those readers, for example, environmental engineers, who don’t have a background in medicine, biology, or the health sciences.

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Risk assessment

Raquel Duarte-Davidson

Learning objectives

This chapter presents a case study to provide an overview of the common features and guiding principles of health risk assessment and summarizes the application of risk assessment. The chapter also explores the principles for the analysis of effects on human health for environmental exposures to:

- ◆ Appraise the terminology and technical basis for risk assessment.
- ◆ Assess the realistic powers and limitations of a tiered approach to risk assessment and gain initial experience in the critical evaluation of studies that use this type of approach.
- ◆ Evaluate the interface between environmental exposure assessment and risk assessment to better understand the relationships between these approaches.

10.1 Introduction

There is increasing public concern that environmental agents may pose a potential threat to human and environmental health. Environmental agents include naturally occurring pathogens and toxins as well as gaseous pollutants, respirable particles, toxic elements, and persistent organic pollutants in air, water, and soil.

Risk assessment is an important tool for evaluating the likelihood and extent of actual and potential exposure to sources of environmental hazards (Institute for Environment and Health, 1999; Department for the Environment, Food and Rural Affairs, 2011). In general, assessing risks involves evaluating, at various levels of detail, the degree of connectivity between the source of a hazard (e.g. an incinerator, waste site, or contaminated land) and a receptor (e.g. humans, buildings, ecosystems) in the environment by studying the exposure pathway(s) between them (Pollard, 2001; Nieuwenhuijsen et al., 2006). This chapter provides an example of this process.

10.2 Case study: assessing the risks to public health from the disposal of carcasses from a foot and mouth outbreak

This case study illustrates a structured approach to dealing with assertions of health effects associated with environmental exposures (Department of Health (DH), 2001).

A tiered approach to risk assessment is followed, involving a rapid qualitative screening assessment of the possible public health risk from the disposal of carcasses following from the foot and mouth outbreak in the UK in 2001. This illustrates the usefulness of prioritizing risks before undertaking a more detailed quantification of the prioritized risks.

10.2.1 What was the original problem?

In April 2001 there was a foot and mouth disease outbreak in the UK which led to the culling and disposal of an unprecedented number of animals. During the outbreak about 4 million animals were slaughtered including 2.6 million sheep; 0.6 million pigs, and 0.8 million cattle. Due to the number of carcasses, it was necessary to use all disposal methods available at the time. It was important to determine the main hazards and exposure routes relevant to all disposal options.

At the time of the outbreak there were four main mechanisms for disposing of the carcasses and an additional option (mass burial) was considered as a means of disposing of large volumes of animals.

- ◆ Rendering is a process that converts waste animal tissue into stable, value-added materials. During the outbreak entire animal carcasses were processed. The rendering process simultaneously dries the material and separates the fat from the bone and protein.
- ◆ Incineration involves industrial, high-temperature burning, at a permanent site or using mobile equipment.
- ◆ Landfill is disposal in a lined pit within a licensed engineered landfill site.
- ◆ Pyre burning involves burning on an open site, either at or away from the site of slaughter.
- ◆ Mass burial on farms is a method that potentially allows for the disposal of tens of thousands of animals at a single site. This is not common practice under normal circumstances as burial of animals in unlined pits is usually only done on a small scale to dispose of a few animals.

10.2.2 What was the scope of the study?

The aim of the study was to investigate the potential public health risks (population living nearby or more generally) of the different disposal options; it did not include occupational exposures (though the study served to emphasize the importance of adequate protection). The findings from the risk assessment were used to determine policy on disposal of carcasses.

Due to the short timescales much of the work had to be desk based, supplemented by first-hand reports of the situation by direct observations (e.g. from pyre burning), site visits, and local interviews (e.g. with disposal contractors and those involved in the response). There was no time to consider novel methods of disposal nor, given the scientific uncertainties, was a full quantitative analysis of all potential hazards undertaken.

10.2.3 Methodology

Risk screening was used to prioritize the main risks following the foot and mouth outbreak and to begin to identify how these risks could be avoided or mitigated. This involved undertaking a qualitative risk assessment to examine the potential public health risks that might arise from using these disposal options on such a large scale (DH, 2001). This was followed by a semi-quantitative risk assessment to further examine the shortlisted hazards. The information obtained from the risk screening process and the semi-quantitative analysis was then used to compare the different disposal methods.

10.2.4 Risk screening

10.2.4.1 Identification of potential hazards

All relevant potential hazards to human health from animal slaughter and disposal were listed and roughly categorized by type of hazard. Data were collated from a wide range of sources to gather basic information on the key characteristics of each hazard. Table 10.1 provides an example (for three groups of chemical hazards) of the information collated in the spreadsheets. The aim was to produce a comprehensive list without pre-judging which hazard might pose the most serious risks. This was then cross checked with a detailed assessment of the pathways produced. Information was also collated on the form of the release including the release mechanism and timescale of the release.

Over 100 hazards (and/or groups of hazards) were identified that may potentially arise from carcass disposal by the various methods available. Biological hazards included *Campylobacter*, *Escherichia coli*, *Listeria*, *Salmonella*, *Mycobacterium*, *Cryptosporidium*, *Giardia*, *Clostridium tetani*, prions from bovine spongiform encephalopathy (BSE), and scrapie. Examples of chemical hazards include methane, carbon dioxide, polycyclic aromatic hydrocarbon (PAHs), dioxins, disinfectants, detergents, hydrogen sulphide, particulates, sulphur dioxide (SO₂), and nitrogen dioxide (NO₂).

10.2.4.2 Identification of exposure pathways

This step involved the identification of the exposure pathways to human for all chemical and biological agents identified. A qualitative source–pathway–receptor–harm qualitative analysis was undertaken and presented in a tabular form (see Table 10.1).

10.2.4.3 Public health consequences of exposures

The potential public health consequences of exposures by biological and chemical agents were considered by taking into account the likelihood of exposure and populations exposed (including high-risk groups), health effects on individuals exposed, and whether there are any existing preventative measures put in place to reduce the risk of human exposure. For example, what population could or would be exposed? What is known about the effects to human health (dose–response, symptoms, populations that may be particularly at risk)? And what would be the leading indicator (if any) of significant exposure and/or adverse health effects?

Table 10.1 Examples of exposure pathways and public health consequences from a number of selected hazards: PAHs, dioxins, and ammonia (and other nitrogen containing substances)

Source of hazard		Release			Exposure pathway	
Hazard	Agent (e.g. bacteria, virus, chemical)	From . . .	Released by (mechanism)	Timescale of release	Likely location of contaminant (e.g. soil, water, air)	Pathways to humans
PAHs (polycyclic aromatic hydrocarbon compounds)	Chemical	Fire	Pyre	Years	Air and food	Expected anyway
Dioxins	Chemical	Combustion products from burning of carcasses, other feedstock chlorinated disinfectants	Pyre burning incineration	Very long-scale dioxins are persistent in the environment and bioaccumulate	Intake from fatty foods produced in contaminated areas Inhalation from contaminated air a minor source of exposure	Acute poisoning will not occur
Ammonia and other nitrogen-containing substances, e.g. nitrates	Chemical	Animal excrement and decay	Burial	Months	Air/water	Inhalation water sources

Public health consequences					
Hazard	Likelihood of exposure (for the given release)	Population exposed, at-risk groups	Leading Indicators	Individual outcomes (health effects)	Existing preventive measures in place that should stop or lessen the risk to human health
PAHs (polycyclic aromatic hydrocarbon compounds)	Inhalation deposition and incorporation in food		PAH monitoring very limited, effect if any on lung cancer wouldn't be seen for years	Small risk of cancer with prolonged exposure, may not be relevant for raised exposure over only a few days	Slight effect by choice of fuels but PAHs will always be present Advice to population as above Site Pyres to avoid residential areas
Dioxins	Likely in any fire. Possible subsequent exposure by consumers of some animal food products from contaminated areas	People living near pyres or consumers of contaminated produce.	Monitoring of soil and/or plants in areas of pyres	Providing intakes are below the tolerable daily intake or only occasionally above, no adverse effects are anticipated. If intakes consistently exceed TDI adverse effects still unlikely but could create substantial risk communication problems	Washing and peeling vegetables will remove deposits. Monitoring by FSA before areas near pyres used again for grazing.
Ammonia and other nitrogen containing substances, e.g. nitrates	Probably inevitable when animals are around	As for air pollutants possible if small amount in fires. For burial surface/ groundwater users	Smell	Health risks unlikely other than at very high concentrations. Nitrates can cause blue baby syndrome but this is very rare in the UK	Water companies are increasing monitoring of supplies. Particularly taste and using powered activated carbon where the facility exists

FSA = Food Standards Agency; TDI = tolerable daily intake.

Data from DH (2001). *A Rapid Qualitative Assessment of Possible Risks to Public Health from Current Foot and Mouth Disposal Options*. London: Department of Health, © Crown Copyright 2001.

10.2.4.4 Preliminary shortlist of hazards

Drawing on earlier stages, a provisional shortlist of the hazards that warranted further analysis was established. Reasons for not including potential hazards in the shortlist were made explicit and kept under review. The following was used to produce this shortlist:

- ◆ If the hazard involved had severe health effects on humans in quantities associated with the disposal operation and
- ◆ if released, the hazard was likely to evade being destroyed or negated prior to human exposure and
- ◆ if the quantity to which humans were to be exposed could be sufficient to cause significant health effects, bearing in mind the type and timescale of exposure
- ◆ then the hazards were prioritized and selected for further examination (i.e. a more detailed semi-quantitative risk assessment was undertaken on the selected hazards).

This risk screening process resulted in a shorter list of potential public health risks from a number of disposal options and exposure pathways. Table 10.2 shows a summary of the potential health risks and relevant pathways of agents to humans associated with the different carcass disposal options. For simplicity some hazards are grouped together.

The disposal option for each group of hazards for which the exposure to humans would be the greatest is shown in dark grey; others that would imply some exposure are shown in light grey. For an example, pyre burning may result in the greatest exposure to particulates, SO₂, NO₂, nitrous particles, PAHs, and dioxins via inhalation, whilst incineration may entail some degree of exposure to these hazards. Pyre burning may also result in the greatest exposure to PAHs and dioxins through the deposition into the food-chain. Other disposal options (e.g. burial or rendering) are unlikely to cause an increase in exposure to these air pollutants via inhalation.

This table also indicates that rendering is the disposal option with lowest exposure risk, assuming that this process is carried out to high standards. Burial of carcasses appears to be the highest exposure risk option as most hazards identified might reach humans via private drinking water supplies. The next step is to undertake a more detailed risk assessment of the hazards of greatest concern identified in Table 10.2 to obtain better estimates of the risks associated with these disposal options.

10.3 Semi-quantitative risk assessment of shortlisted hazards

The next step was a more detailed semi-quantitative risk assessment of the hazards that had been prioritized to estimate the risks more accurately by making use of any additional information or data estimates that were available. This involved refining the assessment by including measured and modelled data, where available, for example, using information available from some of the sites. The assessment for sulphur dioxide is described here as an example.

SO₂ is potentially the most harmful of the various gases released by burning which also include nitrogen oxides (NO_x), hydrogen chloride, carbon monoxide and PAHs. SO₂ has been associated with bringing forward the deaths of those already seriously ill with heart

Table 10.2 Summary of potential health risks, disposal options and pathways

Public health hazards	Disposal option					Pathway of agents to humans
	Rendering	Incineration	Landfill	Pyre	Burial	
<i>Campylobacter</i> , <i>E. coli</i> (VTEC), <i>Listeria</i> , <i>Salmonella</i> , <i>Bacillus anthracis</i> , <i>C. botulinum</i> , <i>Leptospira</i> , <i>Mycobacterium tuberculosis</i> var <i>bovis</i> , <i>Yersinia</i>						Private water supplies Direct contact Recreational water use (Possibly also shellfish)
<i>Cyptosporidium</i> , <i>Giardia</i>						Water supplies (mains and private) Crops, shellfish Direct contact recreational water use
<i>Clostridium tetani</i>						Contact with contaminated soil
Prions for BSE, scrapie						Water supplies via leachate runoff, ash burial
Methane CO ₂						Leakage into housing
Fuel-specific chemicals. Metal salts						Inhalation Deposition into food chain
Particulates SO ₂ , NO ₂ , nitrous particles						Inhalation
PAHs, dioxins						Inhalation Deposition in to food chain
Disinfectants, detergents						Water supply Inhalation of products?
Hydrogen sulphide						Inhalation

Key: within each row disposal option with the greatest exposure of humans to hazards shaded in dark grey, other options entailing some exposure in light grey.

Reproduced from DH (2001) *A Rapid Qualitative Assessment of Possible Risks to Public Health from Current Foot and Mouth Disposal Options*. London: Department of Health, © Crown Copyright 2001.

or lung disease. The key pathway of exposure is through inhalation and, as Table 10.2 highlights, pyre burning is the disposal option likely to be associated with the greatest exposure to humans. In modelling exposures via inhalation a number of different modelling scenarios were carried out using different quantities of animals for disposal.

Initially pyres burned about 250 cattle (or equivalent) and as the outbreak unfolded these were extended to larger pyres which burned 1000 cattle per day for 3 days and then for 20 days (DH, 2001). The quantitative model suggested that burning about half the estimated number of carcasses would add only small percentages to the total normal UK emissions; for example, burning 700,000 cattle, 100,000 pigs and 2 million sheep would add just under 0.3% of the annual UK emissions.

However, the potential local effects of large pyres might be substantial. Assuming that the pollutants emitted from a pyre are roughly proportional to the number of animals burnt on it, then the geographical distribution of airborne pollutants would be affected by the size of the pyres and whether plumes from adjacent pyres overlap. The scenarios modelled suggested air quality standards would be regained at a maximum of 3.5 km downwind of a pyre burning 250 cattle, but would be substantially exceeded at 4 km from a pyre burning 1000 cattle per day. These findings had clear implications for large pyres situated closer to human habitation even through the effects on air quality would only be temporary. Box 10.1 provides a summary of the risk characterization sheets that were prepared for SO₂. Similar sheets were also prepared for other relevant hazards.

Box 10.1 Summary of risk characterization for sulphur dioxide

Description: sulphur dioxide (SO₂) is gas formed during combustion, which oxidizes in water droplets to form sulphuric acid (H₂SO₄). It causes acidification of soil and surface water. If inhaled, SO₂ is a potent bronchoconstrictor. Sulphur in coal is the main source.

Prevalence in foot and mouth disease disposal: there is minimal sulphur in carcasses. SO₂ will mainly be formed during combustion of the fuel. There is more sulphur in low-grade fuel oil than kerosene or natural gas.

Main potential pathway from foot and mouth disease disposal:

- ◆ Inhalation of gas emitted from incinerator/pyre.

Persistence in the environment:

- ◆ Precipitated from the atmosphere usually within several days.
- ◆ Inactivation timescale in the ground—unknown, assumed several months (precipitation as solid salt).
- ◆ Inactivation timescale in water—unknown, assumed as for ground.

Box 10.1 Summary of risk characterization for sulphur dioxide (continued)

Desirable disposal options: methods involving no combustion or low-sulphur fuel. Order of preference for this hazard:

1. = landfill (no combustion)
2. = burial on farm (no combustion)
3. Rendering (no combustion but SO₂ generation from fuel needed for high temperature process)
4. Incineration (combustion, but with effective controls on releases)
5. Pyre burning (less controlled combustion, not necessarily with low sulphur fuel).

Population exposed: workers near to pyres, residents within area affected by smoke/stack emissions.

Health effects: atmospheric exposure to SO₂ is considered to be linked to respiratory symptoms, reduced lung function, bronchoconstriction is most pronounced in people with asthma. May bring forward deaths due to heart and lung disease.

Risk perception: high public concern regarding asthma in children, even given difficulty of demonstrating cause and effect.

Safeguards:

- ◆ Fuels for combustion should be low sulphur as far as possible (e.g. use of kerosene instead of fuel oil for pyres).
- ◆ Pyres should be located in areas of low population density.
- ◆ Workers and nearby residents should be advised to avoid exposure to smoke.

Risk evaluation: exposure appears small relative to other sources of SO₂ provided pyres are well sited and use low sulphur fuels. Acceptability can be improved by further use of the safeguards.

Reproduced from DH (2001). *A Rapid Qualitative Assessment of Possible Risks to Public Health from Current Foot and Mouth Disposal Options*. London: Department of Health, © Crown Copyright 2001.

Based on the more detailed semi-quantitative assessment, the key potential hazards of concern included combustion gases (most importantly SO₂); air-borne particulates (PM₁₀; fine particles with aerodynamic diameter <10 µm); bacteria (e.g. *E. coli* (VTEC), *Campylobacter*, *Salmonella*) potentially spread by water; water-borne protozoa (e.g. *Cryptosporidium* and *Giardia*); and BSE from cattle.

10.4 Comparison of disposal methods

An analysis was undertaken to establish a simple rank ordering amongst the disposal methods listed, based on their (lack of) contribution to the shortlisted public health risks. This allowed for a qualitative comparison of the different disposal options from a public

Table 10.3 Potential public health hazard by disposal option

Potential Public Health Hazard	Disposal option				
	Rendering ^a	Incineration	Landfill	Pyre	Burial
<i>Cryptosporidium</i>					
BSE (older cattle only)					
Sulphur dioxide					
Particulates					
<i>E. coli</i> , <i>Campylobacter</i>					
RANK	1	2	3	4	5

Key: disposal option with the greatest public health hazard are shaded in dark grey, other options entailing some exposure in light grey.

^a Blank cell for rendering is dependent on solid products then going for incineration

Reproduced from DH (2001). *A Rapid Qualitative Assessment of Possible Risks to Public Health from Current Foot and Mouth Disposal Options*. London: Department of Health, © Crown Copyright 2001.

health point of view, taking into account the range of hazards. It had a valuable additional merit in assessing whether the preference order for disposal methods established at the start of the outbreak and based on expert opinion appeared justifiable and robust (DH, 2001). Scientific uncertainties precluded the use of a fully-quantitative analysis and time did not permit the alternative of a full weighting and scoring system based on expert judgement. However, the exercise delivered reasonable conclusions based on the information collected. These are summarized in Table 10.3.

This table shows that licensed engineered landfill is preferable to unlined burial whilst incineration is preferred to pyre burning. One way of arriving at the overall ranking of the disposal options is through a comparison matrix (as shown in Table 10.3) and shows that rendering (rank 1) would be the preferred disposal option as the risks from this option are negligible, followed by incineration, landfill, and pyre burning with burial (5) being the least preferred option, as this posed the greatest human exposure to the given hazard. As the scores presented here are largely qualitative in nature, the results have to be interpreted with caution. Nonetheless the information presented is informative when in the right context.

10.5 Learning points

Risk assessment informs decisions on how to manage risks to and from the environment including humans and therefore it is essential that at the outset of any risk assessment there is clarity about the context, purpose, and decision that the risk assessment is informing (Pollard, 2001). There is practical merit in using logical and systematic methods. The risk assessor should consider at the outset how the output will be used alongside the other influences on the decision on how to manage the risk such as the costs and social acceptability of risk management measures.

Tools and techniques for risk assessments range from straightforward examinations of the connection between the source of the hazard and the receptor to sophisticated

quantitative packages for probabilistic analysis (Pollard, 2001). In practice many risk assessments can be addressed, at least initially, using a qualitative analysis providing the logic is sound and transparent. Complex issues with significant consequences will usually require a combination of qualitative and quantitative analysis because some aspects can be better described in numerical terms than others.

A tiered approach to risk assessment allows for risk screening, prioritization, and a qualitative treatment before undertaking a more detailed quantification of the risks. Because there is often considerable uncertainty involved in assessing environmental risks, particularly environmental exposures and health impacts, resources should be targeted to areas where risks or uncertainties are high, or where the costs of the assessment are justified by the benefits to decision-making. A simple 'risk screening' approach is to determine the initial risks and priorities. If the decision cannot be made based on this approach then more detailed approaches are used, focusing on the key risks identified at screening.

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Chapter 11

Real-time syndromic surveillance

Sam Bracebridge, Alex J. Elliot, and Gillian Smith

Learning objectives

- ◆ Synthesize the concepts and main issues of syndromic surveillance.
- ◆ Assess the role of syndromic surveillance in the practice of health protection.
- ◆ Evaluate the strengths and limitations of syndromic surveillance for epidemiological investigations.

11.1 Introduction

It is likely that at some time every public health official is asked to measure the immediate health effects of an acute environmental event that may affect the population, and to provide reassurance to the public. So, how should this best be achieved? This chapter aims to give a practical guide on real-time syndromic surveillance, when and why one might use it, when not to use it, and where to go for help.

11.2 Case study

There is a large explosion at an oil storage depot, leading to the largest European fire since the Second World War. The fire continues to burn for several days. The resulting plume of smoke potentially contains many toxic chemicals and passes over your area of the country. What are the issues you face? How will you deal with them? What happens in the likely scenario that the plume shifts?

11.3 Immediate issues

The first thing you will want to know is: ‘What is in the plume?’ You will quickly need to understand if there are chemicals in the plume which may pose a danger to health. You will also need to assess the area affected by the plume. The key question in the initial phase, which you will be asked, is ‘How many people are affected?’

In this scenario there has been a large explosion in addition to a potential chemical release. What are your options for measuring health impact?

11.4 Measuring health impact

You assume that there may be some people who have been directly injured by the explosion and others who are immediately affected by the chemicals emitted in the explosion. This will be a limited population around the site of the blast so, in theory, the health effects should be easy to measure by contacting local hospitals and family doctors. However, in practice, real-time information from hospitals is unlikely to be available. You will have to quickly develop a means of capturing the information.

The first thing you need to do is to develop a case definition based on the best available information about the constituent chemicals and their toxicology. There may be uncertainties in the information and these should be clearly defined and understood. As you are developing this case definition on the run you need to ensure you have sufficient detail to allow later refinement once more is known. Collect as much information as you can possibly think of at first, to leave scope for later refinement. Case definition is also discussed in Chapters 15 and 18.

Using the case definition, you could consider designing a questionnaire to be used by health professionals in the affected region to capture data on the number of new cases. Most aspects of this immediate type of cross-sectional study design are described in the study design and field epidemiology chapters (Chapters 14 and 15).

However, as the fire is still burning, and the plume has now moved some distance from the site of the initial explosion, a survey would require a moving population target. What you need in this instance is a routine, real-time, surveillance system which can compare the current numbers and rates of cases (meeting the case definition) in the population at risk and compare this with historical data for the same population. This will answer the question ‘Are there more cases than expected?’ and will give you a very good indication of whether there are any public health effects in the population at risk. Such a system is called syndromic surveillance.

11.5 Common characteristics of environmental events where real-time syndromic surveillance may be used

Events where real-time syndromic surveillance is useful all have the following characteristics:

- ◆ There is a known acute environmental event.
- ◆ There is or may be an acute health impact.
- ◆ There is or may be a public health population impact.
- ◆ You are required to provide estimates of population health effects/reassurance about lack of effects.
- ◆ It may not be possible to identify the level of exposure of individuals.
- ◆ You can identify a symptom, or a set of symptoms, which are associated with the acute environmental event.

- ◆ Existing case-based public health surveillance is not in place or may not be sufficiently timely or flexible.
- ◆ Setting up bespoke surveillance systems may not be sufficiently timely, may be organizationally difficult, have large resource implications, and will not have established baseline data.

Clearly the case study of the explosion at the oil depot fits most if not all of those criteria. Chapters 6 and 9 are illustrations of other types of events that may affect populations where syndromic surveillance could be used.

11.6 What is real-time syndromic surveillance?

Syndromic surveillance is the real-time (or near real-time) collation, interpretation, and dissemination of data to allow the early identification of potential public health threats and their impact, enabling effective public health action. The surveillance is based not on the laboratory confirmed diagnosis of a disease but on the presence of signs and symptoms or proxy measures that constitute a syndrome/provisional diagnosis. The data are usually collected for purposes other than surveillance and, where possible, are automatically generated so as not to impact on the data providers. This surveillance tends to be non-specific yet sensitive and rapid, and can augment and complement the information provided by classic laboratory-based surveillance systems (Triple-S Project, 2011).

Syndromic surveillance may allow early mobilization of public health resources to take action in time to reduce the impact of the environmental event. Importantly the information tends to be available in real-time (usually within a day of the health seeking consultation) and requires no extra work for clinicians providing the data are collected as part of routine clinical practice.

Syndromic surveillance detects ‘alarms’, indicating a statistically significant increase in syndrome(s) for a geographical area that provide early warning of a measurable health impact/monitor the impact of an ongoing event. However, this type of surveillance only provides one piece of the ‘jigsaw’. It must be interpreted alongside other information such as environmental sampling to form a complete picture as possible of the true acute health impact of an environment event.

Over the last decade there has been an expansion in the utilization of syndromic surveillance for tracking the epidemiology of infectious diseases and more countries now host syndromic surveillance systems. Some of the earliest examples of syndromic surveillance systems are in the US where the post-9/11 response included the development of systems able to monitor potential bioterrorist threats. Emergency Department (ED)-based surveillance systems developed in New York were designed to detect this threat by monitoring ‘chief complaints’ recorded during patient attendances. These systems have been used to monitor influenza activity, outbreaks of gastrointestinal disease, and the indirect effects of power cuts on public health. Syndromic surveillance systems monitoring over-the-counter drug sales, absenteeism, and ambulance usage have also been assessed for their potential use in monitoring within national and regional surveillance programmes.

Outside the USA, syndromic surveillance development has also accelerated over recent years. The public health impact of the 2003 European heat wave provided the impetus for the development of an ED surveillance network across France (Oscour®) which provides a national network of over 300 EDs providing daily reports on patient attendance data. The Oscour® network has been used in subsequent heat waves to monitor the effect on public health and has also provided additional real-time surveillance capacity during influenza and gastrointestinal epidemics (Josseran et al., 2009). SIDARTHa is a European collaborative syndromic surveillance system that comprises sentinel EDs across several European countries—this system was tested during the 2010 Icelandic volcanic eruption when the health effects of the resulting ash cloud were monitored in real-time (Brand et al., 2010). Across Europe there is an underlying aim to ensure that syndromic surveillance systems are developed to a set of standards: to achieve this, an EU-funded project is undertaking an inventory of existing syndromic surveillance systems across Europe. It will publish a report containing recommendations and standards required for developing future systems (Triple-S Project, 2011). This initiative will ensure that national syndromic surveillance systems across Europe will be able to monitor similar datasets allowing comparison across countries enabling much more efficient tracking of diseases and other public health issues.

Syndromic surveillance systems have also been used to monitor the health of populations during mass gatherings such as sporting, political, and social events. The Olympic and Paralympic Games (summer and winter) provide major health protection challenges to host countries. Syndromic surveillance systems have demonstrated they can provide reassurance about lack of incident and early warning of alerts during these high-profile events (Tsouros and Efstathiou, 2007).

A rapidly developing area of syndromic surveillance is the use of Internet-based and social media data. Using Internet search engines to monitor influenza-related queries Google Flu Trends have provided accurate predictions of influenza activity (when compared to established sources of influenza surveillance data) (Ginsberg et al., 2009). Internet data can also be used to monitor population health during national emergencies when normal channels of communication and health seeking behaviour may be severely compromised. As the health seeking behaviour of patients changes with increasing use of self-accessed health information, these novel approaches to syndromic surveillance may become increasingly important in monitoring the community impact of infectious diseases or incidents.

The Health Protection Agency (HPA) Real-time Syndromic Surveillance Team (ReSST) provides a national syndromic surveillance service by coordinating a number of national systems in collaboration with external data providers. The systems are described in Table 11.1. The syndromic surveillance systems are used routinely to monitor the activity of common infectious diseases (through the presentation of symptoms e.g. influenza, norovirus), environmental hazards and to respond to public health incidents e.g. flooding and chemical releases. In public health incidents, syndromic surveillance is often used to reassure about *lack* of effect of an exposure in a population, and provide vital key messages to the media and public.

Table 11.1 Syndromic surveillance systems in the UK coordinated by the Health Protection Agency showing the key attributes of each system to demonstrate when syndromic data may be helpful

HPA/NHS Direct Syndromic Surveillance Scheme

‘This scheme monitors the symptoms reported by patients to the NHS Direct telephone health system’ (Cooper et al., 2002).

Coverage	Timeliness	Indicators monitored	Example indicators	Data analysis	Strengths	Weaknesses
England and Wales. All population	Daily data received. Analysis each weekday. Bulletins routinely reported each week	Reasons for symptomatic calls made characterized using a series of protocols. About 10 key protocols routinely monitored but can include any of the symptomatic calls received at NHS Direct.	Vomiting; diarrhoea; cough; cold/flu; eye problems; rash	Syndromic calls analysed as the % of total calls. Daily call exceedances monitored based on 99.5% upper confidence limits (UCL). Data analysed using a process control chart methodology Call outcome e.g. home/self care, GP visit, A&E, 999 analysed to provide indicator of severity. Call volumes enable data to be presented to Strategic Health Authority (SHA) Level (insufficient volumes for finer analyses and robust interpretation on a routine basis)	Provides early warning over other syndromic systems, e.g. GP surveillance. Partial postcodes collected for each call enabling geographical mapping of clusters. Potential to obtain microbiological samples through ‘self-sampling’ (Elliot et al., 2009). Historical data to 2001	Prone to bias from mass media reporting of events. Scheme will be amended as ‘111’ service developed

NHS24 (in collaboration with Health Protection Scotland)

'This is similar to the NHS Direct telephone health line system except that is available to all residents in Scotland' (Meyer et al., 2008).

Coverage	Timeliness	Indicators monitored	Example indicators	Data analysis	Strengths	Weaknesses
Scotland. All population	Daily data received. Analysis each weekday. Bulletins routinely reported each week	The same set indicators as NHS Direct	As NHS Direct	Daily call exceedances monitored based on 99.5% UCL. Data also analysed using exceedances based on 28 day moving average UCL	Historical data since 2004	Prone to bias from mass media reporting of events

RCGP Weekly Returns Service (Sentinel GP Scheme)

'The RCGP spotter scheme is a small sentinel network of GPs. This scheme is one of the oldest running systems in Europe and is considered the 'gold standard' of GP surveillance systems recording consultation data' (Fleming, 1999).

Coverage	Timeliness	Indicators monitored	Example indicators	Data analysis	Strengths	Weaknesses
England and Wales. 900,000 population	Data received and analysed twice weekly. Bulletins routinely reported weekly and during winter twice weekly	Read coded diagnoses mapped to chapters and groups of the ICD9 and presented as a series of 'Alert Conditions'. All morbidity recorded by the sentinel GPs is available for ad hoc analyses	Influenza-like illness; upper respiratory tract infection; asthma; intestinal infectious disease	Weekly consultation rates per 100,000 population. Coverage enables presentation of rates at SHA level. Annual prevalence per 10,000 population is also available for a range of conditions	In this scheme participating GPs are also able to take clinical samples from patients for microbiological testing (e.g. the winter RCGP/HPA influenza monitoring scheme). Validated data quality and representative of national population. Considerable flexibility in the conditions monitored and can link morbidity to prescribing (could be used to monitor severity, vaccine effectiveness, etc.). Historical data to the 1960s	Limited population coverage (ca. 2%) resulting in minimum coverage at SHA level—no Primary care Trust (PCT) coverage available. No statistical analysis routinely performed to determine unusual signals

Table 11.1 Syndromic surveillance systems in the UK coordinated by the Health Protection Agency showing the key attributes of each system to demonstrate when syndromic data may be helpful (continued)

HPA/Q Surveillance National Surveillance System

‘This large GP surveillance system is one of the largest of its kind providing national (UK) coverage and enabling the provision of local surveillance data for health protection’ (Harcourt et al., 2012).

Coverage	Timeliness	Indicators monitored	Example indicators	Data analysis	Strengths	Weaknesses
UK coverage: excellent coverage across England; limited coverage across Wales and Northern Ireland; currently no coverage across Scotland. 24 million UK population covered	Weekly analyses and reports routinely (though see comments re daily reports)	Selection of about 30 diagnoses/ diagnostic groups based on Read coded GP consultations	Vomiting; diarrhoea; wheeze; asthma; ILI; heat stroke; pneumonia with antibiotics; ILI with antivirals	Weekly consultation rates per 100,000 population. Coverage enables presentation of rates at SHA and PCT level. Statistical analyses applied to data to detect unusual signals. Standardized incidence ratios (SIRs) presented by country, SHA and PCT each week	Large population coverage (especially England) enabling robust surveillance at local (PCT) level. Early spread of the 2009 H1N1 pandemic in the UK—use of local syndromic data. Ability to turn on daily reports with 48-hour notice (only in a major incident e.g. influenza pandemic)	Limited ability to add further clinical conditions (with resource implications and necessitates a considerable lead in period of several months)

* Within the UK there are other syndromic surveillance systems that are in existence in Scotland, Wales and Northern Ireland. These systems are co-ordinated by national surveillance leads in each country.

Table 11.2 Clinical presentations and examples of available syndromic indicators for the oil depot explosion

Clinical presentation	Examples of available syndromic indicators (appropriate syndromic system indicated)
Respiratory disease presenting to health care services	Difficulty breathing; cough (NHSD) Respiratory disease (OOH/ED) Upper/lower respiratory tract infection (QS)
Exacerbations of asthma/COPD requiring medication	Difficulty breathing; cough (NHSD) Wheeze; severe asthma (QS/OOH/ED)
Eye problems	Eye problems (NHSD) Conjunctivitis (QS/OOH)
Skin irritation	Rash (NHSD)
Cardiac	Ischaemic heart disease (ED)

ED = HPA Emergency Department System; NHSD = HPA/NHS Direct System;
OOH = HPA GP Out-of-hours System; QS = HPA/QSurveillance System.

Return to our scenario of the exploded storage depot in the case study. Given the likely exposures (smoke, including particulates and volatile organic compounds) the resulting health effects could be monitored using the syndromic indicators described in Table 11.2 using the wide range of symptoms which could be caused by such an exposure.

11.7 How to access syndromic surveillance support and what to expect in the UK?

Syndromic data are produced weekly in a number of surveillance bulletins that are published on the HPA ReSST website (<http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/RealttimeSyndromicSurveillance/>). In the event of an incident, the HPA ReSST can provide a service in support of incidents. The team will be able to suggest potentially useful indicators and, for major and relevant environmental incidents, provide a daily bespoke report including relevant syndromic data. This report will include interpretation on health impact, to be used in incident assessment and incorporated into the incident situation reports (SITREPS). Because these systems run routinely and are used for a variety of environmental/infectious disease early warning/monitoring, historical baselines, statistical analyses and interpretation are also available.

11.8 What was found in the oil depot explosion case study?

Health impacts were monitored through surveillance of NHS Direct calls in the East of England, London, South-east and South-west regions, and through HPA/QSurveillance general practitioner (GP) consultations specifically relating to the areas underneath the plume of the fire. A summary of the measured health impacts is given in Tables 11.3 and 11.4.

In summary, syndromic surveillance was able to demonstrate no substantial increase in health-related consultations in the population at risk during the days that the fire burned. The public were actively reassured, and no further public health action was required.

Table 11.3 Health impact of the Buncefield fire as measured by NHS Direct Syndromic Surveillance System

Date of report	Total calls	Difficulty breathing and cough calls	Outcomes of respiratory calls
12/12/05	Normal volume		
13/12/05	Normal volume	No significant elevation at any NHS Direct site	Proportions recommended to seek further advice similar to period in previous year
14/12/05	Call rate for North Central London was slightly elevated compared to expected	No significant elevation at any NHS Direct site on 11/12/05 or 12/12/05	Proportions recommended to seek further advice similar to period in previous year
15/12/05	Normal volume of calls on 14/12/05	An exceedance in 'cough' calls noted for Thames Valley—not thought to be unusual	Increase noted for London area on 14/12/05, but not significant and not considered unusual.
16/12/05	Normal volume of calls on 15/12/05	No significant elevation at any NHS Direct site	Proportions recommended to seek further advice were at expected levels at all NHS Direct sites

Table 11.4 Health impact of the Buncefield fire as measured by HPA/Q Surveillance System

Consultation type	12/12/05	13/12/05	14/12/05	15/12/05	16/12/05
Wheeze	No concern ¹	No concern ¹	No concern ^a	No concern ^a	No concern ^a
Severe asthma	No concern ¹	No concern ¹	Slightly raised in NW London (but small numbers)	No concern ^a	No concern ^a
Asthma admissions	No concern ^a	No concern ^a	No concern ^a	No activity to report	No concern ^a
Pneumonia	High in SE—but seen in previous week therefore not untoward	No concern ^a	Slight rise in SE (small numbers) not considered to be of concern	No concern ^a	No concern ^a
Upper respiratory tract infection	No concern ^a	No concern ^a	No concern ^a	Slightly raised in Thames Valley—not considered of concern	No concern ^a
Lower respiratory tract infection	No concern ^a	No concern ^a	Slightly raised in potentially affected areas—but not considered of concern	No concern ^a	No concern ^a

No concern;^a: no concern in potentially affected area.

11.9 Caveats and incidents where syndromic surveillance will not be appropriate

Note syndromic surveillance systems will only ever provide a part of the ‘jigsaw’ of information needs in an incident. There are important caveats to consider when using syndromic surveillance for a particular incident:

- ◆ The indicators monitored routinely tend to be non-specific (e.g. vomiting) and are based upon either the symptoms experienced by patients presenting or diagnoses/aggregated of diagnoses made in clinical practice—hence there will not be clear ‘case definitions’.
- ◆ For most of the schemes the population coverage and call or consultation rates do not enable the impact of small localized incidents to be monitored.
- ◆ The schemes tend to be better at detecting events with a potentially wide population health impact rather than individual cases of a specific disease. For example, Legionnaires’ disease can present with fever, influenza-like illness, pneumonia, or diarrhoea. New cases are likely to be spread across a variety of presenting syndromes or symptoms and hence are more likely to be detected through established surveillance systems (laboratory confirmation or case reporting) than by syndromic systems.
- ◆ In an acute event, these systems use existing indicators and routinely collected data which have been set up to provide information on generic conditions to support both environmental and infectious disease indicators. Establishing new syndromes (for which there are no baselines) and which require additional work for the data providers will not be provided during an acute event.
- ◆ Beware of using and interpreting syndromic surveillance data before understanding the source of the data and the intricacies surrounding its recording. The benefits and potential caveats and limitations, of using the data for specific incidents should be discussed with those coordinating the syndromic surveillance schemes.

11.10 The future and other uses of syndromic surveillance

Syndromic surveillance is continually developing with opportunities to access data through novel sources or to access data from other areas of the health care system. Within the HPA, one of main drivers for these developments was to increase the intelligence available during the London 2012 Olympic and Paralympic Games, with particular focus on London. Events such as the Olympics provide unique challenges. The Games attract large numbers of visitors who may not have ready access to GP services and with different health care seeking behaviour from local residents. This needed to be addressed by the syndromic systems monitoring population health. New developments included national ED and out-of-hours GP attendance surveillance systems. In addition to developing new syndromic surveillance systems, there were regular changes to improve the collection, analysis, and dissemination of syndromic data including:

- ◆ Improving the robustness and statistical analysis of existing syndromic surveillance systems.
- ◆ Developing novel ways of interpreting, displaying, and disseminating syndromic surveillance data, e.g. dashboards with speedometer-type displays.

Table 11.5 Syndromic surveillance systems in the UK developed primarily for the London 2012 Olympic and Paralympic Games by the Health Protection Agency

HPA Out-of-Hours GP Syndromic Surveillance Scheme

‘This system aims to monitor the gaps in routine GP surveillance by providing vital data covering GP out-of-hours activity.’

Potential population coverage	Conditions monitored	Likely timeliness	Comments	Added benefit
Aim at 20 million	List of aggregated read codes used by out-of-hours contacts	Daily	London coverage will be assured first	Provide GP data during evenings and weekends/ public holidays. Provides more acute episodes compared to in-hours GP systems

Emergency Department Syndromic Surveillance System (EDSSS)

‘This system will monitor the attendances of patients across a sentinel network of Emergency Departments across England.’

Potential population coverage	Conditions monitored	Likely timeliness	Comments	Added benefit
Sentinel scheme—aim to involve 20 Emergency Departments (EDs) by 2012.	Major symptoms/syndromic groups, e.g. respiratory, gastrointestinal, etc. Depends on the coding used in the ED, joint work with the College of Emergency Medicine is working towards a common dataset	Daily	Focus initially on London and major urban EDs	Will provide monitoring of more severe presentation of disease. Covers mass gathering events where visiting populations have limited access to GP services

Over-the-Counter Surveillance Scheme

‘The sales of over-the-counter drugs can provide early warning over other surveillance systems; this project aims to assess the value of monitoring of sales to provide ‘proxies’ for disease activity.’

Potential population coverage	Conditions monitored	Likely timeliness	Comments	Added benefit
To be determined, though likely to involve major supermarket chains	A selection of sale volumes for common over-the-counter remedies such as paracetamol, cold/flu remedies, anti-diarrhoeal preparations, etc.	Aiming for daily	Scheme roll out will depend on ability to obtain data and assessment of the added value of the information	Will provide a proxy for patients self-medicating and potential early warning of events, e.g. patients who self-treat before seeking further medical advice. Also could provide useful indicator for mass gatherings with visitors, e.g. Olympics

NHS Direct web-based surveillance

'This system aims to utilize the self checker algorithms on the NHS Direct website, where patients are able to input their symptoms to obtain e-health advice.'

Potential population coverage	Conditions monitored	Likely timeliness	Comments	Added benefit
England	Limited number of syndromes, e.g. cold/flu, vomiting	Aiming for daily	To undergo a feasibility study. Aiming to utilize the use of self checking algorithms on the NHS Direct and NHS Choices website	Changing health seeking behaviour of population—increasing use of web-based medical resources. More patients use NHS Direct website than telephone service and therefore this will provide complete burden on NHS Direct

Note: at the time of writing, several of these schemes are still to be evaluated to assess whether they provide added value over existing systems.

- ◆ Development of thresholds at national and, in particular, local level to improve early warning.
- ◆ Developing new systems to accommodate the anticipated challenges in monitoring the mass gathering and changing population characteristics.

The real-time syndromic surveillance systems developed to increase intelligence during the London 2012 Olympic and Paralympic Games are listed in Table 11.5.

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Chapter 12

Routine data

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Learning objectives

- ◆ Appraise the types of routine health and environment data currently available.
- ◆ Critically evaluate the uses and limitations of such data sources.
- ◆ Evaluate the advantages and limitations of the environmental public health tracking approach and its utility in environmental epidemiology.
- ◆ Assess the use of long-term surveillance systems such as cancer registers.

12.1 Introduction to routine environmental and health data

Relatively little is known about the complex interactions between lifestyle, environmental factors and hazards, and the associated burden of disease. By comparison our knowledge in the fields of infectious and communicable hazards is well developed and benefits from work done by many eminent figures in public health in the past. The role of the contemporary environment in health is complex and multifaceted and therefore requires innovative methods for assessment of risk and management of public health interventions.

There are several ways to investigate the health effects of an environmental exposure:

1. Ad hoc investigation of the specific alleged association at one point in time using routine data: this is the most common scenario encountered by local public health practitioners asked to address public concerns or complaints relating to alleged pollution or the effects of industrial processes on the health of a population or specific group of people.
2. Formal epidemiological investigation which may utilize routine data as well as carry out additional targeted data collection.
3. Environmental public health tracking (EPHT): this is a relatively novel methodology which involves the integration of routine data sources for both health and environmental indicators.

We consider here the value and limitations of routine data for environmental epidemiology and environmental public health tracking. Methods for epidemiological investigation are dealt with elsewhere in this book.

12.2 Case study

A public health practitioner has expressed concern over a number of seemingly unrelated fatal accidents due to carbon monoxide (CO) poisoning in a large housing estate in his area. Apart from the spatial relationship, albeit in very large geographical area, there are no obvious temporal or demographic associations to link the cases. This chapter explores how we can use routine data on health and environment to assess the potential association between reported cases and identifiable physical and other hazards to inform the need for intervention.

CO is a common environmental hazard in the UK and is a known cause of a significant number of fatalities and hospital admissions from accidental poisoning (Wilson et al., 1998). Some of the associated symptoms are not well characterized as poisoning and it is often undiagnosed (Davies and Beasley, 2010). Fig. 12.1 provides estimates of the overall burden of disease related to accidental exposure to CO in domestic dwellings. These figures exclude the very large numbers of fatalities recorded each year in England attributable to suicides and deliberate exposures. Only some of the elements of the disease burden are available from routine statistics (e.g. mortality), and even those may not be accurate (in particular for CO which is known to be under-reported) (Davies and Beasley, 2010).

Demographic factors can also significantly affect potential for hazard and accidental exposure. For example, many local areas share common risk factors for CO poisoning, in

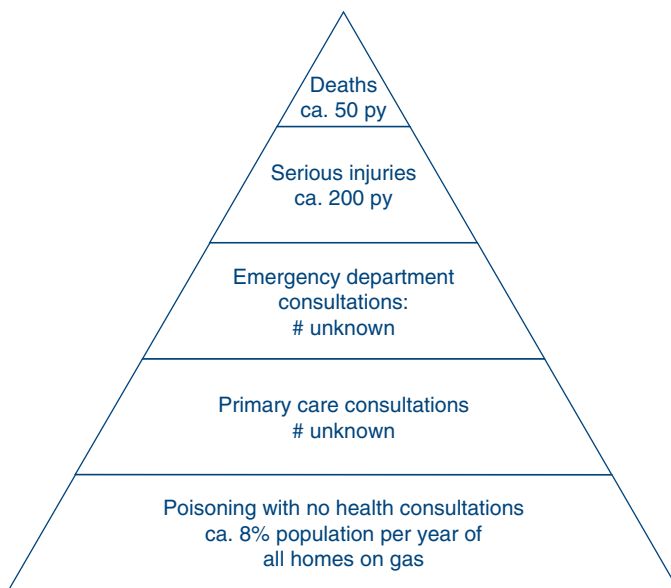


Fig. 12.1 The burden of disease related to CO. py = person years.

Data from Davies, S. and Beasley, C. (2010). *Carbon monoxide poisoning: Needless deaths, unnecessary injury*. Department of Health © Crown copyright 2010 and Croxford, B., Leonardi, G.S., and Kreis, I. (2008). Self-reported neurological symptoms in relation to CO emissions due to problem gas appliance installations in London: a cross-sectional survey. *Environ Health* 7:34.

particular age of the housing stock, type of tenure (large concentrations of young people/houses in multiple occupation/low income), and ownership (private landlords/elderly owner occupier/poor maintenance).

12.3 Types of routine data

Routine data sources include both monitoring and surveillance data. Surveillance has been defined as ‘the systematic, regular collection, analysis and interpretation of data for a given population, to detect changes in patterns of disease or determinants of disease, with action taken if predefined criteria or thresholds are met’ (South East Public Health Observatory (SEPHO), 2009). This differs from monitoring, as it encompasses both monitoring and taking action when abnormal patterns are found. The Public Health Surveillance Working Group for South East and Eastern England (SEPHO, 2012) maintains a database of surveillance systems in the UK which is a valuable resource for identifying sources of health outcome and disease determinant data.

Information from several data sources may need to be analysed and considered to build a complete picture of the incidence of disease related to CO poisoning in private dwelling houses in the local area.

Routine health data may provide some evidence to confirm or refute the alleged increase in deaths. However even if the increase is confirmed it is important to evaluate the potential environmental risk factors to identify whether there is a common cause.

12.4 Routine data sources for carbon monoxide

A significant and varied amount of information is available to support investigation and review of the incidence and prevalence of mortality and morbidity associated with accidental exposure and CO poisoning. Routinely collected data which may be of value for the evaluation of health outcomes due to carbon monoxide are shown in Table 12.1. Routine data systems which record environmental indicators relevant to CO are shown in Table 12.2.

The data in Tables 12.1 and 12.2 could be analysed in a variety of ways, for example:

- ◆ Comparison of deaths in the local geographical area with other areas of the country with a similar demographic profile to identify ‘hot spots’ or statistically significant excesses.
- ◆ Comparison of recorded deaths in the local geographical area with evaluation of local housing quality according to English House Condition Survey.
- ◆ Evaluation of housing quality according to CO relevant indicators, compared with other areas of the country.
- ◆ Evaluation of primary care CO consultations according to housing indicators.
- ◆ Longitudinal analysis of CO deaths related to interventions such as campaigns to install CO monitors in domestic houses.

The choice of analysis and data used depends very much on the quality of the data for the particular outcome and exposure being studied (in this case CO). Decisions have to

Table 12.1 Examples of routine health data sources

Data source	Brief description of data	Uses of data	Limitations of data
Office for National Statistics Mortality data	Statutory requirement for all suspected or confirmed deaths from CO poisoning to be reported to the coroner	To identify deaths caused by CO poisoning. Data on source is not available in the published information	Based on ICD10 codes, several codes may apply to CO poisoning. Includes fire-related and work-related deaths
CO Gas Safety Society Database	Unintentional deaths from non-fire related CO poisoning in England, Wales, Scotland, and Northern Ireland since 1995 from 'cuttings and media' service, coroners' reports, and direct notification from victims' families	The data are publicly available and include information on the source of CO, location of the incident, and age of victim	Data collection is not complete and is likely to severely underestimate the total number of deaths. Data is based on press reports and verified with coroners where possible
Hospital episode statistics (HES)	Data containing information on hospital admissions and outpatient attendances in England	Can be used to consider how many hospital admissions and attendances are related to CO	Aggregated statistics not able to distinguish between accidental and non-accidental incidents CO is clinically underdiagnosed
Emergency Department attendance data (Department of Health experimental dataset)	Emergency Department attendance data within HES records. Emergency Department attendances at major Emergency Departments	This dataset can be used to identify Emergency Department attendances related to CO, figures can be extrapolated to provide a UK figure (Planned for inclusion in new HPA environmental public health surveillance system)	Currently only an experimental dataset, 15 Primary Care Trusts using ICD codes. National estimates extrapolated from these figures however, not sure if they are representative. CO is clinically under-diagnosed
Health and Safety Executive data	Data reported to HSE under the Reporting of Injuries, Diseases and Dangerous Occurrences Regulations (RIDDOR)	Records fatalities and some 'near misses' involving extended hospitalization	Not available in datasets below national level. Periodic reporting, most likely annually CO is clinically under diagnosed

(continued)

Table 12.1 Examples of routine health data sources (*continued*)

Data source	Brief description of data	Uses of data	Limitations of data
NHS pathology departments' data	Carboxyhaemoglobin concentration, and related clinical information	Invaluable as an automatic source of data on CO-related health endpoints. Validation of clinical diagnosis and evaluation of CO exposure	Incomplete. Not all suspected cases will be tested. CO has a short half life and unless the test is performed as soon as the patient presents it may not be present. Not routinely reported by all pathology departments. Underascertainment. Raised carboxyhaemoglobin concentration could be due to smoking
Primary care data	Including GP consultations, plus data from other clinics and weekend/night visits	Provide an idea of the number of primary care consultations from CO	Consistency in the coding of this data. CO is clinically underdiagnosed

be made about whether deaths or deaths plus morbidity should be investigated; which aspects of housing quality are the best indicators of higher risk for CO exposure; and what the most appropriate comparison population is. Such decisions will be informed by knowledge about the quality and completeness of the data (Chapter 16).

12.5 Values and limitations of routine data

A major advantage of epidemiology based entirely on analysis of routine data is avoiding the time and cost involved in collecting ad hoc data. This may be particularly important for answering local community health concerns such as an excess of CO deaths, where a rapid answer is required and there are no resources for in-depth epidemiological studies. Routine mortality data could at least identify whether there is a real increase in deaths (with caveats described later in this section). Data may be valuable to establish a baseline for CO deaths or consultations which can then be use for monitoring the situation over a longer time period. An example is a study on 10 years of Office for National Statistics (ONS) data which identified clear differences between regions of England and Wales and between age groups and sexes and an overall declining trend in CO deaths. (Dabke et al., in press) Even the use of a database which has recognized problems can generate interesting hypotheses. An example is a study on the data collected by the CO Gas Safety Society identifying a high relative risk of non-mains gas sources (Juniac et al., 2012). This study also points to the importance of recognizing clustering in CO deaths (sometimes more than one

Table 12.2 Examples of routine environmental data sources

Data source	Brief description of data	Uses of data	Limitations of data
English House Condition Survey—Department of Communities and Local Government	Housing tenure by type, occupation, age of property, standard of fitness and physical condition	Identifies specific areas of unfit and substandard housing and types, e.g. flats, houses in multiple occupation	Sample survey, not house specific
Local authority housing records	Inspection reports of Individual unfit and substandard houses	Facilitates detailed comparison of houses and tenure to identify common types of heating appliances, design layouts and other potentially hazardous aspects	May not be updated regularly or in sufficient detail to identify hazards such as types of heating appliances or other gas equipment which may be implicated
Local authority complaints registers	Details of complaints about housing fitness standards, faulty appliances or suspicious odours/fumes, or other nuisances in private sector dwellings including statutory notices served	Provide focus on past history of households and in particular complaints and events leading up to fatal or non-fatal incidents	May include personal and sensitive information covered by data protection requirements
Housing association maintenance and repair records	Social landlord property inspection and maintenance information	Records of faulty heating or cooking appliances, tenants complaints, etc.	May not be updated regularly. Variation in detail of data collected
Gas safety inspection reports	Records of mandatory installation and annual safety checks	Verification of competent installation and effectiveness of annual maintenance and repair	Records held by issuer and not collated nationally. (Incomplete as reports may not be available from landlord/owner of property)

member of the family dies) which is currently not noted in any database. These studies have recognized their inherent limitations but are good for hypothesis generation.

It is important to understand the limitations of routine data which is not collected specifically for environmental epidemiology. For example, reporting of carboxyhaemoglobin levels by NHS pathology laboratories is a function of diagnosis and treatment of potentially exposed individuals. Whilst these data are routinely collected and available to clinical toxicologists, they are not assembled in a way that is readily translated for the surveillance of blood carboxyhaemoglobin levels in the wider population. Environmental data may be more problematic than health data due to a wider variability in geosociopolitical

boundaries; e.g. local authorities in the UK use political boundaries such as electoral wards, townships, and counties whilst national agencies such as the UK Environment Agency collect data on the basis of river catchment areas (corresponding to the administrative boundaries of the Agency in the discharge of its responsibility for clean water). Comparison of different datasets may mean aggregating data down to a very low level and building them back up to population level.

Access to routine data may also be problematic. Although information is routinely collected by many agencies, some of it on a statutory basis (ONS mortality, Coroners reports, Health & Safety Executive notifications of deaths and dangerous occurrences, local authority public health nuisance and decent housing standards notices), it may not be routinely published in a way in which it can be readily used without extensive cleaning and validation, or may need to be accessed by special request. There is often further difficulty in accessing anonymized patient identifiable information that can be related to a specific exposure without breaching confidentiality (Chapter 18).

A number of key issues have been identified which should be considered when evaluating any routine data system (Goodyear and Malhotra, 2007). These include:

- ◆ Accuracy—to what extent are the data that are present accurate? What biases may be present?
- ◆ Precision—what level of uncertainty is in the data? Have appropriate measures of uncertainty been included (e.g. 95% confidence intervals)?
- ◆ Completeness—how complete is the dataset? How much missing data is there?
- ◆ Timeliness—when were the data collected? Is this sufficiently recent to still be relevant?
- ◆ Coverage—is the whole population of interest covered? If not, who is missing?
- ◆ Analysis—what analysis has been applied to the data? Have appropriate techniques been used (e.g. for direct or indirect age standardization)?
- ◆ Accessibility—who has access to the data? Who controls this access?
- ◆ Confidentiality—can individuals be identified from the data?
- ◆ Original purpose of collection—personal data may only be used for the purposes for which it was collected. NHS data registrations generally include improvement of the health of the population and management of the NHS among their purposes, but non-NHS data may not.

Routine health data are often not sufficient to provide the level of detail required to establish the overall burden of disease related to CO poisoning due to errors and inconsistency of coding. There are also difficulties in interpretation, for example, in the case of a house fire the actual cause of death may be indeterminate if the fire was due to a leak or malfunctioning gas appliance. Cause of death may be attributed to smoke inhalation or exposure to toxic substances generated by thermal degradation of the materials used in household furnishings. Detailed toxicological analysis may not be sufficient to identify the primary cause of death which could therefore be coded to any one of a range of exposures.

Therefore epidemiological analyses based entirely on routine data must be interpreted with caution. They often need to be supplemented with additional epidemiological data available collected specifically for the purpose of the epidemiology investigation.

12.6 Environmental public health tracking

A novel approach that aims to make routine data more widely available to those interested in environmental hazards to health is environmental public health tracking (EPHT). EPHT has been defined as:

‘The ongoing collection, integration, analysis, and interpretation of data about:

- ◆ Environmental hazards
- ◆ Exposure to environmental hazards and
- ◆ Human health effects potentially related to exposure to environmental hazards.

It includes dissemination of information learned from these data’ (Centers for Disease Control and Prevention, 2010).

In England, the Health Protection Agency (HPA) (2011) have expanded this definition to encompass:

- ◆ Hazard identification and mapping
- ◆ Exposure assessment and quantification
- ◆ Development of biomonitoring
- ◆ Systematic review of health outcomes and disease surveillance
- ◆ Horizon scanning
- ◆ Development of environment and health indicators.

This differs from the traditional approach to epidemiology by bridging the gap between routine health outcome data, exposure assessment, and quantification of the environmental hazard. The relationship between routine data on environment and health and their interpretation is a key aspect of EPHT and can include both tracking health outcomes (looking for plausible environmental causes) and tracking hazards (using information on the type and number of disease events attributable to that hazard to motivate actions by public health workers to validate exposures through measurement or assessment and thus allow public health interventions) (see Box 12.1).

In the carbon monoxide case study tracking would aim to facilitate surveillance of health events coded as having been caused by CO and to relate these events with known hazards at population level such as factors related to the building (gas appliance failures and ventilation defects), factors related to individual behaviour (use of cooking sources and other combustion within the home), and interventions available to address these problems. EPHT, through design and implementation of a systematic environmental public health surveillance system, will facilitate linkage of data from Emergency Department attendances and NHS pathology laboratory reports requested by clinicians and reported CO exposure incidents. Routine collection of information from data sources collected on an ongoing basis will support population estimates. This is how the actual incidence might be verified and extrapolated to provide estimates of the overall burden of disease.

Box 12.1 Environmental public health tracking

Health outcome tracking

Disease ➤ Cause

Example: CO poisoning in private dwelling houses (e.g. mortality data coded as CO poisoning), and related potential causes of such deaths within private dwellings (faulty gas appliances, poor maintenance of heating systems).

Hazard tracking

Cause ➤ Disease

Example: arsenic in private drinking water supplies.

12.7 Further data collection

Where the routine data systems are insufficient to answer the specific question, it may be possible to supplement the routine data with ad hoc epidemiology investigations, for example, review of a sample of individual cases (e.g. from coroners' records) to identify further information concerning the cause of death, such as the source of CO, or to establish the potential for miscoding and other recording errors in the routine sources used. Such studies would be useful in retrospective evaluation of mortality data rather than real-time investigation of an incident. Biomonitoring studies might be used to estimate personal exposure in identifiable at risk populations.

New sources of data may become available for use in ad hoc evaluation of environmental exposures; for example, several local authorities in England have managed to fund CO alarms in all of their housing stock. By monitoring the alarm activations and investigating the levels of CO from faulty appliances, it is possible to begin to understand the community burden of CO. The effectiveness of the interventions can also be evaluated and compared.

The threshold of effect in acute CO exposures is well understood but low-level, long-term health effects are still poorly understood. Ad hoc studies using the EPHT model of measurement and validation of actual exposure may assist in improving the understanding of the burden of disease associated with chronic CO poisoning.

12.8 Use of routine data in formal epidemiological studies

Routine data on non-communicable diseases may be of value for many types of epidemiological investigations. One of the most common epidemiological approaches based on routine data is the cross-sectional study, but case-control, cohort studies, intervention studies in the community, and other designs can all be conducted with a contribution from routinely available data (Chapter 14). However the caveats on routine data relevant for ad hoc investigations are just as important for formal studies and data quality (Chapter 16) must be carefully evaluated.

12.9 Conclusions

The role of environmental hazard data for the interpretation of routine health data, and vice versa, is key in an environmental public health service. Hazard data must be considered to produce a valid interpretation of the spatiotemporal pattern of a non-communicable disease in relation to that hazard. Vice versa, interpretation of health hazard data without consideration of the baseline routine health data runs the risk of not being relevant or applicable only to a specific situation. Valid interpretation of routine health and environment data as part of surveillance usually requires collaboration between different professional groups; on one hand those familiar with patterns and methods for interpretation of routine health data and on the other hand those familiar with patterns and interpretation of routine environmental hazard data (Chapter 7).

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Geographic information systems

Leslie Jones

Learning objectives

- ◆ Describe key features of geographic information systems.
- ◆ Understand basic application and assessment of geographic information systems in epidemiology.
- ◆ Evaluate strengths and limitations of geographic information systems in epidemiology.

13.1 Introduction

A geographic information system (GIS) is a computerized information system that contains geographic data representing various aspects of the real world categorized and described spatially (e.g. disease case locations, populations, or environmental hazards). These separate data *layers* in a geographic database can be brought together (or *integrated*) within a GIS to explore relationships between them, enabling generation and analysis of hypotheses using spatial techniques. GIS can also act as a valuable communication tool, enabling visual and intuitive presentation of results.

GIS have a wide range of uses in environmental epidemiology and public health in descriptive and analytical studies, and may complement standard methodologies. Whether considering a point source, such as a polluting site, or a network such as heavily-trafficked roads, GIS can be used to derive individual or group exposure estimates based on distance, and also to integrate modelled or measured hazard and exposure data. GIS can also be used in disease surveillance to examine spatiotemporal links and clusters, and in outbreak investigations to assist in source identification.

13.2 Case study: Legionnaires' disease outbreak

This case study considers investigation of a hypothetical outbreak of Legionnaires' disease similar to several outbreaks and investigations published in the literature (e.g. García-Fulgueiras et al., 2003; Nguyen et al., 2006; Castilla et al., 2008; Nygård et al., 2008).

A public health unit is notified by a local hospital of an unusually high number of patients ($n = 18$) with pneumonia admitted over the last few days, with three confirmed

with Legionnaires' disease at time of notification. Cases reside in or near two neighbouring towns and preliminary interviews have revealed no common exposures. The unit initiates an outbreak investigation immediately.

Legionnaires' disease is a severe and uncommon form of pneumonia caused by inhalation of aerosolized droplets containing *Legionella pneumophila*, a bacterium which thrives in water under certain conditions, especially in buildings and associated water systems. The source and airborne pathway by which people are infected may be indoors (e.g. spa pools) or outdoors (e.g. industrial cooling towers); the latter may potentially infect people over a range of several kilometres. Transmission of *Legionella* occurs directly from environment to human; the disease is not contagious. Legionnaires' disease has an incubation period of usually 2–10 days, with a varying and relatively high case fatality rate. Known risk factors include (older) age, male gender, smoking, pre-existing chronic respiratory illness, and being immunocompromised. *L. pneumophila* can also cause a much milder, normally self-correcting, flu-like illness called Pontiac fever, with a higher attack rate than Legionnaires' disease; the term *legionellosis* can be used to describe Legionnaires' disease and Pontiac fever separately or together.

Legionnaires' disease cases most often occur sporadically; although space-time clusters are observed which cannot be linked to any common source and may well have arisen by chance. Legionnaires' disease outbreaks with a common source can have major public health implications and cause great alarm in the community. The key aim of an outbreak investigation is to identify the source as quickly as possible and take action to prevent continuing exposure.

The initial investigation therefore concentrates on obtaining, for each case, information on potential exposure sources in the 2 weeks preceding the onset of symptoms (Box 13.1), as well as environmental and microbiological investigation.

Three days after the initial outbreak notification several new cases were notified; at this stage, with active case finding and ongoing confirmatory testing, 27 cases have been confirmed. After several more days a total of 52 Legionnaires' disease cases were confirmed and environmental investigation has identified a number of potential sources.

13.3 How GIS aids the outbreak investigation

GIS is particularly useful for outbreak investigations where a common outdoor source has been implicated. Since the agent (aerosolized *Legionella*) tends to decrease in concentration as it disperses further from its source, this gives rise to clustering of cases around the source. GIS provide the capability to map, visualize and analyse the outbreak spatially.

The chosen study design may inform GIS data preparation; hence close collaboration with a GIS specialist is required from an early stage. For an outbreak investigation speed and accuracy of mapping are a key consideration. Therefore it is important to know what GIS resources are already available in terms of software, data, skills and existing tools and procedures. Often GIS may be available with routine and other potentially relevant data set up and ready to go.

Box 13.1 Legionnaires' disease investigation in the UK

Patient data

- ◆ Demographic and clinical data (including underlying conditions, date of onset).
- ◆ Two-week travel history both abroad and in UK including travel routes.
- ◆ Exposures to: hotels, hospitals (visits or stay), whirlpool spas/hot tub, air conditioning, showers, water displays in shopping or garden centre, fountains, food displays with water mists, car washes, jet washes.

Microbiological data

- ◆ Characterize and compare isolates from patients and potential sources to see if a match can be found.

Environmental data

- ◆ Test domestic water supply.
- ◆ Locate, investigate, and sample cooling towers and other potential sources.

Data from Lee, J.V. and Joseph, C. on behalf of the PHLS Atypical Pneumonia Working Group (2002). Guidelines for investigating single cases of Legionnaires' disease.

13.4 Assembling and preparing GIS data

Conceptually, physical geography may describe collections of discrete 'objects' with defined boundaries distributed in space, e.g. urban or administrative areas, roads and houses. Geography can also describe continuous 'surfaces': phenomena varying continuously in space without boundaries, e.g. population density, temperature, or pollutant concentrations in the soil or atmosphere. GIS represents discrete objects as collections of points, lines, and polygons (*vector data*), and surfaces as regular grids (*raster data*) in which each grid cell takes a value. Whether an 'object' or 'surface' model is used depends on the nature and context of what is being represented (and may sometimes be different ways of looking at essentially the same thing).

Preparing GIS data for outbreak investigation involves converting information from the patient questionnaire which is spatially *implicit*, e.g. an address or postcode in a line listing, to data which is spatially *explicit* (geographic data). For point locations this may be done through an automated process of *geocoding*, whereby a spatial reference (such as a postcode) within a record is matched to a reference dataset. Decisions must be made on whether and how to code and represent case locations and travel routes (e.g. whether to digitize or infer through network analysis). Such decisions and interpretation of strengths and limitations of different methods are beyond the scope of this chapter, and require collaboration and discussion with a GIS specialist. The kind of information needed is listed in Box 13.2.

Box 13.2 Geographic data of potential relevance

- ◆ Legionnaires' disease cases (e.g. case residence points, case travel route lines).
- ◆ Potential sources of *Legionella* (hazardous site points).
- ◆ Backdrop (topographic) mapping at various scales.
- ◆ Demographic data by small area (especially for estimating population-at-risk).
- ◆ Census/administrative boundaries.
- ◆ Meteorological data (especially wind direction).
- ◆ Imagery (e.g. aerial photos or satellite imagery).
- ◆ Postcode centroids and address locations (reference datasets).
- ◆ Detailed road network data.

Whilst there is always a temporal element to geographic data, GIS emphasizes spatial over temporal aspects, and can be challenging to apply when dynamic spatiotemporal processes are involved.

13.5 Exploring and analysing data in GIS

There are several levels of complexity in using GIS to evaluate outbreak data; these are listed in Box 13.3.

13.5.1 Initial visualization and hypothesis generation

GIS is particularly strong in this area, in which we start to explore and answer questions such as: 'How many people were infected and where did they live, travel or work?'; 'What were the most likely sources of infection?' (Engeset and Jensen, 2008). We need to think about how to display and present the data and interpret the results. We may also aim to set up questions as formal hypotheses for more rigorous testing.

13.5.1.1 Spot maps

Typically data are presented as a spot (or dot) map (Fig. 13.1), showing case residences over backdrop mapping and including relevant data such as suspected sources. This may identify notable patterns and clustering.

An initial evaluation of the data may assume that infectious exposure is more likely to have occurred at or close to home for many of the patients, so that the first case data mapped are case residences. More complex case data to map might include case travel routes (with places visited) during the incubation time period.

If data on suspected sources are available these should be added to the spot (or spot plus travel routes) map. This is an example of visual *overlay* of geographic data layers; useful to identify (potential) relationships between different data. Data on suspected sources including, for example, local authority registers of cooling towers (a legal requirement in the UK since 1992), may be readily available in implicitly spatial form (e.g. spreadsheet

Box 13.3 Summary of suggested steps in using GIS in an outbreak investigation

1. Simple description of place

Spot map showing case residence points over backdrop mapping, possibly including location of suspected sources, and travel routes. May highlight spatial clusters and possibly trends.

2. Choropleth mapping by small area

Represents rates rather than numbers; symbolize to highlight patterns and trends (may standardize rates by age and/or sex).

3. Case activity spaces

Optionally, represent (as lines) travel routes and locations visited by each case during their probable incubation period for the disease; particularly useful for ‘outlier’ cases who live far from a suspected source.

4. Atmospheric dispersion modelling (ADM)

Optionally, results from ADM may be integrated within GIS, refining hazard and exposure estimation by taking into account meteorological effects on dispersion from a suspected source.

5. Formal analytical epidemiological study

A variety of possible designs using distance as a proxy for exposure may be used, e.g. case–control using distance from source (e.g. García-Fulgueiras, 2003); comparison of disease rates in zones at different distances from point sources (e.g. Nygård et al., 2008); or point-pattern statistical analysis (e.g. Martínez-Beneito et al., 2006). Where needed, population denominators may be generated within GIS.

with addresses or postcodes, which can be geocoded) or as geographic data. Data may also be captured in GIS (as with case data) through geocoding or digitizing, or in the field using global positioning system (GPS) technology.

The 52 case residence points on the spot map (Fig. 13.1) appear to cluster in two areas: to west and east—corresponding to towns A and B respectively (grey areas on the backdrop mapping). Nine potential sources identified by the outbreak investigation are also shown. The existence of two different sources is possible (though unusual) since under certain conditions airborne *Legionella* from one facility may colonize another. Microbiological investigations are valuable here to identify whether the causative organisms derive from the same or more than one source; age-specific attack rates (AR) may also be calculated, expecting higher attack rates with older age for a town or area where an actual source is located (Nygård et al., 2008).

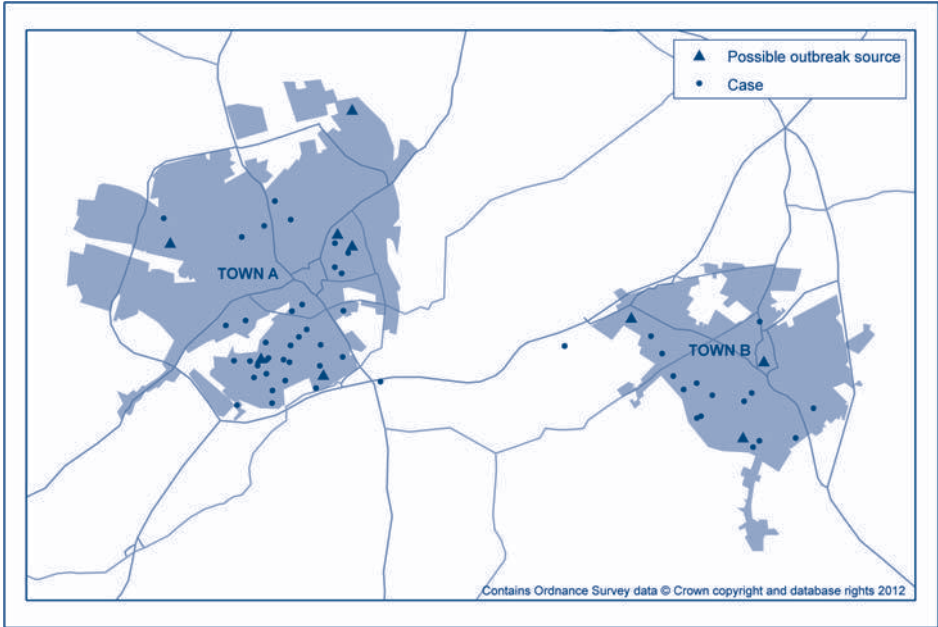


Fig. 13.1 Hypothetical spot map for a Legionnaires' disease outbreak (including backdrop map and suspected sources).

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Whilst a spot map can suggest the location of clusters of cases, particularly if there are many cases then point patterns can be more difficult to visually interpret. Wind direction (which may vary considerably) may further complicate the interpretation. Spot maps based only on case residence are also limited by not considering case travel movements, which is particularly important for Legionnaires' disease as exposure may not always relate to residence. Furthermore, spot maps show only cases without considering underlying population at risk; hence they can be misleading (spatially analogous to using count data for epidemiological purposes, rather than rates). This can be alleviated to a certain extent by adding backdrop mapping indicating populated areas, and therefore approximate population distribution; alternatively, *choropleth maps* may be produced.

13.5.1.2 Choropleth maps

To take underlying population size into account, rates are generated by selecting suitable small area geography, counting case points (numerator) within each small area and dividing by total population at risk (denominator). The denominator may often be derived from census or mid-term estimates, and is therefore an approximation to the population at risk. For a disease such as Legionnaires' disease it may be useful to also standardize by age and sex, given that the risk group for this disease is age- and sex-specific and a relatively small proportion of the population are susceptible.

Once calculated, ARs by small area can be shown as a number in each mapped small area, (e.g. Jansà et al., 2002), or more usually displayed as a choropleth map to view patterns and trends more easily (e.g. García-Fulgueiras et al., 2003; Nguyen et al., 2006;

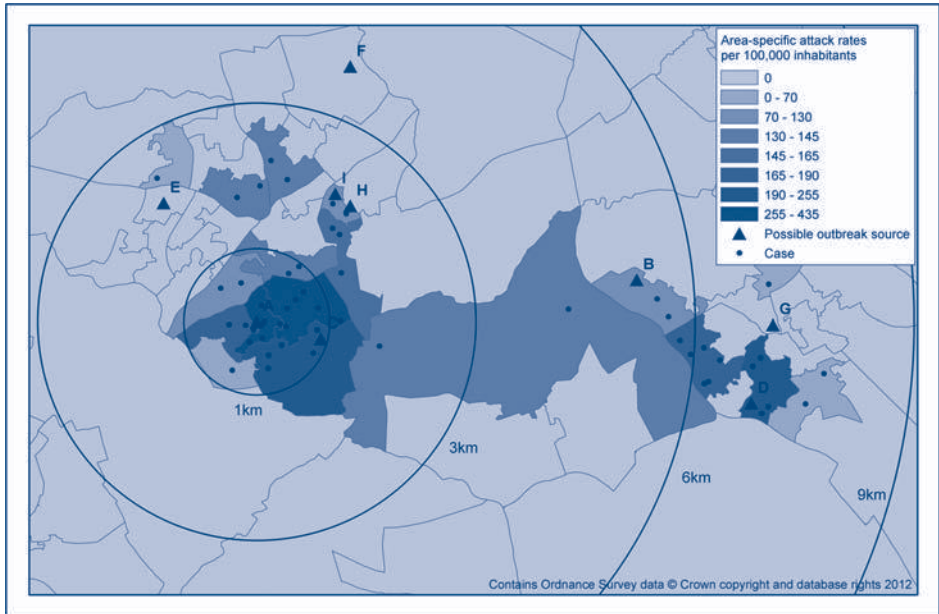


Fig. 13.2 Choropleth map for hypothetical Legionnaires' disease case study (including circular buffer zones around suspected source A).

Contains Ordnance Survey data © Crown copyright and database right 2012.

Castilla et al., 2008) (Fig. 13.2). This requires suitable data ranges and symbology to be chosen. Choropleth maps have the advantage that, subject to certain limitations, and provided a meaningful classification scheme and symbology is chosen, patterns and trends can be more clearly seen especially if suspected sources are included. As with spot maps, we can start to form hypotheses about the general area in which to look for sources, or about specific suspected sources. These may be further informed by environmental and microbiological investigations.

If the investigation is assuming a single source and risk proportional solely to distance of residence from the source, the choropleth map shown in Fig. 13.2 would suggest source A (located within the zone with the (equal-) highest attack rate) as the most probable source of the outbreak. In some published outbreaks (Nguyen et al., 2006; Castilla et al., 2008), choropleth maps have in this way highlighted the location of what was eventually proven to be the source. However, as for spot maps, other factors such as meteorology and case travel may confuse the visual interpretation.

Whilst choropleth maps can be very useful, a practical limitation of rate mapping for outbreaks is that relatively large case numbers may be required to produce meaningful results. Another potential limitation is what geographers call the modifiable areal unit problem (MAUP). This problem derives from the calculation of rates using pre-defined census or administrative areas, which are arbitrary with respect to the investigation. Using different geographical boundaries may give different answers, indicating an element of randomness in the results. A third potential limitation of area rate mapping is that, whilst its aggregation of data is useful in making patterns and trends clearly visible,

it also loses information at individual level. Care must thus be taken with the scale of the areas used: too detailed and overall patterns can be hard to make out; too generalized and important information may be lost.

13.5.1.3 Case activity spaces

Another visualization which may be useful is case travel routes, or *activity spaces*. Whilst these data are particularly time-consuming to produce, this may be done alongside mapping case residences. Mapping activity spaces can be particularly useful for ‘outliers’ to the investigation; for example, patients who live far from the area may be found to have travelled close to a particular source during the probable exposure time window (derived from the epidemic curve).

13.5.1.4 Atmospheric dispersion modelling

A further refinement uses dates of onset of illness in conjunction with meteorological conditions and/or atmospheric dispersion modelling (ADM). Modelled concentrations can be added to GIS as another data layer for comparison with spatial distribution of cases. Externally modelled data is often integrated with GIS to help infer exposure within epidemiological studies generally. Use of monitoring point data, which can be interpolated to a continuous surface within GIS, is also commonly seen.

Note that uncertainty around the source term means that ADM can only really model relative, rather than absolute, *Legionella* concentrations. With *Legionella*, there is also great uncertainty as to what constitutes infectious dose, so even if data is available to model releases fairly accurately, it is hard to relate the results to pathologically significant exposures. ADM requires levels of data and expertise which may be difficult to obtain during an outbreak; however, if available, it may offer very useful support to distance-based methods in GIS, and environmental and microbiological investigation.

13.6 Hypothesis testing

A major benefit of GIS is that it enables calculations to be performed for bespoke areas, such as circular *buffer zones* representing distances around prospective sources (Fig. 13.2), which can be generated routinely in GIS more easily than in spatial statistics packages.

13.6.1 Spatial analysis of relative risk

Spatial analysis for each of the suspected sources is based on the assumption that, for the true source, there should be a negative association between the risk of Legionnaires’ disease and distance from the source. One analytical approach, as used in the cluster investigation of Nygård et al. (2008), generates a sequence of distance zones around each source and then compares Legionnaires’ disease rates in each zone looking for a dose–response relationship. An alternative approach, as used in an investigation of sporadic Legionnaires’ disease (Bhopal et al., 1991), generates and compares observed and expected age- and sex-specific rates of Legionnaires’ disease in small population areas

classified according to distance from suspected sources (with expected rates derived from rates in a wider geographical area and applied to the age/sex profile in the small areas).

GIS can be used to estimate underlying population (at-risk) in various ways, using small area data (such as census output areas) and/or commercial datasets, though estimating population brings some uncertainty and possible error into the calculations.

A dose-response relationship for the relative risk (RR) through distance bands or for small areas at varying radii or distance from a prospective source (with Chi-squared tests for statistical significance of any identified trend), together with a strong association with distance, provides evidence for the source of the outbreak (Nygård et al., 2008). Further environmental and microbiological investigation may assist in confirming the relationship.

Table 13.1 illustrates the analysis principle for a subset of three of the prospective sources (in reality, more than three radii would probably be used). Prospective sources A and C are located fairly close to one another, and it is hard to tell from the spot or choropleth map which is the more likely source. The table of relative risk shows that A is the only prospective source with a clear trend of decreasing relative risk with distance from source which, having also (marginally) the highest relative risk closest to source, may make it a strong candidate for being the true source.

In Table 13.1, the radial zones include the preceding ones, thus diluting any apparent dose-response relationship. An alternative (arguably more rigorous) way to calculate relative risk using buffer zones is to take populations within doughnut-shaped rings moving outwards from the prospective source to be the exposed groups, and to compare their attack rates with those of a single ‘unexposed’ population at some greater distance away.

Table 13.1 Table of relative risk with distance from prospective sources for hypothetical Legionnaires’ disease outbreak

		Suspected source		
		A	C	H
< 1 km	AR(exp)	234	243	62
	RR	9.1	8.7	1.5
	Cases	24	21	6
	Population (est.)	10,240	8,640	9,690
<3 km	AR(exp)	85	79	77
	RR	4.1	3.5	3.5
	Cases	36	35	36
	Population (est.)	42,570	44,280	46,610
<6 km	AR(exp)	53	56	53
	RR	2.0	3.5	3.8
	Cases	41	46	48
	Population (est.)	77,600	82,020	90,730

AR(exp) = Legionnaires’ disease attack rate within zone; RR = relative risk; Cases and Population refer to within radial zone.

Although these analytical methods are powerful, there are several potential limitations which may need to be addressed. Estimating uncertainty (e.g. by calculating confidence intervals) around relative risks produced through spatial analysis may be tricky due to uncertainties around both count numerator and estimated population denominator. A practical limitation is that sites may need to be some distance from each other for the method to be sensitive enough to distinguish between them. There is also a limitation of MAUP for buffer zones (i.e. potentially arbitrarily different results if different radii are chosen) unless sensitivity analysis is carried out, using various distances from hypothesized source. A major potential limitation of the exposure estimate shown above is that it is purely based on distance away from site. It therefore does not take into account meteorological conditions (e.g. wind direction) or case travel movements (which would require the use of case activity spaces and ADM as discussed in section 13.5.1.3/4). If different age or sex structures exist in the populations being compared to calculate relative risk, this should be taken into account (see e.g. García-Fulgueiras, 2003; Castilla et al., 2008).

13.7 Benefits of GIS

GIS is a unique medium which can be used to systematically organize, integrate, analyse and present data from the different multidisciplinary approaches involved in an outbreak investigation or epidemiological study. GIS normally complements and overlaps with other approaches such as epidemiological, environmental, and microbiological investigation. GIS can potentially speed up investigations by automating production of map data and enabling rapid interactive mapping to discover spatial relationships. GIS supports analytical investigation of spatial aspects of a problem by allowing aetiologically-relevant areas to be generated rather than being confined to arbitrary pre-defined areas such as districts or census tracts.

In outbreak investigation, using GIS as soon as possible can potentially help find the source of an outbreak more quickly, and possibly improve public health outcomes as a result. GIS can provide useful supporting evidence, both visual and analytic, to complement evidence from other parts of the investigation, whether used early on as an active part of the investigation, or afterwards for retrospective confirmatory analysis.

GIS also helps in surveillance and managing information. By mapping disease cases as they are notified, a geographic database can be built up of cases in an area over a period of time. This systematic approach may potentially enable connections to be made where they might otherwise not be seen; it may also indicate if seemingly-sporadic cases that have occurred further apart in time could actually be linked to a common source (Bhopal, 1991).

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Section 3

Environmental epidemiology design and problem analysis

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Study designs for public health investigations: basic concepts and practice

Irene A. Kreis and David A. Cromwell

Learning objectives

- ◆ Synthesize the main types, including the main hybrid forms, of epidemiological studies and apply to examples.
- ◆ Appraise the main strengths and limitations of various designs.
- ◆ Assess the relation between study design and data analysis.
- ◆ Evaluate various theoretical models for consideration of causality.

14.1 Introduction

Many questions can be posed to a public health (environment) practitioner from various sources—the public, health managers, and public officials. Each may have their own perspective and demands for information. The art of public health practice is to translate these questions into ones that can be researched using an appropriate and feasible study design. A major part of this process is listening to and working with those involved to agree upon the main research question. It is only once this has been achieved that the process of developing a detailed study protocol can proceed. But it will be time well spent. Clarifying the main question increases the likelihood of the results being accepted and, if needed, acted upon.

The type of question to be answered will differ from situation to situation. Sometimes, the aim is to understand the causes of a disease or the effects of various exposures. In other situations, the aim is to determine how big a problem a community faces. Of the many questions being posed, most (if not all) are valid and could be evaluated, given enough time and money. However, it is typically necessary to set priorities among those questions.

The type of question selected influences the outcome measure and choice of study design, and the relationship between these will be explored in this chapter. The methodological issues will be illustrated in the context of asthma research but they also apply to any exposure or disease-centred topic.

14.2 Asthma epidemiology in brief

Asthma is one of the most common chronic conditions affecting both children and adults, yet much remains to be learned of its aetiology. The definition of asthma is widespread reversible airways obstruction resulting from bronchial smooth muscle contraction (Weatherall et al., 1990). The epidemiological definition is related to the frequency of occurrence of wheeze (Lai et al., 2009). The burden of asthma in both children and adults varies between countries, with low prevalence rates (2–4%) in Asian countries and high rates (15–20%) in developed countries (particularly UK, Australia, and New Zealand) (Lai et al., 2009).

In developed countries, the incidence of asthma has increased over the past few decades. This increase together with the geographic variation are both reasons why environmental factors are believed to play an important role in the current asthma epidemic. These include exposure to allergens as well as lifestyle factors. Observations on migrating populations (such as Asian students to Australia and New Zealand) strongly support the role of local environmental factors as they start showing increased prevalence rates but not quite those of the local populations (yet) (Subbarao et al., 2009).

Risk factors for asthma occur throughout a person's life. Early childhood wheezing has been consistently associated with prenatal maternal smoking, and this effect is increased when combined with postnatal smoke exposure. There is some evidence for the influence of diet including breastfeeding on the risk of atopy and asthma but this remains controversial (Subbarao et al., 2009).

Asthma in adults may have persisted from childhood, it may present as a relapse of childhood asthma, or it may occur *de novo* as adult-onset asthma. Adult-onset asthma may have environmental (especially occupational) causes with or without allergen sensitization. Asthma related to workplace exposures has been documented in many occupational settings. Commonly associated occupations and exposures include car painting (isocyanates), hairdressing (various chemicals), domestic and commercial cleaning (cleaning solutions), health care professions (latex), and baking (flour dust) (Subbarao et al., 2009).

New-onset asthma can occur at any age, without prior illness or concomitant disease. Atopy as a risk factor for asthma becomes less common with increasing age, although occasionally it is the dominant trigger. Similarly, air pollution is a factor that typically worsens pre-existing asthma rather than causing incident asthma. Exposure to environmental tobacco smoke consistently worsens asthma symptoms and is a risk factor for severe asthma. Total serum immunoglobulin E level, a surrogate for allergen sensitivity, has been associated with the incidence of asthma. Sensitization to aeroallergens, particularly house dust mite, cat, and cockroach allergens, is well documented as being associated with asthma (Subbarao et al., 2009).

14.3 Possible environmental epidemiology research questions for asthma

When beginning a public health investigation, the first questions being asked may not be sufficiently clear to investigate. A phase of exploration and problem-shaping is required.

For instance, at a public meeting about local air pollution, residents may ask ‘Is it safe to live here?’. The notion ‘to live here’ needs refining, and this question could be developed in the following ways:

- ◆ ‘Do I have asthma because I live here?’
- ◆ ‘Do I have asthma because I grew up here although I don’t live here anymore?’
- ◆ ‘I don’t have asthma but what is my risk of getting asthma if I continue to live here?’
- ◆ ‘What risk to my health will I face because I just moved to the area?’

In general, the questions that an investigation adopts fall into three basic groups: those related to the cause of a disease, those related to the burden or risk posed by a disease, and questions about what type of intervention might be required.

Causal type questions might be:

- ◆ Does a diet high in milk contribute to becoming an asthmatic?
- ◆ Does living with dust mites affect the frequency and severity of asthma attacks?
- ◆ Does air pollution generated by diesel motors increase the frequency and severity of asthma attacks?

Burden type questions might be:

- ◆ What is the level of asthma/poor lung function among our school children?
- ◆ What is the impact of chronic obstructive pulmonary disease on the health status of our elderly?
- ◆ What is the demand for respiratory health services/health promotion?

Intervention type questions might be:

- ◆ Would reducing the exposure to allergens in the first year of life reduce the likelihood of an infant becoming asthmatic?
- ◆ Would increasing the general level of exercise through stimulating bicycle travel among asthma sufferers reduce the impact of asthma?

14.4 Measuring disease and health status

When developing research questions, it is essential to consider the most appropriate way to measure disease or health status. Asthma is an illness that can affect individuals to different degrees, and its severity is often reflected by physiological changes in a person’s lung function. It is a chronic disease with acute exacerbations which can range from mild, intermittent impairments of lung function to a severe asthma attack that can result in death. These exacerbations can be triggered by various exposures, such as air pollution.

A general representation of the different prevalence of exposure, physiological changes and disease in a population is given in Fig. 14.1. This is an adaptation from a model presented by Health Canada (2006). When designing a public health investigation, it is necessary to review which of these levels are most relevant, and to select appropriate measures. This is likely to involve making trade-offs. For example, measurements of

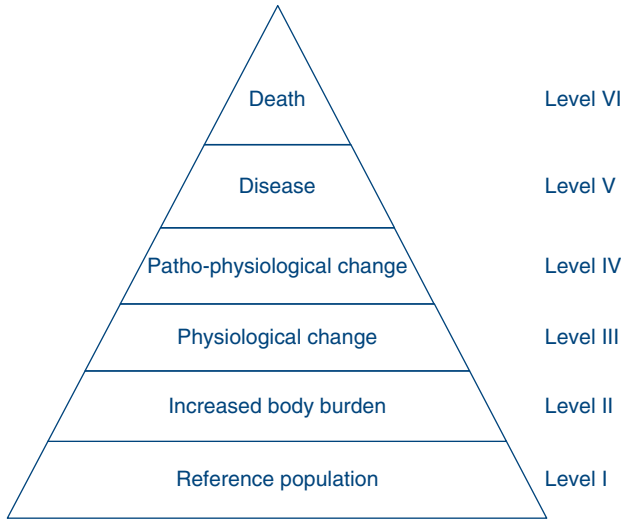


Fig. 14.1 Health pyramid.

specific mortality or disease are directly related to health status. However, they may prove difficult or expensive to collect because they are relatively rare unless routine data can be used. Therefore, it may be necessary to use a surrogate measure like lung function which is an associated physiological measure. This is strongly associated with worse health on average, but poor lung function is not something that an individual might recognize as ‘bad health’.

14.5 How do questions translate to study designs?

Public health investigations into environmental issues can use a variety of study designs. There are some standard types but elements of these may be mixed together to produce a hybrid design. Nonetheless, the main study designs can be differentiated by considering the following characteristics:

- ◆ Do we know the disease status of people already?
- ◆ Was the exposure (or intervention) allocated to individuals by researchers or did researchers observe what was happening?
- ◆ What is the reference or control population?
- ◆ Are the measurements available for individual people or only for groups?

14.5.1 Group level designs without information on individuals (ecological studies)

At the start of an investigation, it is common to explore the possible association between a disease (or outcome of interest) and possible exposures in a population by collecting statistics from public documents or from routine data sources such as statistics on admission to hospital, general practitioner (GP) attendances, or the sale of medication.

Collating this information enables the creation of a dataset of exposures and health outcomes but it will only be available for pre-defined groups, such as people within certain age ranges, or who live in neighbouring regions. Data will not be available on individuals. A study in which data are only available at a group level is called an ecological study.

Ecological studies are often cheap and fairly quick to undertake, particularly if the data required are routinely published by regional or national bodies. But efficiency is not the only reason for using an ecological design. An investigation may also be interested in effects that occurs at an ecological level, such as exposure to air pollution in a neighbourhood. In this situation, it is common to use a similar group or community as a reference population, or to consider variation across a number of groups. Studies of this type are called multigroup ecological studies. The association between the exposure and outcomes is typically analysed using a regression model, which can incorporate data on possible confounders such as age and sex.

It is important to remember that this multigroup design is essentially cross-sectional. For example, a study might find an association between the incidence of asthma-related hospital admissions and the sale of tobacco but there is no information about whether the exposure to tobacco smoke came before the hospitalizations for asthma. As such, multigroup ecological studies do not support inferences about cause and effect, and they are generally considered to generate hypotheses for further evaluation.

Ecological studies can be used to examine patterns over time. These studies collect data at numerous points in time (generally more than 20) and are known as time-series studies. The study might involve a single time-series. For example, we may know when a new source of air pollution began, and by collecting observations on hospital admissions for asthma before and after this event, we can estimate whether there has been a health effect. We could improve this design by collecting time-series data on levels of air pollution and assessing the correlation between (say) daily levels of air pollution and daily hospital admissions. Because we know the timing of events, both single and multiple time-series studies can provide some evidence of cause and effect. However, their results are subject to various biases and have to be interpreted with caution. For example, results may reflect changes in diagnostic patterns and coding rather than changes in morbidity.

14.5.2 Individuals followed over time whilst monitoring their usual exposure and health effects (cohort studies)

A common component of a public health investigation is the collection of data from individuals on their exposure to some environmental factor and their health status. Typically, there is no intention to interfere with the level of exposure, and consequently, such studies are referred to as ‘observational designs’. A cohort study is one common type of observational study (the other types are considered in sections 14.5.3 and 14.5.4).

Cohort studies are characterized by enrolling individuals based on exposure to a determinant of interest. For example, we can define a cohort as a group of school children based on their exposure to air pollution. The cohort will typically contain individuals who have different levels of exposure (e.g. some play outside much more than others), and it is

common for those individuals with a low exposure to be defined as the reference (control) population. In an air pollution study, the pupils from one school may not differ sufficiently from each other in exposure to gain insight into possible effects. An alternative way to create a reference population would be to enrol individuals from a distinct but similar region known not to have the environmental factor (a school in a non-polluted area).

The study then proceeds by obtaining measurements of exposure, with measurements of health status being made at one or more time points subsequently. In a study of the health effects of air pollution on asthma in children, measurements can be made by the investigator (lung function), by the children (daily diaries on medication use), or obtained from the health system (hospital admissions or GP visits). The exposure is often measured by air pollution monitoring systems but could be conducted by personal monitoring and exposure assessment can be done using activity diaries and extrapolating from those. The results of cohort studies are usually expressed as a risk ratio (Chapter 17).

It is common to distinguish between two forms of cohort studies based on how the data were collected. Prospective cohort studies describe investigations in which measurements are taken from individuals after they have been enrolled in the study. This has the advantage of allowing measurement protocols to be standardized and data collectors to be trained. One of the hybrid forms of study design is a special case of the prospective cohort called a case crossover study. This describes a particular way in which prospective cohort data are analysed. In a case crossover study, a period of effect is identified (such as a period in which individuals suffer low lung function or there have been particularly high hospital admissions for asthma) and this is then compared to a predetermined time period before or after. An advantage of this approach is that demands on data completeness are less stringent, and it can be particularly well suited to settings in which there are difficulties collecting data.

Retrospective cohort studies describe investigations which make use of existing data sources, such as historical medical records. The historical data are used to identify which patients meet the eligibility criteria, and then the required data on these patients are extracted. No new measurements are made. Consequently, these studies might face problems due to missing data or inconsistent data definitions (see Chapter 16).

In asthma research, prospective cohort designs are more common than retrospective cohort designs because there are often insufficient data on asthma cases or levels of exposure. They are more common for diseases like cancer for which there are registries that can be used to identify all incident cases. Retrospective cohort designs can be useful if the research question can be answered using a routine dataset in which exposed individuals can be readily identified and which captures the outcome of interest (e.g. death, disease).

14.5.3 Comparison of individuals with and without a disease (case-control study)

An efficient way of collecting information on determinants of illness is to use a case-control study. This enrolls individuals based on the outcome of interest rather than the exposure. It begins with the identification of cases (e.g. those newly diagnosed with

asthma) and then a number of controls (often between one and four) are selected for each case. Data on the exposure to the environmental factor are then collected for both the cases and controls (e.g. the level of dust mites in the house or a history of (parental) smoking) and the measure of effect is estimated as an odds ratio (OR) (Chapter 17).

The distinction between a case and control is clear in many situations. However, this is not always so. For example, enrolling patients with asthma poses problems of consistency due to the intermittent nature of the acute exacerbations and the broad spectrum of severity that exists for this disease. Consequently, this design is not common in asthma research. Defining a good control population can also be difficult. Ideally, in a case–control study, one would want all the cases and the controls to be drawn from the same population, and to differ only with respect to their disease status. This could be achieved by selecting controls from a population-based register or civil administration database that refers to exactly the same population as the medical database that the cases came from. Many countries do not have such registers and the only practical option is to identify individuals from hospital records. For example, in an asthma study, patients identified from admissions to a respiratory ward may be compared with controls from another type of ward (such as an orthopaedic ward). However, if hospitals take in people for elective care from a wider population than those admitted for acute conditions, there may be systematic differences between cases and controls.

Another problem with identifying controls for case–control studies in environmental epidemiology is a lack of variation in exposure which reduces statistical power. For example, if people are enrolled from a single region to investigate air pollution effects, the gradient in exposure may be small. Enrolling individuals from multiple centres can widen the range of exposures and has the additional advantage of enabling a larger number of cases to be enrolled (or a more rapid accumulation). Common practice in multicentre studies is to select the controls from the same region as the cases. For the air pollution investigation, this could negate the effect of the wider range of exposure and would need to be solved with a joint-source case–control study but the practicalities of this design are beyond the scope of this book.

In case–control studies, people are assessed individually for their (past) exposure to the relevant environmental contaminant. Questionnaires are often used to assess exposures because historical data from biological monitoring is often unavailable. Some environmental data may be routinely collected although this is context specific. According to some statistical advisers this has major consequences for the power of the study but individual exposure assessment can solve the problem. In many situations, the information collected on exposure does not specify whether it occurred before the disease or health outcome. Consequently, these studies cannot support inferences about cause and effect.

Case–control studies can be done within an existing cohort study. Both cases and controls are identified within the cohort, and only then is the exposure information analysed. These nested case–control studies are very efficient, particularly in the context of expensive bio-monitoring of body burdens such as persistent organic pollutants. They also have the advantage of having exposure data collected prior to knowledge of which individuals are cases and controls, which minimizes the risk of recall bias. A disadvantage of the

nested design is that it may rely on bio-banking and collecting samples that might not be analysed has ethical implications.

14.5.4 Individuals with unknown disease (or exposure) status before the investigation (cross-sectional studies)

A common design in asthma/lung function research is to collect data on health and determinants in people who are not defined by ill health or by exposure. People are asked to participate in the study and then information (or measurements) about health (e.g. lung function, having the diagnosis of asthma) and exposure (e.g. time spent outdoors) are collected at that time. This may involve participant questionnaires, or biological sampling such as lung function measurement, blood samples, etc. Such studies are referred to as cross-sectional designs. As with the other observational designs, the analysis estimates the association between health status and the level of exposure.

In many cases, the information collected on exposure does not capture whether or not it occurred before the disease or health outcome. Consequently, these studies cannot support inferences about cause and effect. Some historical information on exposure can be collected at the time of the investigation. For example, a study could reconstruct lifetime residential history or how much school children were exposed to pollution from nearby roads by playing outside. However, these reconstructions may be difficult to verify and this also limits inferences about cause and effect.

Cross-sectional investigations can be conducted at a single location but population selection can be flexible. Studies can be defined to capture people with a wide range of exposures and cover multiple sites. For example, a survey on childhood asthma can be organized within different schools, or different towns, or locations in different countries as long as each site uses identical protocols.

14.5.5 Allocating specific exposures and following people over time (trials)

A public health practitioner can be called upon to implement an initiative to reduce the effect of environmental pollution. In these circumstances, an evaluation of the initiative is not limited to simply observing its effect. Participants can be allocated by the researchers to either an intervention or a control group. Such studies are known as controlled trials. For example, an initiative could be implemented to reduce exposure to allergens during the hypothesized period of asthma development, and study participants could be allocated to either the active treatment (mite-proof cushion covers) or to a placebo. Another example could be a community education programme to reduce levels of dust mite or cockroach allergens giving one town the intervention (the education campaign) and another town not. If the allocation is random, the study is referred to as a randomized controlled trial.

All controlled trials involve prospective data collection as outcomes can only be measured after participants have been allocated to the intervention or control group. Disease or health status is measured over time, and these data may be performed by the researcher or obtained from routine medical records. Participants are followed-up over

Box 14.1 Synonyms for major study design in epidemiology

Used in this text	Synonym
Ecological	Geographic
Prospective cohort	Concurrent follow-up or longitudinal
Retrospective cohort	Non-concurrent follow-up or historical cohort
Case–control	Case–referent or patient–control
Cross-sectional	Survey
Trial	Experimental cohort

the course of the trial, and the association between the intervention and outcome is typically expressed as an (incident) risk ratio (Chapter 17).

14.5.6 Study design names

In epidemiology there are about as many names for study designs as there are epidemiologists. A common set of names is used in this chapter (Porta et al., 2008). However, the sections are named with the process rather than the design name to ensure all readers focus on the content and not the label. Common synonyms used in epidemiological studies are shown in Box 14.1.

14.6 Sources of bias related to the designs

In conducting an investigation, we want to avoid drawing the wrong conclusion. Therefore we need to limit the possibility that the results are due to errors (bias) related to the measurement of data, the selection of samples, or confounding.

Measurement bias can arise in various ways and is difficult to control. There are techniques that can minimize but not eliminate measurement errors. Unfortunately, it cannot be removed by statistical means.

Measurement bias can be due to flaws in the data collection instruments or the expectations of respondents and observers. Questionnaires should be piloted to check their clarity and appropriateness. Laboratory tools and field instruments need to be calibrated and people trained to collect data in a standard manner. Overall, instruments need to possess adequate levels of validity and reliability. Poor reliability will introduce greater levels of random variation. This can be dealt with by increasing sample size. However, bias cannot be removed statistically. Because of this, it is generally better to use an instrument with little bias and adequate reliability than an instrument with greater bias and excellent reliability.

Various forms of bias arising from the respondents can occur. They can give answers they believe that you want to hear, they may not disclose information related to sensitive or taboo subjects, or they may not recall facts accurately. The last problem is most prominent in studies where respondents know their health status may be related to the exposure being investigated (as in case–control studies where they may have pondered on possible causes of their illness). Recall bias is unavoidable to some degree but its effect can be

mitigated by using neutral questions and asking for information that can be corroborated from other sources.

Observer bias can arise when the observer has an influence on the information recorded. This can occur when the outcome being measured is subjective. Recording accuracy may depend on the perceived importance of the participant or location or expectations/knowledge of the exposure a person has received. This also applies to interviews as observers may be more or less inclined to ask follow-on questions. Blinding observers to certain information about participants' state of health or exposure can reduce the likelihood of this occurring.

Observer bias may also arise if observers are inconsistent in following the format of an interview. For location-related studies, which are common in environmental epidemiology, switching well-trained teams regularly and ensuring close adherence to protocols are the main ways of reducing this bias. This issue can be avoided by using self-administered questionnaires.

Another threat to the validity of a study is selection bias. Some designs are more sensitive to specific sources of selection bias than others. In controlled trials, researchers can ensure the intervention and control group are similar by randomly allocating participants to each group. However, in observational studies, it is extremely difficult to ensure patient groups are similar, even if baseline patient characteristics are recorded. There is always the danger of bias from unmeasured confounders.

Another source of selection bias is loss to follow-up. This will arise if participants drop out of the study for non-random reasons. It is crucial, therefore, that the follow-up of participants in the study is as complete as possible and drop-out rates should be similar for patients with different exposure levels. Loss to follow-up can be a major problem for cohort studies, particularly those that measure outcomes a long time after the exposure or those that require a great commitment from the participants such as keeping diaries.

In case-control and cross-sectional studies, there may be selection bias due to (selective) non-response. Response rates need to be adequate and should not differ too much between groups. It is unrealistic to expect 100% response rates in most situations but efforts should be made to achieve as high a rate as possible. Some investigators calculate the number of respondents required to obtain a sufficient power and then increase this to compensate for non-response. However, it is preferable to improve response rates, and so reduce the risk of differential non-response. The effort should go in reaching all potential participants and, if they refuse, find out why and who they are to aid the interpretation of the results.

A specific bias in cross-sectional studies is prevalence bias. Cross-sectional studies will identify people with the illness at that point in time. Those that have died or who have left the environment will not be captured. As those who remain are a subset of all those who develop disease, they may differ systematically from those who have been lost to follow-up. If so, the study results will be biased. The size of this bias will depend on the type of health effect being studied. It is less of a concern in studies on asthma because asthma is rarely lethal and most people do not move house very often (and typically not because of

developing asthma). In case–control studies, this type of bias is avoided by using new (incident) cases only.

Confounding is inherent in most studies and needs to be measured and controlled for in the analysis. A determinant is a potential confounder if it is an independent cause of the disease. It becomes a confounder if it is also associated with the exposure of interest (Rothman et al., 2008). The issue of confounding needs to be considered when planning studies. Confounders need to be measured and taken into account in the analysis. All observational study designs are sensitive to confounding. However, those designs where little is known about the individuals (ecological studies or retrospective cohort studies) are particularly susceptible.

Epidemiological studies often collect large amounts of data. It is tempting to perform extensive analyses, and make multiple comparisons. This can easily become a ‘fishing’ expedition. Some statistically significant associations will occur by chance rather than reflecting a causal relationship. Consequently, every study protocol should define an analysis plan including the variables to be compared, and the potential confounders. This should be based on a review of the literature.

14.7 Relating study designs to evaluation of causality

Various models have been proposed to capture how disease in populations can arise and spread. Rothman et al. (2008) proposed a model of disease that is based on necessary and complete causes. This model recognizes that, for a disease to occur, a number of events need to happen either at the same time or in a certain sequence. For example, for a disease to occur, people need to be vulnerable to the disease and then exposed to the trigger at a certain time. Risk factors for a disease may occur together, in a cluster or in context. For instance, men are more likely to have specific occupational exposure than women (although this can change over time and will differ between societies) and children will often have different exposure profiles because of their behaviours.

In the evaluation of individual suspected causative agents, researchers often use the Bradford Hill considerations. They should be used as a framework for evaluation. They are explicitly not criteria and should not be used as a checklist (Bradford Hill, 1965). The nine considerations are divided in those related to the exposure itself such as *strength of the association* (the magnitude of the relative risk or OR), *dose–response relationship* (which should be shown), and *cessation of the exposure* (which should result in a cessation of the effect). In environmental epidemiology, using these considerations can be problematic because of measurement errors and because of the long-term effects, sometime over generations. Of the remaining considerations, the most essential one is *temporality*: the exposure should occur before the effect. Air pollution-asthma research has been able to demonstrate this requirement. This was partly because of investment in good air pollution monitoring systems and the fact that some of the effects (notably changes in lung function) occur relatively fast. The temporality consideration favours cohort studies and controlled trials. The other five considerations are important but less directly related to individual study designs and more to overall evidence from other studies.

14.8 The role of the proposal

Many choices need to be made when designing a study in environmental epidemiology. A detailed study proposal needs to be written to ensure the design is coherent and feasible, and can be communicated to everyone involved (which includes stakeholders, local communities, and funders as well as the study team).

The core components of study proposals include:

- ◆ *Aim and study questions:* it is good practice as a public health practitioner faced with the range of questions discussed earlier, to formally consider them here. This makes it easier to defend the choice of design and study questions (Chapter 4).
- ◆ *Background:* this should provide a review of the existing evidence to support your study design and plans (Chapter 3).
- ◆ *Population description and selection:* a detailed evaluation of the source of the participants (e.g. school or nursing home) and the participant selection process is crucial to limit selection bias. This should contain a discussion of choices and their consequences, such as which schools, which years in those schools, how to handle refusals to participate, etc.
- ◆ *Data to be collected:* these needs to be spelled out and demonstrate measurement of confounders and all relevant exposures and outcomes. Methods to reduce potential bias should be mentioned. Both exposure and outcome should be addressed.
- ◆ *Structure of databases and coding:* the coding manual will develop over time but a framework should already exist at the planning stage (Chapter 16).
- ◆ *Analysis plan:* a preliminary analysis plan is used as a final check to ensure all relevant data are collected. It is useful to create sample empty tables to prevent essential variables from being overlooked (Chapter 17).
- ◆ *Time plan:* produce a simple chart that depicts the number of things to do and how long they will take. This will help to ensure you can report back in a timely way (Chapter 15).
- ◆ *Ethical and privacy consideration:* (Chapter 18).

The main proposal is often fairly concise. However, it is typically accompanied by a series of appendices which provide the methodological details. These may include: the search strategy and review criteria for the literature review, letters of invitation to participate, the participant questionnaires and disease measurement scales, the standard operating procedures for field and lab procedures, and codebooks. See also Chapter 15.

14.9 Conclusion

Constructing and conducting an environmental epidemiological investigation is a balancing act between ideal methodological designs and practical constraints. Success requires clarity about the research questions, options, and the methodological limitations. Choices and decisions should be carefully documented and discussed. This will prevent unrealistic expectations and help to ensure the study addresses the correct issue in a feasible and rigorous manner.

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Field epidemiology: logistics

Helen Maguire, Irene A. Kreis, and Virginia Murray

Learning objectives

- ◆ Appraise the key preparations necessary before deployment to the field.
- ◆ Review the logistics involved in conducting an epidemiological investigation and collecting original information; the key elements needed for a successful deployment to the field.
- ◆ Distinguish issues associated with site visits and pilot/scoping studies.
- ◆ Evaluate the differences between various forms of field epidemiology such as those related to incident investigation and those of planned research.

15.1 Introduction

The aim of field epidemiology logistics is to ensure adequate preparation and provide operational independence in the field. This includes the operational requirements for conducting an epidemiological study, obtaining relevant samples for testing as well as communications. Often the need is for very rapid deployment of incident response teams or field study coordinators. Sometimes, a sustained period in the field is needed, for weeks or even months. A safe and secure environment in field operations must be ensured and this is especially important in developing countries where there may be political unrest or other unfamiliar hazards. Deployed teams must be prepared for unstable situations (political and environmental) and have resilience to deal with change and uncertainty. An early advance visit to the problem location to assess the local organization and political environment is always valuable for any epidemiological investigation. As any field investigation may lead to legal redress and prosecutions, all records must be kept to the highest standards from the start and stored appropriately.

15.2 Case studies

The case studies examined in this chapter are based on an urgent outbreak investigation of a Legionnaires' disease cluster in London contrasted with a longer-term investigation of blood lead levels in children in an urban Australian setting.

15.2.1 *Legionella* outbreak investigation

Legionellosis is a potentially fatal infectious disease caused by Gram negative, aerobic bacteria belonging to the genus *Legionella* (Health Protection Agency (HPA), 2012a). Currently between 200–300 laboratory confirmed cases occur annually in England and Wales, but the number of cases may be higher. More cases occur in the summer and early autumn, but it can happen any time of year. The early symptoms of Legionnaires' disease include a 'flu-like' illness with muscle aches, tiredness, headaches, dry cough, and fever. Sometimes diarrhoea occurs and confusion may develop.

Diagnosis is made through urinary antigen testing and a chest X-ray is helpful. Legionnaires' disease cases can be treated successfully with antibiotics but has a mortality rate between 5% and 15%.

Legionella bacteria are found naturally in the environment, usually in stagnant water, growing best in warm water. They can be found in hot tubs, hot water tanks, large plumbing systems, or parts of the wet air-conditioning systems of large buildings (e.g. cooling tower water systems). These usually only become a problem when the temperature allows the organisms to grow rapidly, such as in water systems which are not properly designed, installed, and/or maintained. Outbreaks have also been associated with smaller-scale hot water systems such as spa baths and in holiday accommodation. Information about past outbreaks and how to investigate them can be found on the HPA website (HPA, 2012b). The case study is based on an outbreak in Piccadilly Circus, London 1989 with 33 confirmed cases, including five deaths (Watson et al., 1994).

15.2.2 Child blood lead survey

This case study was a child blood lead survey conducted in Wollongong, Australia in 1994 (Kreis, 1994). The area was at risk of lead contamination due to its proximity to heavy industry, particularly a copper smelter. Children are particularly sensitive to the neurotoxic effects of lead (Chandramouli et al., 2009) with the World Health Organization (WHO) identifying lead as one of the five major environmental hazards (WHO, 2009). Several lead blood surveys had been conducted before in this area, but with poor or unknown response rates.

15.3 Preparation

All epidemiological investigations need a clear case definition as soon as possible so case finding and collection of basic epidemiological data can begin. Developing a case definition requires a clear understanding of the health concern and possible causes. This must be explicit to enable information to be gathered for cases and any possible risk factors. Further work will aim to prove or disprove such associations.

Key points for consideration in terms of preparation in either situation include:

- ◆ security (personal and transport/data/equipment)
- ◆ site visits and pilot scoping studies
- ◆ equipment and protocols

- ◆ data and specimen collection
 - human resources
 - specimen handling and transport.

Investigation of most Legionnaires' or other infectious disease outbreaks is urgent because the source of infection needs to be found as soon as possible to prevent more cases. Many agencies may be involved. Findings from the outbreak investigation may influence legal proceedings thus making quality control and documenting evidence crucial.

In the blood lead case study, speed is of less concern but quality control and documentation are still important. Public health may be adversely affected if a source of contamination persists without identification and control. Therefore the political and societal consequences can be substantial. However, it is not always possible to move quickly if ethical approval is needed because the study is classed as research (Chapter 18). However in an urgent outbreak investigation, the health of the public is at immediate risk and formal ethical approval is usually not required.

In both case studies the main focus of logistics should be: ensuring security in the field; deployment of personnel and specialist equipment; provision of transport and communications; and adherence to (standard) operating procedures where they exist. If protocols do not exist it is useful to develop them. Planning in advance is key and it is important to establish early on what the local arrangements are as well as understand local politics and consider how best to reflect these.

Equipment including computers should be ready for deployment in the field, with the required software already loaded. This could include Epidata (or EpiInfo), Stata, R, and mapping software (QGIS).

Planning and protocols for specimen collection and the containers, transport media, and packaging are also required. This might include kits and packaging for specimen collection and storage (e.g. blood, urine, faeces). In nutritional surveys or environmental epidemiology studies, measurement tools may be needed, e.g. callipers, scales, or peak-flow meters.

Before field deployment ascertain the reasons for inviting support to the field. Clarify the terms of reference for the investigator's involvement and what logistics are required. In the context of the Legionnaires' disease outbreak scenario (and similar situations) there will usually be a need to investigate quickly. There will be pressure for rapid answers, there may well be a media spotlight and legal implications. All these aspects should be considered and planned for in advance. Find out what is going on as far as you possibly can. Ask questions including if you can have terms of reference for your involvement and get up to date with relevant scientific literature.

It is important to ask about what the expectations from the field work are and what local expertise and resources are available. You also need to know about the tasks envisaged and identify the specific role of the field investigator. You need to ask about timescales and what has already been done, what resources you need to bring, who is in charge, and to whom the investigator needs to report.

For the Legionnaires' disease investigation, it was useful to write a short one-page outline of the objectives of the field trip or study before setting out. An initial meeting on

arrival was arranged in advance with senior local public health staff. In the blood lead levels survey additional preparations included a full protocol and the materials required such as standard letters of invitation for participation in the investigation and questionnaires. These were drafted and signed off by peers, project steering committees, and the ethics committee as relevant.

In both scenarios consider what you need both to bring (Box 15.1) to the field and what you expect to be there already so you can check what is actually there (Box 15.2).

15.3.1 Security

Working in pairs is good practice. Some locations may require advance security clearance or other specific training for international investigations which may pose challenges,

Box 15.1 Resources for field investigation include:

- ◆ Computer, calculator, mobile phone (including charger and appropriate plugs)
- ◆ Software
- ◆ USB (universal serial bus) storage device, compact discs
- ◆ Notebook and pens/pencils
- ◆ File templates
- ◆ Standard questionnaires
- ◆ Handbooks, relevant articles
- ◆ Telephone address list to include reference centres and contacts of authorities and experts
- ◆ Camera (including charger and spare storage media)
- ◆ (Laboratory equipment)
- ◆ (Sample containers and sample taking equipment)
- ◆ (Sample storage equipment)
- ◆ Maps, geographic positioning system (GPS)
- ◆ Others . . . (money, 'health kit').

Box 15.2 Equipment available on location should include:

- ◆ Computers with Internet connection
- ◆ Telephones, telefax
- ◆ Copy machine
- ◆ Reference materials
- ◆ Office furniture and stationery.

especially in developing countries. A field office with complete and robust information technology and communications (satellite telephony, radio communications, and, if possible, field video-conferencing capacity) can be invaluable. You may also need specialized protective equipment and medical supplies. For international deployment vaccinations and visas may need to be obtained.

15.3.2 Site visits and pilot scoping studies

The main benefit from site visits is to gain a real appreciation of what is actually going on, including the scale, nature, as well as wider dimensions of the incident, such as any medical or political imperatives. The 'feel' that a site visit gives is very helpful. It offers an opportunity for assessment and reflection on the circumstances of the concern and allows initial consideration of health impacts using concepts such as the source–pathway–receptor model (Chapter 9). It is important to be aware of local sensitivities, so being appropriately dressed, being respectful of, and behaving appropriately to support local customs and values are vital, especially in a foreign country. Reporting back to those who have deployed the field team is essential as they will need to feed back to stakeholders and their parent organizations.

Routine formal communication plans should be put in place as a priority. You need to be aware before you attend any meeting what you should say in terms of the aim of your future involvement. Consideration should be given to meeting stakeholders such as politicians, community elders, health and educational professionals, as well as other crucial social groups. The public rumour mill can be very active and strange people and their vehicles, for example, can attract attention.

15.3.3 Equipment and protocols

Coordination and logistics support should be agreed by prior development of operational protocols and agreed standards. This might apply for specialist equipment and software as well as the basic approach to investigation, research, and evaluation. Prior training in use of equipment and technical facilities is essential to ensure familiarity, confidence, and reliability in the field.

Sample collection and testing processes in laboratories usually are well documented with standard operating procedures (SOPs). It is important to know which laboratories can and will carry out the tests, where they are, what their requirements are for submitting samples, and who has the responsibility for keeping SOPs up to date.

For example, in the Legionnaires' disease scenario reliance was placed on already existing protocols and SOPs. In the blood lead scenario additional SOPs might need to be drawn up, e.g. for blood sampling and storage of the specimens in the field. If possible use questionnaires that have been used before (ideally ones that have been validated). Other standardized documents such as invitation letters can be developed in advance. Population sampling strategies need to be developed and included as part of the proposal.

15.3.4 Data and specimen collection

You should ask if any microbiological or environmental investigations have already been started before the field investigation. You need to know what sort of human samples

might be required, how these will be collected, and where analysis will be done. If environmental samples are needed it is vital that the legal power to enter premises or areas is arranged in advance. This was relevant to both case studies.

Consultation should take place with colleagues (e.g. microbiologist, vet, environmental, and toxicological experts) to determine who leads the team and what support will be provided back at base and to whom the team is directly responsible. An additional area to explore is whether there are any mandatory local guidelines or procedures to be followed, e.g. in relation to confidentiality or data handling.

Data requirements should ideally be ascertained during the site visit and scoping study and a draft questionnaire or checklist of data items prepared (the computer database or Excel data collection file could be set up in advance). This was not possible in the Legionnaires' scenario where deployment was rapid but for the blood lead scenario this was all agreed with stakeholders before any field investigation. Line listings of cases with essential data can be invaluable and should be kept up to date and easily accessible. The data might include:

- ◆ cases/contacts/affected individuals
- ◆ basic sociodemographic details
- ◆ laboratory results
- ◆ key dates including onset of illness
- ◆ whether questionnaires available or requested.

Pre-piloted, validated simple questionnaires should be used where possible. All questions should be clear, unambiguous, and not leading. Analytical studies also need information about potential confounders, e.g. age and sex. Team members should be trained in administering the questionnaires and any sampling methods to ensure uniformity. Data should be immediately plotted as epidemic curves showing confirmed and probable cases over time overlaid with key events.

15.4 On arrival in the field

It is essential to have a systematic approach. Leaders for key aspects of the investigation should be identified. The field investigation team should meet with the local stakeholders early; preferably arrange this before leaving base. Soon after arrival, establish communications with your base/headquarters. Identify the best location in which to establish the field work and ensure its accessibility and security.

The links between various potential actors and their likely inter-relationships are depicted in Fig. 15.1. The activities involved can rapidly become complicated as the work proceeds. It is important to understand this dynamic mix as well as the political context. A key aspect is to ensure dedicated administrative support for the field work and do not neglect nutritional support, as a hungry team will not work as well as one that is fed and watered!

It is good practice at an early stage to prepare for an eventual orderly departure from the field. Systems developed at the start should be documented to ensure that others can retrieve relevant data and records when the team have left.

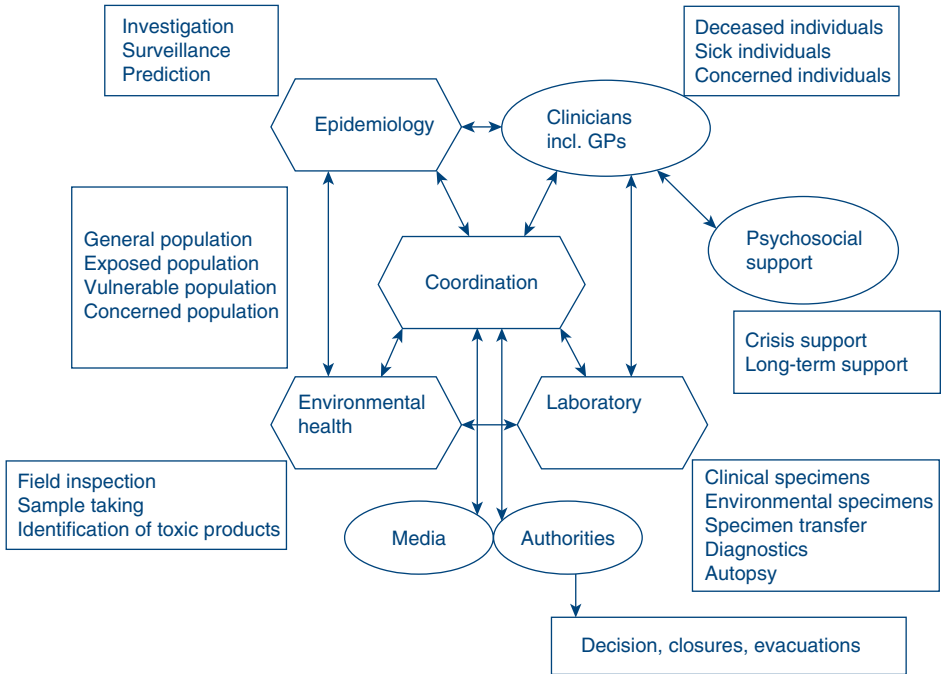


Fig. 15.1 The inter-relationships of potential field team members and their various functions. Entities in ovals are predominantly local, in hexagons mostly the field team, and squares are tasks/responsibilities.

Significant expertise among local professional colleagues and stakeholders should be identified early on. The field investigation team should share responsibility and work with local colleagues using agreements and protocols, clarifying who leads before any investigation is undertaken. This allows the field investigation team to facilitate local learning and development and make transfer of responsibility back to the local team easier when the investigation team leave. Within this approach it may be helpful to compartmentalize aspects of the investigation, for example, by clarifying issues related to the media and who will respond to press enquiries.

15.4.1 Process and mechanisms required in rapid field investigations

The timelines for reporting should be discussed and agreed at the outset. Regular meetings should be properly minuted with the agreed actions and those responsible listed. It is important to document all decisions and the rationale used to make them including what information was available at the time. Developing a 'battle rhythm' for the reports and updates that are required makes it possible to schedule key field work and meet all the internal and external demands for reports and summaries in good time. For example, it is often useful to release statements to the media around midday to fit with their publication schedules in print or visual media. There may also be other senior committees that

need summaries (situation reports; (often abbreviated to SITREPS)) at end of the day or by mid afternoon.

Operational information will also be required and should include:

- ◆ Local and other professional contacts: name, position, contact details.
- ◆ As a minimum operational records should include:
 - epidemiological (protocols, questionnaires)
 - methodological notes—sampling strategy for studies, control selection if analytical studies planned
 - data analysis plans—descriptive or analytic
 - interview notes, meeting minutes, press statements
 - emails
 - raw data (epidemiological, microbiological, or environmental) e.g.
 - epidemiological data collected
 - urinary tests for *Legionella* antigen and environmental samples taken and tested as well as their results (e.g. cooling tower, fountain or spa)
 - blood sampling for lead poisoning and environmental sampling for lead in soil, dusts or other pollutant pathways.

Tasks that need to be done include managing information (databases), collecting data and specimens/samples, and collating and interpreting results to provide briefings or reports to aid health protection decision-making.

Management of data and databases includes data entry and validation, confidential storage, and documentation of procedures. It should be clear who has the overall responsibility for data management and an inventory of files and log books.

15.4.2 Leaving the field

Departure from the field should be planned well ahead of time, and discussed and agreed between the team supervisor and colleagues. Before leaving it is essential to prepare a preliminary report and ensure it is clear how and who will produce a final report. It is also vital to archive data securely and with clear documentation. Databases and any personal information (PII) within them need to be secure and PII kept to a minimum and only retained where necessary. Ways of collecting outstanding laboratory or clinical results need to be agreed so they can be incorporated into final reports. There should always be a debriefing meeting on arrival back at base.

15.4.3 Rapid field investigation of Legionnaires' disease

The case–control study done in the outbreak associated with Piccadilly Circus, London 1989 showed cases were more likely to have visited a certain area in the 2 weeks before onset of symptoms. There were 33 confirmed cases, including five deaths (Watson et al., 1994).

The focus in the Piccadilly Circus outbreak was on certain cooling towers in the area where cases were known to have visited or passed by within a certain distance. The registers and maintenance records for such towers (if they existed) needed to be examined, the towers visited, and sampling planned, specimens taken and tested while the epidemiological investigation was going on. The inspecting and sampling strategy changed as more information became available. The organism, *Legionella pneumophila* serogroup 1, was isolated from six patients and also from water samples from five wet cooling towers in the area. Many of the cooling towers examined were inadequately maintained. All cooling towers in the area were shut down and only allowed to restart after appropriate inspection and maintenance.

15.4.4 Field lead poisoning survey

The Wollongong survey on child blood lead entailed identifying children of relevant age (in the example used here under 6 years) and taking a venous or a finger-prick blood sample. A questionnaire was also used to identify possible sources and other information such as residential history and parental occupations. Quality control and reduction of bias is crucial in such studies. Therefore attention should be paid to participant selection and ways to limit observer and responder bias.

Protocols and procedures were agreed in advance and all members of the team, as well as the local relevant authorities and the media, had seen, read, and understood the full protocol including all the SOPs, letters, other procedures with location maps, and plans (Kreis, 1994; Willison, 1994). Following meetings held with authorities, members of the public (including the parents and grandparents of children invited to participate, heads of schools, and local health care professionals) were given summaries of the protocols which were also shared at press-conferences.

Quality was assured by:

- ◆ Documenting all aspects of the field work, including log book and photographs where permissions were obtained.
- ◆ All materials and procedures were routinely checked independently for quality control purposes as agreed in the protocol.

Table 15.1 Door-knock effort in the Wollongong lead study

	Number of personnel	Roughly estimated hours	Number of days
Letterbox drop	2	40	4
1st round	10	424	14
2nd round	3	160 (incl. weekends)	16
3rd round	2	88	9
4th round	1	10	2

Reproduced from Kreis, I.A. (1994). *Protocol for the Illawarra Child Blood Lead Study, 1994*. University of Wollongong, Illawarra Environmental Health Unit 1994 with permission of the author.

Table 15.2 Publicity efforts in the Wollongong lead study

Category	# identified	# visited/contacted	Time period
Local press	?	12?	06/06/94–30/12/94
Ethnic/social groups	25	19	04/06/94–18/08/94
Medical establishment	18	17	21/07/94–21/11/94
(Pre-)schools/ child care/playgroups	13	13	23/06/94–10/08/94

Reproduced from Kreis, I.A. (1994). *Protocol for the Illawarra Child Blood Lead Study, 1994*. University of Wollongong, Illawarra Environmental Health Unit 1994 with permission of the author.

- ◆ With more than one location for the investigation, attention was paid to co-ordination between staff and the tools they used to make sure no systematic differences were created them.
- ◆ Media contact was planned to ensure good participation rates alongside other methods to reduce selection bias outlined in Tables 15.1 and 15.2 (Chapter 4).

An overall response rate of 68.5% was achieved with the assessment of 698 children (either exposed or control). Some of the control group children were also identified as over the guideline level and a cluster outside the initial problem area was identified and later investigated.

15.4.4.1 Long-term investigations

A particular feature of a longer-term investigation identified in the field lead case study was the sustained contact between members of the team and the community they were working in.

15.5 Conclusion

Field investigation is exhilarating and challenging. Preparation is essential and good organizational skills help. It is important to stay organized and use pre-prepared plans in a flexible way whilst working with local stakeholders. Help from many local colleagues should be sought as the occasion demands. Focusing on what outputs are required helps orientation and prioritization of activities. Where findings are shared in the scientific literature the work of the full investigating team should be acknowledged and ethical approvals may need to be set up at the start to allow this to happen. Such reports are vital to improve health protection practise in the future.

15.6 Further reading

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Chapter 16

Data quality

Araceli Busby

Learning objectives

- ◆ Synthesize key principles of data management in epidemiology.
- ◆ Appraise quality management processes for data collection and analysis.
- ◆ Evaluate the effect of poor quality data on study outcome in environmental epidemiology.

16.1 Introduction

When any epidemiological study is carried out it is vital to be aware of the potential for inaccuracy in the data collected and the likely effect of such inaccuracies on the outcome. Environmental studies of congenital anomalies provide a good example of the rigour with which data must be collected and evaluated. This chapter considers an investigation into anophthalmos and microphthalmos (congenital eye defects) carried out in the UK that can illustrate data quality issues.

16.2 Anophthalmia case study

Anophthalmos/microphthalmos are rare congenital anomalies of the eye: anophthalmos is the complete absence of the eye and associated ocular structures and microphthalmos is a smaller than normal eye. Together these eye anomalies account for less than 1% of all congenital anomalies (with a prevalence in Europe of around 1 per 10,000 births; see e.g. EUROCAT, 2011). Anophthalmos/microphthalmos may be of considerable clinical significance; the majority of babies with moderate to severe anophthalmos/microphthalmos will be severely visually impaired or blind, and also require extensive surgical procedures to ensure normal growth of the bony orbit.

In 1985 a Welsh study investigated claims of a cluster of babies born with microphthalmos in the vicinity of a hazardous waste incinerator (Welsh Office, 1985). The study was unable to find any evidence of a cluster but concluded that their data were not sufficiently complete to refute a possible cluster. In 1988 the Scottish Office conducted a similar investigation into clusters of microphthalmos reported near a chemical incinerator. Again data

quality was not considered adequate to refute a possible cluster although the study did not confirm any increase either (Dolk et al., 1993).

Both these studies were reported in the press, but a report in *The Observer* (Paduano et al., 1993) suggesting a link between anophthalmos/microphthalmos clusters and the fungicide benomyl brought the matter to the public's attention. The newspaper cited a toxicology study (Kavlock et al., 1982) in which anophthalmos/microphthalmos had been induced in the offspring of rats fed high oral doses of benomyl. The story was rapidly taken up by other newspapers, with further allegations that the number of babies born blind in the UK had doubled in the previous 10 years (Boulton, 1993).

The media reports identified nine children born within a 40-mile radius of a village in North Lincolnshire within a 12-year period; three within 4 years of each other. Other cases identified by the media ('described by one US expert as an epidemic'; Paduano et al., 1993) were of varying ages. Diagnoses included anophthalmos, microphthalmos and optic nerve disorders. Two cases were from the same family but no further information about family history or associated anomalies was reported.

16.3 The initial investigation

The first step in evaluating the allegations that benomyl causes eye anomalies was to investigate the apparent cluster(s) in detail. Three key allegations had been made by the press reports:

16.3.1 'The number of babies born blind has doubled'

Data from the UK Blindness Registration was reviewed and showed a considerable increase in blindness registrations in adults. However, very few registrations are for children or babies (Dolk et al., 1993) therefore the data are not relevant to congenital anomalies. It is clear that time trend data require careful evaluation to assess consistency of recording over time and relevance to the group under study and this is a key issue in data quality.

16.3.2 'There are clusters of anophthalmos in rural areas in the UK'

Preliminary investigation into anophthalmos/microphthalmos birth rates evaluated data from the Office for National Statistics (ONS) Congenital Anomaly returns and UK regional congenital anomaly registers. The ONS National Congenital Anomaly System (ONS, 2010) began recording data in 1964 and is based on passive reporting (there is no mandatory requirement to report babies with anomalies and no active follow-up); ascertainment is therefore low. The various regional registers were more recently set up and perform active data collection, with consequently better ascertainment. However, at that time, regional registers were only recently set up and hence of limited value for the evaluation of time trends.

Further difficulties in evaluating these routine data arise from the fact that anophthalmos/microphthalmos is a feature of many conditions and syndromes therefore a baby classified with a specific diagnosis (e.g. 'Patau's syndrome') may not have individual

anomalies listed. Babies with multiple anomalies may be spontaneously or therapeutically aborted and detailed information on individual anomalies is not recorded.

Comparison of the newspaper reported cases with the rates reported by ONS and regional registers did not indicate any excess in the rates seen at county level for those counties containing the alleged clusters (Dolk et al., 1993). As discussed in Chapter 19, it is not considered valid to examine a single cluster (or localized excess) in isolation, due to the tendency of rare diseases such as anophthalmos/microphthalmos to cluster as a result of natural, random variation. Evaluating the anophthalmos/microphthalmos ‘cluster’ required data on all anophthalmos/microphthalmos over a wider geographical area to identify whether the condition demonstrated greater spatial or spatiotemporal clustering than expected. Clearly such an examination would require complete, consistent, and accurate ascertainment of all babies born with this condition, as well as sufficient information on each baby so that alternative causes (genetic, other environmental causes) could be excluded. ONS data available at the time did not meet this requirement.

16.3.3 ‘Benomyl is a human teratogen and causes eye defects’

The evidence for the link to benomyl was based on one toxicology experiment in rats and an identified ‘increase’ in cases in the UK which was alleged to mirror a rise in pesticide usage.

Neither a cohort study of farming communities in Norway (Kristensen et al., 1994) nor an ecological study of pesticide use and anophthalmos/microphthalmos in Italy (Bianchi et al., 1994) supported a link between pesticide exposure and anophthalmos/microphthalmos. However, the Italian study was ecological (thus considered to be a relatively weak argument for causality) and the Norwegian cohort study, whilst being a stronger methodology for identifying causal relationships, used proxy exposure data based on common farming practices, thus risking exposure misclassification (see Chapters 8 and 14).

The evidence for exposure to benomyl in the reported cases was limited: one mother reported spraying strawberries in her garden with a fungicide and several families lived near farm land. There was no evidence in UK congenital anomaly data of any change in anophthalmos/microphthalmos prevalence over the time period when benomyl (and the related fungicide carbendazim) use increased a thousandfold (Gilbert, 1993). The epidemiological and toxicological data in 1993 were therefore considered not sufficient to adequately assess the likelihood of benomyl being a human teratogen (Gilbert, 1993).

16.4 Next steps in the investigation

The decision to continue with further investigation was prompted by the high-profile media attention and level of public concern (see Chapter 4) combined with the absence of adequate data, rather than any convincing scientific evidence for an association between the condition and exposure.

Rather than institute a full epidemiological study it was decided to first conduct a data gathering exercise so that the presence or absence of geographical variation and clustering in anophthalmos/microphthalmos (which might suggest an environmental cause) could be evaluated.

16.4.1 Data collection needs for a study of congenital anomalies

In order to be able to investigate anophthalmos/microphthalmos it is essential to define the aim of the investigation, have a clear case definition, and understand the epidemiology of the disease in question; including information on incidence and prevalence, the main recognized causes and any potential confounders.

16.4.1.1 Epidemiology of anophthalmos/microphthalmos

The causes of congenital anomalies are broadly divided into genetic and environmental, although around 20% of major congenital anomalies are thought to be multifactorial (environmental factors influencing genetic predisposition). Genetic causes involve damage to the genetic material which then cause errors in embryonic or fetal development. Non-genetic anomalies are caused by direct damage to the developing cells which overcomes the ability of the embryo or fetus to repair. The causes of up to 60% of congenital anomalies are unknown (Moore and Persaud, 2007).

Whilst certain causes (more commonly genetic) give rise to recognizable syndromes (a specified group of anomalies associated with that cause) it is not possible to accurately diagnose aetiology from phenotype (the observable pattern of anomalies). For example, not all babies with apparent Down syndrome have an extra chromosome 21 on genetic testing; similarly not all Down syndrome babies have all the features of the syndrome.

Anophthalmos/microphthalmos is a rare congenital anomaly, usually associated with other anomalies in the same child. The majority of cases of anophthalmos/microphthalmos have unknown aetiology (Busby et al., 1998). It is a component of a wide range of genetic syndromes which, other than Trisomy 13, account for only a small proportion of cases. The best established environmental causes in humans are certain maternal infections including non specific hyperthermia, rubella, toxoplasmosis, and cytomegalovirus, but these account for only a small proportion of cases. Microphthalmos is an established feature of the fetal alcohol syndrome spectrum of anomalies and maternal exposure to thalidomide, isotretinoin, toluene abuse, and insecticides have been reported to be associated with microphthalmos but with less extensive evidence (Busby et al., 1998). There is little evidence to support pesticides or fungicides as an important cause.

16.4.1.2 Data quality

The epidemiology of anophthalmos/microphthalmos suggests a number of key issues for data quality because of losses of severely affected babies before birth and the multiple alternative causes for anophthalmos/microphthalmos and are summarized as:

- ◆ *Completeness of recording of early fetal deaths:* early fetal deaths may be difficult to identify and recording is variable: not all women will know they are pregnant;

clinical examination of miscarriages vary in their detail; and recording practices vary. Studies of congenital anomalies therefore specify a gestational age cut-off such that (it is assumed) all babies born after this gestational age are certain to have been recognized, usually around 20 weeks. *In utero* deaths after 20 weeks are designated stillborn. Babies selectively aborted for fetal anomaly (who might otherwise have survived to later in the pregnancy or even to term) must be included on the assumption that they would otherwise have been born after 20 weeks and thus become a case. Data sources must therefore be chosen carefully to include all relevant babies and the limitations of individual sources must be clearly understood (e.g. a child health register may be a valuable resource for living children but will provide no information on therapeutic abortions, stillbirths, or babies who have died). It is particularly important to be aware of differences in recording early fetal deaths and terminations as any variation between sources can result in spuriously higher or lower prevalence in time or space simply due to this alone.

- ◆ *Identifying alternative causes:* as a first step it is common in congenital anomaly research to identify and exclude inherited genetic conditions, chromosomal anomalies, and well-established environmental causes from analysis as this would introduce misclassification. This requires detailed information on family history, maternal exposures, health, and age (more important for chromosomal than for non-chromosomal anomalies), clinical tests, and differential diagnosis. Information on early fetal deaths or terminations is likely to be limited compared with data on living babies and children.
- ◆ *Which anomalies to included or exclude?* Information on the phenotype may provide clues as to aetiology but should be interpreted with caution. It is common, however, to analyse congenital anomalies in clinical subgroups (e.g. according to organ system) as this may allow specific patterns to emerge; much as an occupational study of cancers in a chemical industry might look separately at lung cancers and bladder cancers. Because severe congenital anomalies are rare a compromise is often needed between having adequately exposure-specific or aetiologically relevant groups and having large enough numbers to achieve statistical power. Patterns of associations between certain defects (e.g. cardiac defects combined with neural tube defects) may be more important than gross divisions between organ systems because an environmental exposure can affect several different developing organ systems. Subgroup analyses need detailed information on all malformations which are present so these must be fully and accurately recorded (and coded).
- ◆ *Exposures requiring investigation:* for anophthalmos/microphthalmos a wide variety of exposures have been (weakly) associated. For this reason the investigation did not focus on a particular exposure but aimed to look at the more general issues of geographical variation and clustering on the assumption that any environmental exposure (whether pesticides or another) would result in identifiable geographical variation. The geographical location of the individual cases, ideally at the critical time for exposure, is thus a key piece of information. Address at delivery is generally used

as a proxy for location during pregnancy but 23% of women may move house during pregnancy (Hodgson et al., 2009). Additionally place of residence may be a poor representation of exposure (consider the case of pesticide exposure, for example: someone living in an urban environment may make frequent visits to rural locations for work or recreation).

16.5 Data quality for a case register and investigation

To determine whether there is a link between a health effect and an exposure there are three essential pieces of information:

1. Individuals with the condition (cases).
2. Individuals without the condition (controls or population).
3. Information about exposure in cases and controls/population.

The study design determines how cases are collected. In a case–control study, for example, it is important to identify sufficient cases and controls to ensure statistical power. In geographical studies or cluster analysis it is vital that case ascertainment is as complete as possible for the time/geographical boundaries specified.

For anophthalmos/microphthalmos, geographical variation and clustering were the key issues which made completeness of ascertainment especially important. Completeness is also an important aspect of data quality since commonly the higher the levels of ascertainment the better the overall quality of the data. Hence the decision was made to create a complete case register for a specified time period (1988–1994) of all cases born in England.

16.5.1 Cases

A clear case definition that can be simply and consistently applied was needed to ensure that all relevant cases were included on the register, and all cases on the register were genuine. The key issue with anophthalmos/microphthalmos was the lack of an existing clinical definition for mild microphthalmos and the potential for diagnostic variability. Whilst anophthalmos is also difficult to distinguish from severe microphthalmos this was less of a concern since both conditions were relevant. After discussion with expert clinicians, microphthalmos was classified as mild, moderate or severe with mild defined as having eyes more than two standard deviations smaller than average for gestational age (Busby et al., 1998). Clinicians were provided with a pictorial guide supplemented with questions about ocular size and age at measurement. Cases defined as mild were analysed separately from moderate to severe and anophthalmos, so that any effect of variation resulting from inconsistent recording of mild cases could be evaluated.

As discussed, cases with known causes (other than that under investigation) must be excluded from analysis. This requires detailed information on each baby, including clinical diagnoses, family history, genetic testing, and information about all the associated congenital anomalies (not just anophthalmos/microphthalmos).

The final case definition for the study was: ‘All babies in England whether live born or stillborn on or above 20 weeks’ gestation with anophthalmos or moderate to severe

microphthalmos (defined as ocular diameter 15mm or less at term) with or without other anomalies.’

16.6 Evaluation of data sources

Ideally case ascertainment would be prospective, allowing for accurate information to be collected at the time when it is most readily available. However this is beyond the resources (both time and cost) of most epidemiology studies and retrospective sources must be used. In the anophthalmos/microphthalmos study, data collection was retrospective, using both routine and ad hoc data sources. Routine sources offer the advantage that recording should be consistent over time (with important caveats) but often lack detail and may or may not be complete. Ad hoc data sources (e.g. clinician surveys) may allow for the collection of greater detail but are rarely consistent over time and must also be carefully evaluated for completeness, especially for data collected retrospectively. Each data source should be carefully evaluated so that the likely sources of error and inaccuracy are identified.

The anophthalmos/microphthalmos study used multiple data sources (Box 16.1) so that basic information identifying each case was then supplemented with data from expert clinicians and other sources (e.g. pathology reports). Evaluation of reporting rates from different sources (Busby et al., 1998) suggested that clinician reporting rates were higher in the more recent past (due to better recall) whilst routine registries provided more cases in earlier years of the study period (due to the time delay for individuals to be recorded and the data to be available). Overall this resulted in a fairly stable prevalence rate of anophthalmos/microphthalmos over time but this disguised a variety of reporting biases.

Box 16.1 Multiple data sources used for case ascertainment

- ◆ Birth notifications
- ◆ Death certificates
- ◆ Maternity records
- ◆ Neonatal and other hospital discharge records
- ◆ Pathology records
- ◆ Cytology records (for abnormal chromosome notifications).
- ◆ Specialist clinical departmental records, e.g. paediatric surgery, paediatric cardiology, clinical genetics, ultrasound.
- ◆ Community health records (records of child health, disability).
- ◆ Special notification from clinicians or other health care professionals, e.g. BPASU, or ad hoc surveys.
- ◆ Specialist routine registration systems e.g. congenital anomaly registers.

16.6.1 Data quality issues

Issues to consider when evaluating the quality of the data acquired through any one source include:

- ◆ *Relevance*: are all cases likely to be included? E.g. post-mortem records will not include living children; child health records will not include children who died at or before birth.
- ◆ *Accuracy*: are the data in agreement with data on the same individual from other sources? What evidence is there from the source that data are accurate and have been validated?
- ◆ *Completeness in space and time*: e.g. Moorfield's Eye Hospital register of children only included those referred to the hospital for expert treatment; clinician surveys are unlikely to provide much information on children seen in the distant past.
- ◆ *Use of standard terminology, definitions, and coding*: coding systems may not be precise enough to pick up a single anomaly particularly if it is part of a syndrome; clinical and coding definitions may change over time when coding systems change or clinicians change; coding systems used by different sources may not be comparable.
- ◆ *Follow-up of cases*: often important for routine sources which collect data at one single point in time such as birth certificates: incorrect diagnoses may not be corrected at a later date.
- ◆ *Quality control*: most routine data sources have quality control procedures and a quality assurance framework in place. This is documented by records of coding systems and possibly as a coding summary, so that consistency testing and any issues with identifying and dealing with any outliers is explicit and clearly recorded.

16.7 Quality issues in managing the data

Data acquired from multiple sources must be carefully processed to ensure that information is collated consistently, with the minimum of error and without compounding any existing quality problems. Issues of data quality for a derived registry are essentially the same as those described earlier for data sources with the additional necessity of having to combine data from different sources which may not always agree. Standard protocols must be developed for the translation of data from different sources into the registry database format, for standardized coding (including written coding manuals) and for quality control.

16.7.1 Setting up the computer system

A computerized database may incorporate data entry rules which reduce the possibility of random data entry error; for example, variable fields can be limited to a specific valid range (e.g. limiting the gestational age field range to between 1 and 44 weeks); certain core variables can be made mandatory so that the case cannot be saved unless the field is completed; drop-down boxes can be provided (e.g. for associated

congenital anomalies) containing detailed descriptions and coding guides to reduce coding errors.

16.7.2 Duplicates

A duplicates protocol might specify, for example, which variables should be used to identify a duplicate individual (e.g. date of birth and postcode). Procedures for identification of duplicates should be standardized and documented.

16.7.3 False positives and conflicts in information from different sources

Where information from different sources appears to conflict, a protocol may be required for deciding which data source takes precedence. For the anophthalmos/microphthalmos study, for example, an ophthalmologist's judgement of microphthalmos severity was considered to override that of the paediatrician, whilst the judgement of any clinician who had seen the child was given priority over information from a routine data source. What is most important is that the protocol is documented and followed by all individuals who enter data.

16.7.4 Evaluation of completeness

Evaluation of completeness may be possible using a variety of methods. For the anophthalmos/microphthalmos register prevalence rates derived from registry data were compared with published literature and routine data sources in other countries. Capture-recapture methods were used to evaluate completeness by statistically analysing the level of overlap between different data sources (Armstrong et al., 2002). Despite extensive use of multiple sources and thorough follow-up estimates of completeness suggested that up to 25% of cases might be missing from the register (Busby et al., 1998; Armstrong et al., 2002), which emphasizes the difficulties of collecting data on single conditions on an *ad hoc* basis.

16.8 Conclusions

The investigation into an alleged cluster of anophthalmos/microphthalmos in England provides a good illustration of the difficulties of ensuring data quality in environmental epidemiology. It is clear that data quality underpins the validity of any epidemiological study but particularly in environmental epidemiology which is often required to evaluate very low levels of exposure and poorly defined health outcomes. It is essential that data quality is given primary importance from the very start of any investigation and the likely effect of any uncertainty is well characterized and clearly communicated at the outset to those with an interest in the study outcome.

The analysis of geographical variation did not find any evidence for either large-scale regional variation in rates of anophthalmos/microphthalmos or localized clustering (Dolk, 1998). Although the data were acknowledged to be incomplete this would not be expected to introduce spurious geographical variation and since none was seen it is

doubtful whether the results would essentially have changed with complete ascertainment. The difficulty of achieving complete ascertainment using retrospective data and the resources required highlights the value of high-quality routine registration for rare conditions such as congenital anomalies which can generate high levels of anxiety amongst communities where there are suggested increases or clusters.

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Applied statistical techniques

Dominik Zenner

Learning objectives

- ◆ Have a good overview of the statistical methods of data description and analysis common in environmental epidemiology and evaluate their relation to study design and variable choice.
- ◆ Apply some specific methods such as power calculation and standardization techniques and explain them in their context.
- ◆ Specify and apply statistical methods for hypothesis testing in case–control and cohort studies.
- ◆ Interpret and critique selected statistical methods, such as logistic, linear, and Poisson regression for advanced analysis as used in the literature.

17.1 Introduction

The chapter provides a practical guide for using statistical and epidemiological methods to investigate environmental hazards. It provides worked examples of relevant methods based on two published investigations. The studies can be found in the further reading section (section 17.5); some of the data have been simplified.

The chapter covers a selection of basic methods which are commonly used and should be within the capability of a practitioner in the field. There are suggestions for studying more advanced statistical methodologies in the further reading list.

17.2 Case study 1—dealing with categorical data: a cancer cluster

A cluster of haematopoietic cancer cases (cancers of the blood system) was observed in a rural Dutch community (Aalsmeer). Fourteen cases of leukaemia and lymphomas occurred within approximately 12 years. All lived within 1 km of each other. Public health practitioners were notified by the parents of one of the cases, because they felt that these illnesses could have been caused by an exposure to pesticides. This particular part of Netherlands is a world-renowned flower growing area. One possible source of exposure

was swimming in a walled pool on the edge of a lake. The possible role of air pollution in causing these illnesses is not considered here (Mulder et al., 1994). This cluster is also used as a case study in Chapter 19.

17.2.1 Descriptive analysis

The first step is to describe the cluster of cases by specifying *the observations in time* (when did the cases occur?), *person* (are specific groups of persons more affected than others?), and *place* (where do the cases live in relation to each other and to the implicated source?). In this example, all cases were children or young adults and occurred within about 12 years of each other.

The first thing to do is to create a ‘spot map’ of the cases (Chapter 13). Here the dots indicate cases by residence. The map can not be shown for privacy reasons (Chapter 18). Cases can be mapped by place of work or other relevant factors, depending on the hypothesis. Maps can become more informative if important geographical features, e.g. industrial areas of interest, are also displayed. It is almost always helpful to use graphs and maps to illustrate and describe the cluster. This visual approach often allows associations to be seen. One such association is revealed through plotting age at diagnosis against year (Fig. 17.1). The weak positive association suggests a possible point source affecting cases all around the same time, relatively early in the period under investigation.

Graphical representations such as Fig. 17.1 can be extremely useful in generating hypotheses about causes. At this stage, any indication of causal association is tentative.

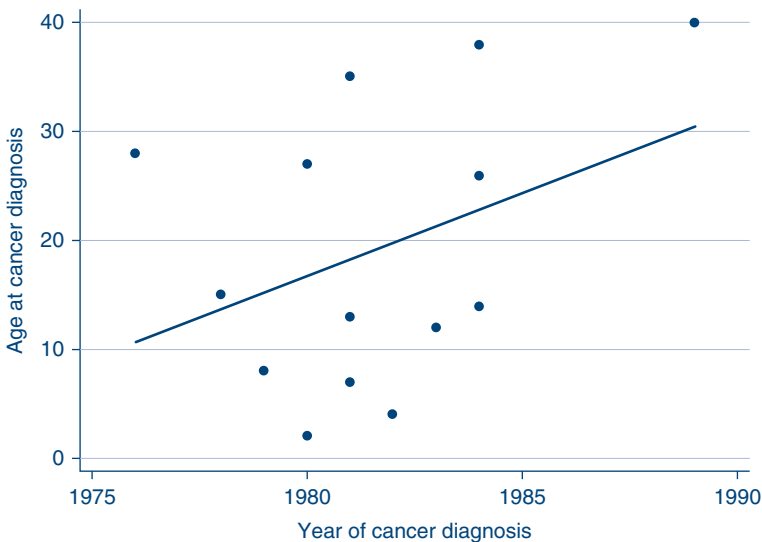


Fig. 17.1 Scatter plot with a regression line, illustrating the relationship between age and year of diagnosis. 14 cases.

Data from Mulder, Y.M., Buoy, M., and Kreis, I.A. (1994). A case-control study on the association between a cluster of childhood haematopoietic malignancies and local environmental factors in Aalsmeer, The Netherlands. *J Epidemiol Community Health* 48:161–5.

It is necessary to establish whether the number of cases is more than would be expected in the area during this time period. This can be done by comparing the data with a reference population, e.g. national rates.

17.2.2 Incidence and standardization

To compare the number of cases to a reference population raw counts are usually converted into rates. One such rate is the incidence density; the number of new cases (numerator) is divided by the total time from all persons who are at risk during the specific period of time (denominator). Incidence density is expressed as:

$$\frac{[\text{New cases over specified time}]}{[\text{Total person time at risk}]}$$

Times when persons were not at risk, (e.g. moved out of the area) need to be excluded from the denominator.

The total population of Aalsmeer in 1990 was estimated as 22,167. Fourteen cases occurred over a period of 12 years. For illustration, let's assume that everybody was at risk; no one moved out or in, was born or died. Then the incidence density would be $14/(22,167 \cdot 12) =$ about 5.3 per 100,000 person years (py). In real life you would need to use information on movements (in and out of the risk cohort) to calculate the total time at risk.

A standardized rate is used to establish whether this observation is above what would be expected for this area and time compared to national or other reference rates. Rates are usually standardized for age and sex.

There are two approaches to standardizing. You could adjust the rates, using the age and sex composition of a known reference population. This process is called direct standardization and it simply produces a weighted average of the rates in each stratum, e.g. age/sex groups. You could then compare this to similarly adjusted rates of other populations.

The directly standardized rate (DSR) is calculated as follows:

$$DSR = \sum_{stratum} \frac{Rate_{stratum} \cdot N_{stratum}}{\sum N_{stratum}}$$

where $Rate_{stratum}$ denotes the stratum-specific rates in the research population and $N_{stratum}$ denotes the number of persons in each stratum of the reference population. This can be laid out as a table; in Table 17.1 the population is stratified by age only. More commonly, both age and sex would be used. The DSR is the sum of expected cases divided by the total reference population.

The first step is to calculate age-specific incidence rates for each age group (e.g. 4/2782 for the under 10-year-olds). You can then apply these stratum specific rates to the proportion of the Netherlands population to calculate the stratum-specific contribution to the DSR. The sum of these stratum-specific contributions gives an age-standardized rate of 5.26 per 100,000 person years, very similar to the crude rate, as the age distribution in Aalsmeer is very similar to that in the Netherlands population.

Table 17.1 Calculation of directly standardized rates by calculation of stratum-specific rates and calculating expected cases for each stratum

	Netherlands population	Proportion	Aalsmeer population	Cases	Incidence rate (100,000 py)	Weighted contribution
<10 years	1944693	0.1255	2782	4	11.98	1.504
10–19 years	1826916	0.1179	2614	4	12.75	1.503
20–40 years	4938040	0.3187	7065	6	7.08	2.255
Over 40 years	6784240	0.4379	9706	0	0.00	0.00
Sum	15493889	1.0000	22167	14		5.26

Data from Mulder, Y.M., Buoy, M., and Kreis, I.A. (1994). A case-control study on the association between a cluster of childhood haematopoietic malignancies and local environmental factors in Aalsmeer, The Netherlands. *J Epidemiol Community Health* 48:161–5.

The other way to standardize is called indirect standardization. This directly compares observed numbers of cases with those we would expect to see by applying rates from a reference population. The result is a ratio, often called a standardized mortality ratio (SMR) which cannot be directly compared, unlike the DSR.

The 2007 combined rates for all lymphomas and leukaemias in the Netherlands was 25.8 per 100,000 persons. First you must calculate the number of expected cases. You can do that by applying the stratified national cancer rates to your stratified population.

$$\text{Expected number of cases in each stratum} = \frac{\text{Rate}_{pop} \cdot N_{sample}}{(\text{per } X \text{ py})}$$

Where Rate_{pop} denotes the stratum-specific rates from the standard population and N_{sample} the stratum sizes from the study population (Table 17.2).

Table 17.2 Calculation of expected cases by applying the known stratum-specific rates of a reference population to the stratum-specific denominator of the sample population

Age group	Rate per 100,000 py	Denominator	Expected numbers
<10	6.50	33384	2.170
10–19	6.65	31368	2.086
20–39	10.60	84780	8.987
Overall	25.8		

Data from Mulder, Y.M., Buoy, M., and Kreis, I.A. (1994). A case-control study on the association between a cluster of childhood haematopoietic malignancies and local environmental factors in Aalsmeer, The Netherlands. *J Epidemiol Community Health* 48:161–5.

If we sum the expected numbers you would expect 13.2 cases in the 12 years observed. The indirect standardized ratio is simply the numbers of observed cases divided by the number of expected cases,

$$(\text{Indirectly standardized ratio SMR}) = \frac{\sum_{\text{stratum}} \text{Observed}_{\text{stratum}}}{\sum_{\text{stratum}} \frac{\text{Rate}_{\text{pop}} \cdot N_{\text{sample}}}{(\text{per } X \text{ py})}}$$

e.g. $14/13.2 = 1.06$ or 106%. The number of observed cases is about 6% higher than the background rate in Netherlands. This ratio is unlikely to show a statistically significant effect, but could prompt further investigations.

17.2.3 Developing a hypothesis

More cases than expected suggests a possible public health issue requiring further investigation to find a cause, take action to mitigate it, and prevent further cases. The null hypothesis is (by convention) the default position that there is no association between exposure and outcome. For example, *there is no association between pesticide exposures in the area and developing a haematopoietic cancer during the period at risk*. The alternative hypothesis is that there is an association between the pesticide exposure in the area and haematopoietic cancers.

An analytical study needs to be designed to assess whether there is an association, i.e. sufficient evidence to reject the null hypothesis. The outcome could be considered to be a binary variable (i.e. leukaemia yes or no). Exposure variables can be either categorical (e.g. swimming in the pool) or continuous (e.g. age). The design of epidemiological studies is discussed in chapter 14. Here the focus is on the techniques to analyse case-control studies.

17.2.4 Sample size and statistical power

First you need to decide how many cases and controls you require for your study. Sample size calculations are essential, to determine the minimum size of study needed to identify what is considered to be the smallest clinically important effects, therefore minimizing costs and resources. The number of subjects needed for the study depends on:

- 1 The smallest acceptable effect size.
- 2 The expected variability of the sample.
- 3 The ratio of cases to controls. (As a simple guide, a study with four times as many controls as cases is useful, especially when there are few cases.)
- 4 The significance level or false positive error rate you are prepared to accept.
- 5 The statistical power. (This is commonly set as 80%.)

Power and significance level are usually chosen by convention. The effect size which the analysis is designed to detect should be determined clinically or using a literature search. The expected variability could be assessed in pilot studies, or through a literature search.

Once the parameters above are known, sample size calculations can be performed quite simply, using standard statistical software packages such as EpiInfo, STATA, or SPSS (see further reading, section 17.5).

If the sample size is limited by the natural occurrence of a disease, you can calculate the expected statistical power for the sample size you have, thus allowing your results to be interpreted within the context of a limited sample size.

17.2.5 Proportions and confidence intervals

Commonly, both the outcome variable (case or control) and various exposure measures are binary (Table 17.3). To analyse such data, we need to assess whether cases and controls show different patterns for these exposure measures. We can do this using confidence intervals for individual proportions, or for differences between proportions. In the latter case, odds ratios and their associated confidence intervals are the preferred analysis tools.

A formula to calculate a confidence interval for a proportion is:

$$\hat{p} \pm z_{\left(1-\frac{\alpha}{2}\right)} \cdot \sqrt{\frac{\hat{p}(1-\hat{p})}{n}}$$

where \hat{p} is the estimated proportion from the sample, $z_{\left(1-\frac{\alpha}{2}\right)}$ is the deviate of the standard normal distribution for the significance level α , and n is the sample size. So the 95% confidence interval for the proportion of cases living near a greenhouse (row 1, Table 17.4) is:

$$0.71 \pm 1.96 \sqrt{\frac{0.71(1-0.71)}{14}}$$

Therefore the estimated proportion of cases living near a greenhouse is 0.71, and the 95% confidence interval is 0.47 to 0.95. In other words from the sample taken you estimate that 71% of the cases would live near a greenhouse (point estimate), but you are not so certain about this and you calculate that the true proportion could lie somewhere in

Table 17.3 Numbers and proportions of cases and controls by exposure

	Case		Control	
	Exposed	Not exposed	Exposed	Not exposed
Lives near greenhouse	10 (71%)	4 (29%)	25 (45%)	31 (55%)
Playing in greenhouse	4 (29%)	10 (71%)	9 (16%)	47 (84%)
Holiday job in greenhouse	4 (29%)	10 (71%)	14 (25%)	42 (75%)
Exposure to pesticides (yes/no)	2 (14%)	12 (86%)	8 (14%)	48 (86%)
Exposure to pesticides (>3 hours/week)	2 (14%)	12 (86%)	3 (5%)	53 (95%)

Data from Mulder, Y.M., Buoy, M., and Kreis, I.A. (1994). A case-control study on the association between a cluster of childhood haematopoietic malignancies and local environmental factors in Aalsmeer, The Netherlands. *J Epidemiol Community Health* 137:663–7.

Table 17.4 Percent and 95% confidence intervals for various exposures in cases and controls

	Percent of cases exposed		Percent of controls exposed	
	Point estimate	95% CI	Point estimate	95% CI
Lives near greenhouse	71	47–95	45	31–59
Playing in greenhouse	29	5–52	16	8–28
Holiday job in greenhouse	29	5–52	25	14–38
Exposure to pesticides (y/n)	14	0–33	14	6–26
Exposure to pesticides (>3h/wk)	14	0–33	5	1–15

Data from Mulder, Y.M., Buoy, M., and Kreis, I.A. (1994). A case-control study on the association between a cluster of childhood haematopoietic malignancies and local environmental factors in Aalsmeer, The Netherlands. *J Epidemiol Community Health* 48:161–5.

the range 0.47 to 0.95. Non-overlapping confidence intervals for the proportions among cases compared to those of the controls usually indicate that differences in the proportions are significant. The size of the confidence interval depends on the sample size and (much less so) on the proportion size. Small sample sizes have wide confidence intervals. You could modify the table as outlined in Table 17.4.

17.2.6 Odds ratios

Remember this is a case–control study. Since you selected controls from a population, you cannot know the exact size of your population at risk. It is therefore not possible to calculate attack rates (the proportion of cases amongst the exposed), nor is it possible to calculate risk ratios (the ratio of the attack rates in exposed to unexposed). So you have to *estimate risk* in the study using odds and odds ratios (ORs). It should be noted that the odds ratio is a reliable proxy for a risk ratio if the disease is relatively rare (this is the case here) and the case–control study is population based as in this example. If the disease is more common, the OR overstates the risk and should only be interpreted as a risk with much caution. However, the OR is a perfectly acceptable measure of association. The easiest way to calculate ORs is to draw up a 2×2 table. For the first exposure in Table 17.4, your 2×2 table would look like Table 17.5.

Table 17.5 A 2×2 table of the odds of becoming a case if leaving near a greenhouse

	Near greenhouse	Not near greenhouse	Sum
Case	10 (a)	4 (b)	14 (a + b)
Control	25 (c)	31 (d)	56 (c + d)
Sum	35 (a + c)	35 (b + d)	70 (a + b + c + d)

Data from Mulder, Y.M., Buoy, M., and Kreis, I.A. (1994). A case-control study on the association between a cluster of childhood haematopoietic malignancies and local environmental factors in Aalsmeer, The Netherlands. *J Epidemiol Community Health* 48:161–5.

‘Odds’ is the term used for the ratio of the probability of an event (being exposed) to the probability of not having that event (not being exposed). The OR is the ratio of odds for two groups, here cases and controls, and can be designated as:

$$\frac{\text{Odds of becoming a case if exposed}}{\text{Odds of becoming a case if not exposed}}$$

that is $(a/c)/(b/d)$ or $(a*d)/b*c$. In Table 17.5 the odds of living near a greenhouse (exposure) in the cases are: $(10/14)/(4/14) = 10/4 = 2.5$ while for the controls the odds are: $(25/56)/(31/56) = 25/31 = 0.81$. So the estimated odds ratio of becoming a case if you live near a greenhouse is $(10/4)/(25/31)$ or $2.5/0.81 = 3.1$. So the odds of becoming a case when living near a greenhouse is more than 3 times larger than if not living near a greenhouse.

This estimate is subject to sampling variation, so you should also calculate 95% confidence intervals (CIs) for these odds ratios. All standard statistics packages provide this automatically, but a step by step approach for calculating this is given here.

$$\exp\left(\ln(OR) \pm z_{\left(1-\frac{\alpha}{2}\right)} \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}\right)$$

where exp is the exponential function, ln is the natural logarithm, $z_{\left(1-\frac{\alpha}{2}\right)}$ is the deviate of the standard normal distribution (as earlier), and a, b, c, and d are the four individual cell counts of the 2x2 table (Table 17.5). In this example the 95% confidence interval will be given as:

$$\exp\left(\ln(3.1) \pm 1.96 \sqrt{\frac{1}{10} + \frac{1}{4} + \frac{1}{25} + \frac{1}{31}}\right)$$

So the estimated OR with its 95% confidence interval is 3.1 (0.87; 11.08). The CI includes 1 (the value that represents the null hypothesis) and is very wide.

None of these ORs has a corresponding CI that excludes the value 1. Thus, the analysis of ORs shows no significant evidence of difference between cases and controls (Table 17.6).

Table 17.6 Crude odds ratios (ORs; unadjusted for confounding) and 95% confidence intervals (CIs) for various exposures in cases and controls

	Estimated (crude) OR	95% CI
Lives near greenhouse	3.10	0.87–11.08
Playing in greenhouse	2.09	0.54–8.15
Holiday job in greenhouse	1.20	0.32–4.44
Exposure to pesticides (yes/no)	1.00	0.19–5.33
Exposure to pesticides (>3 hours/week)	2.94	0.44–19.60

Data from Mulder, Y.M., Buoy, M., and Kreis, I.A. (1994). A case-control study on the association between a cluster of childhood haematopoietic malignancies and local environmental factors in Aalsmeer, The Netherlands. *J Epidemiol Community Health* 48:161–5.

17.2.7 Adjusting for confounding

Up to now each variable was evaluated on its own merits. This completely ignored the fact that these variables may not be independent of each other. A confounder is a ‘third factor’, associated with exposure and outcome and not on the pathway between exposure and outcome and as such ‘confounds’ the observed effect in a single variable analysis. Children who live near a greenhouse may be more likely to play in a greenhouse than children who do not live nearby. For those who play in a greenhouse, you may be exaggerating the impact of the exposure of living near a greenhouse because living near a greenhouse is confounded by playing in a greenhouse. In the earlier analysis (‘single variable analysis’) crude ORs and crude p-values were calculated, assuming there are no confounding effects.

There are three main ways of dealing with confounding. Options not discussed here include matching for the confounders at the design stage (be careful not to over-match), or restricting analysis to particular strata (difficult in environmental epidemiology as numbers of cases are usually limited). The method used here to adjust for confounding is *stratification and regression analysis*. A stratified analysis (e.g. two strata—living near to a greenhouse and living far from a greenhouse) would give estimates of effect for each stratum separately and also provide an adjusted OR which combines the two strata but gives different weights according to the size of the stratum.

17.2.8 Logistic regression analysis

The other way of estimating risk and adjusting for confounding is by using regression modelling and for binary outcome data logistic regression is recommended for multi-variable analysis. The logistic regression model calculates the probability of a particular outcome given a set of predictor variables using an extension of the ideas of multiple linear regression:

$$\text{logit}(\hat{p}) = \ln\left(\frac{\hat{p}}{1-\hat{p}}\right) = a + b_1x_1 + b_2x_2 + b_3x_3 \dots + b_kx_k$$

Using the example of swimming in the eastern pool and living in the eastern neighbourhood, the model estimates the constant (a) and the logistic regression coefficients (b_1 and b_2) (Table 17.7).

Table 17.7 Results of a logistic regression analysis to model the association between swimming east and residence and becoming a case

	Coefficient	95% CI	p-value
Constant	-2.096	-3.051 to -1.141	<0.0001
Swimming east >2h/week	1.649	0.308–2.990	0.016
Eastern neighbourhood	0.467	-0.834 to 1.768	0.48

Data from Mulder, Y.M., Buoy, M., Kreis, I.A. (1993). Patient-control study: the relationship between local environmental and hematopoietic malignancies in young people in Aalsmeer. *Ned Tijdschr Geneesk* 137:663–7.

Table 17.8 Results of a logistic regression analysis to model the association between swimming east and residence and becoming a case—coefficients have been transformed to odds ratios

	OR	95% CI	p-value
Swimming east >2 hours/week	5.2	1.4 – 19.9	0.016
Eastern neighbourhood	1.6	0.4 – 5.9	0.48

Data from Mulder, Y.M., Buoy, M., and Kreis, I.A. (1994). A case-control study on the association between a cluster of childhood haematopoietic malignancies and local environmental factors in Aalsmeer, The Netherlands. *J Epidemiol Community Health* 48:161–5.

Using this information, for a person who lives in the eastern region and swims east the $\text{logit}(\hat{p})$ could be estimated as:

$$\text{logit}(\hat{p}) = -2.096 + 1.649 * 1 + 0.467 * 1 = 0.02$$

Note that the logit is just the natural logarithm of the odds (section 17.2.6). We are not particularly interested in the logit but using the fact that the $\ln(A) - \ln(B) = \ln(A/B)$ allows direct estimation of an odds ratio, adjusting for all the other variables in the model. If the disease is relatively rare, the ORs would provide a reasonable estimate of the risk ratio for that exposure. As the coefficients are the expected increase in the logit for a unit increase in the exposure (exposed compared to not exposed in the case of a binary exposure), their antilog is the estimated OR (e.g. $e^{1.649} = 5.2$) For the earlier example the estimated ORs using a logistic regression model are illustrated in Table 17.8.

The model estimates the OR of becoming a case, adjusting for region of residence of swimming in the eastern swimming area in the lake, is 5.2. The corresponding p-value is 0.016, as measured by the Wald test, one of several statistical approximate methods used in this context. Therefore there is evidence to reject the null hypothesis and it is likely that there is an association between swimming in the eastern swimming area and becoming a case, even after adjusting for the (not separately statistically significant) neighbourhood in this model. You could also adjust for multiple other potential confounding variables.

Although you can adjust for multiple variables, the final model should only contain variables which significantly add to the explanatory power of the model or are confounder, because otherwise the model can become complex to understand. Therefore it is advisable to think carefully about the hypothesis being examined, the potential confounders, and effect modifiers when including predictor variables in a logistic regression model.

17.3 Analysing incidence rates and rate ratios

In the previous analysis the data were treated as binary—some people had an event (cases) and others did not (controls); this ignores the fact that the exposure times may have differed between people. The ideal design to examine the *incidence per person time*

Table 17.9 Number of haematopoietic cancer events, person years, incidence and confidence intervals per 100,000 person years at risk

	Events	Person years	Incidence	95% CI
Swimming east >2 hours/week	7	38875	18.01	7.24–37.1
Not swimming east	7	249669	2.8	1.13–5.78
Eastern neighbourhood	8	103613	7.72	3.33–15.21
Western neighbourhood	6	184931	3.24	1.19–7.06
Total	14	288544	4.85	2.65–8.14

Data from Mulder, Y.M., Buoy, M., and Kreis, I.A. (1994). A case-control study on the association between a cluster of childhood haematopoietic malignancies and local environmental factors in Aalsmeer, The Netherlands. *J Epidemiol Community Health* 48:161–5.

at risk is a cohort study. For demonstration purposes the case–control data from the study has been transformed to include the person years at risk (i.e. generating a 13-year hypothetical cohort data from 22,167 persons to reflect a full hypothetical ‘population’ of Aalsmeer).

A crude incidence rate can be calculated by dividing the number of events ($n = 14$) by the total person time at risk in the cohort (288,544 years, 22,167 persons with their total follow-up time). Here the crude incidence rate is 4.9 per 100,000 person years. The person years are less than $22,167 \times 14$, because some individuals had to be censored when they moved in or out of the area for various reasons (e.g. birth, death, and migration).

In this analysis you are interested in *rates*. With these cohort data you can now calculate incidence rates per 100,000 person years and 95% CIs for different strata as illustrated in Table 17.9. The Aalsmeer population is divided into two clear neighbourhoods: east (where the glasshouses are) and west (the main village). Each has a swimming area in a lake, only the eastern one is thought to be contaminated.

The incidence rate for people engaging in swimming east is much higher compared with those not swimming east (18.01 vs. 2.8 per 100,000 person years). This was expected from the results of the case control study, but with cohort study data it can be quantified directly.

17.3.1 Comparing incidence rates

These two rates are compared using a rate difference (18.01 – 2.8 per 100,000). The rate difference is 15.2 per 100,000 (CI 1.7–28.7) and the CI does not include zero; it is likely that the rate difference is significantly different from zero; hence we reject the null hypothesis.

More commonly, rates are compared using an incidence rate ratio. Here it is $18.01/2.8 = 6.42$ (CI 1.92–21.46), which is significantly different from 1, the neutral point of this risk ratio. So people who engaged in swimming east were about 6½ times more likely to develop a cancer of the haematopoietic system compared to those that did not. The null hypothesis that there is no difference between the rates in the two strata, or equivalently that the incidence rate ratio is 1 is amenable to statistical testing. A test of this hypothesis

gives a p-value of 0.001, indicating evidence to reject the null hypothesis in favour of the alternative hypothesis, that the rates in the two strata are different.

This analysis could also adjust for possible confounders. As already discussed, living in an eastern neighbourhood may be associated with swimming to the eastern swimming area, but it may also be associated with haematopoietic cancers (the incidence rate ratio is about double). These confounders are adjusted for using a Poisson regression analysis. The formula is very similar to the logistic regression formula and is derived from calculating a slope in the same way:

$$\ln(c) = \ln(py) + a + b_1x_1 + b_2x_2 + b_3x_3 \dots + b_kx_k$$

with re-arranging

$$\ln(c) - \ln(py) = \ln\left(\frac{c}{py}\right) = \ln(r) = +a + b_1x_1 + b_2x_2 + b_3x_3 \dots + b_kx_k$$

Where c is the count, py is the person years, r is the incidence rate, a is the constant (i.e. natural logarithm of the background rate), b_1, b_2 , etc. are the regression coefficients, and x_1, x_2 , etc are the observed values of explanatory variables. Looking at the variables ‘swimming to the east’ and neighbourhood of residency, the Poisson regression analysis would give the following result as shown in Table 17.10.

The coefficients can be used to calculate individual risks, or a mean risk for all variables using the formula. For example an individual who lives in an eastern neighbourhood and regularly swims to the east the risk would be: $\ln(r) = -10.759 + 0.663 * 1 + 1.764 * 1 = -8.332$. The rate is therefore is the antilog (e^x) of -8.332 , i.e. 24.1 per 100,000 person years. As with the previous logistic regression, the coefficients can be transformed (anti logged) to give a direct estimated of the incidence rate ratios for each predictor variable (Table 17.11).

Thus, after adjusting for the neighbourhood, the risk of becoming a case when swimming to the east is still nearly six times higher (highly significant). Conversely, living in the eastern neighbourhood is not significantly associated with becoming a case after adjusting for the swimming activities. The results are similar to those derived from the logistic regression analysis, but here we are calculating rates and rate ratios and hence taking person-time at risk into consideration.

Table 17.10 Results of a Poisson regression analysis to model the effect of swimming east and residence and becoming a case

	Coefficient	95% CI	p-value
Swimming east >2 hours/week	1.764	0.705–2.823	0.001
Eastern neighbourhood	0.663	–0.407 to 1.732	0.225
Constant	–10.759	–11.673 to –9.846	0

Data from Mulder, Y.M., Buoy, M., and Kreis, I.A. (1994). A case-control study on the association between a cluster of childhood haematopoietic malignancies and local environmental factors in Aalsmeer, The Netherlands. *J Epidemiol Community Health* 48:161–5.

Table 17.11 Results of a Poisson regression analysis to model the effect of swimming east and residence and becoming a case. Coefficients have been transformed to incidence risk ratios

	IRR	95% CI	p-value
Swimming east >2 hours/week	5.8	2.0–16.8	0.001
Eastern neighbourhood	1.9	0.7–5.7	0.23

Data from Mulder, Y.M., Buoy, M., and Kreis, I.A. (1994). A case-control study on the association between a cluster of childhood haematopoietic malignancies and local environmental factors in Aalsmeer, The Netherlands. *J Epidemiol Community Health* 48:161–5.

17.4 Case study—dealing with continuous data: polychlorinated biphenyl

Polychlorinated biphenyls (PCBs) are lipid-soluble organic compounds, which can accumulate in fatty tissue. Because many have a similar toxicity to dioxins, they are banned in many countries. They can remain in the environment for a long time so there has been concern about their persistence in human tissue, their potential excretion in human breast milk, and possible toxicity to breastfed babies. It is important to know whether there are particular risk factors for high concentrations in breast milk. Higher maternal age (given longevity of the contaminant) might be a risk factor and previous breastfeeding may lead to lower excretion. If this was confirmed advice to bottle feed could be given to mothers at particular high risk (Aalbers et al., 1996).

This could be addressed by a cross-sectional study (see Chapter 14 on study design for details) using a systematic sample (first 12 women planning to breastfeed) in widespread locations around a country (30 birth centres in the Netherlands). PCB levels in breast milk samples would be analysed with exposure information from questionnaires, completed by the women.

17.4.1 Measures of centre and spread

PCB levels were measured as a concentration (mg/kg human fat). This yields continuous data, i.e. observations can take any value, except negative values. Continuous data are usually described using two measures: one which estimates the ‘middle’ of the series of observations and another which estimates the spread.

Frequently, series of observations on a continuous variable have a (near) normal distribution (‘Gaussian distribution’). This is important, because the mathematical properties of the Normal distribution are well described and 68.3% of observations lie within one standard deviation either side of the mean. This information can be used for statistical calculations based on probability theory. The easiest way to explore the distribution of the data is to plot it, for example with a histogram.

Two parameters, the mean and standard deviation, are sufficient to completely describe the Normal distribution in a population. You could calculate a mean from a population

or—as done in this example—from a sample and you will use analogous sample statistics. The sample mean is the average value and can be denoted as follows:

$$\bar{x} = \frac{\sum_{i=1}^n x_i}{n}$$

For example:

$$\bar{x} = \frac{(2 + 3.5 + 5.6 + 8.9 + 17)}{5} = 7.4$$

The standard deviation is used to provide a measure of the spread of the distribution. The standard deviation is the square root of the variance (the average of the distance of individual measurements from the mean) and is defined as follows:

$$s = \sqrt{\frac{\sum_{i=1}^n (x_i - \bar{x})^2}{n - 1}}$$

For the same data for which the mean was calculated:

$$s = \sqrt{\frac{(2 - 7.4)^2 + (3.5 - 7.4)^2 + (5.6 - 7.4)^2 + (8.9 - 7.4)^2 + (17 - 7.4)^2}{4}} = 5.96$$

When data clearly do not follow a Normal distribution, alternative measures of centre and spread are sometimes used. The median is the modal value of the ordered observations, and is 5.6 (the third observed) in our sample.

You could also define spread by quoting the minimum and maximum values (2 and 17) and their difference, (range) = 15, or the value on the 25th or 75th percentile. In this example the 25th percentile would be $(2 + 3.5)/2 = 2.75$ and the 75th percentile $(8.9 + 17)/2 = 12.95$. Their difference, the inter-quartile range, is a useful alternative measure of spread (IQR = 75th percentile – 25th percentile = 10.2).

The data from this study allow the examination of the distribution of one particular PCB, a recognized carcinogen (2,2',3,4,4',5,5'-heptachlorobiphenyl (PCB-180) CAS Number: 35065-29-3, abbreviated PCB-180 here). In all, 95 observations were available, ranging from 16 mg/kg to 232 mg/kg. Plotting the data gives the following histogram, on which a Normal distribution with the same mean and standard deviation is superimposed (see Fig. 17.2).

Data analysis is most straightforward if data are approximately normally distributed but these data are considerably right-skewed (positive skew) and do not reflect a Normal distribution. Analysis options for these data include non-parametric procedures, e.g. those related to the median. However, right-skewed distributions can often be transformed to a Normal distribution, for example, by taking the natural logarithm which

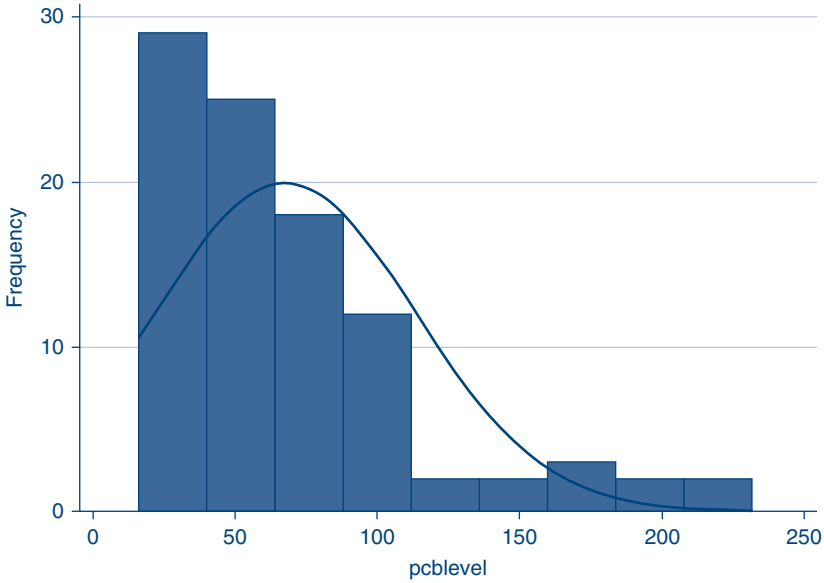


Fig. 17.2 Histogram of PCB levels in breast milk; Normal distribution overlaid.

Data from Albers, J.M., Kreis, I.A., Liem, A.K., and van Zoonen, P. (1996). Factors that influence the level of contamination of human milk with poly-chlorinated organic compounds. *Arch Environ Contam Toxicol* 30:285–91.

then allows parametric tests based on the normal distribution model to be used. If you take the natural logarithm of the PCB-180 data, you can plot the histogram in Fig. 17.3.

This transformation has produced an approximately a Normal distribution; and hence parametric analyses can be used. It is perfectly valid to calculate a mean as above and then transform (exponentiate) the data back. This is called the geometrical mean, (here 55.6 mg/kg). The geometrical mean is much closer to the median (56.9 mg/kg) than the mean (67.8 mg/kg). For normal distribution models, which are symmetric, the mean and median take the same value.

17.4.2 Analysing relationships between continuous variables

In order to explore a possible relationship between maternal age and PCB-180 levels, which may accumulate over time, we could transform age into a categorical variable with just two groups (15–29 and 30–45).

A *two-sample t-test* is appropriate when assessing the equality of the means of two independent groups. Here your null-hypothesis would be that there is no significant difference between PCB-180 levels in women aged 15–29 and those aged 30–45. To calculate a *t*-statistic you would use the following formula:

$$t = \frac{\bar{x}_1 - \bar{x}_2}{s_{pooled} \sqrt{\frac{1}{n_1} + \frac{1}{n_2}}}, s_{pooled} = \sqrt{\frac{(n_1 - 1)s_1^2 + (n_2 - 1)s_2^2}{n_1 + n_2 - 2}}$$

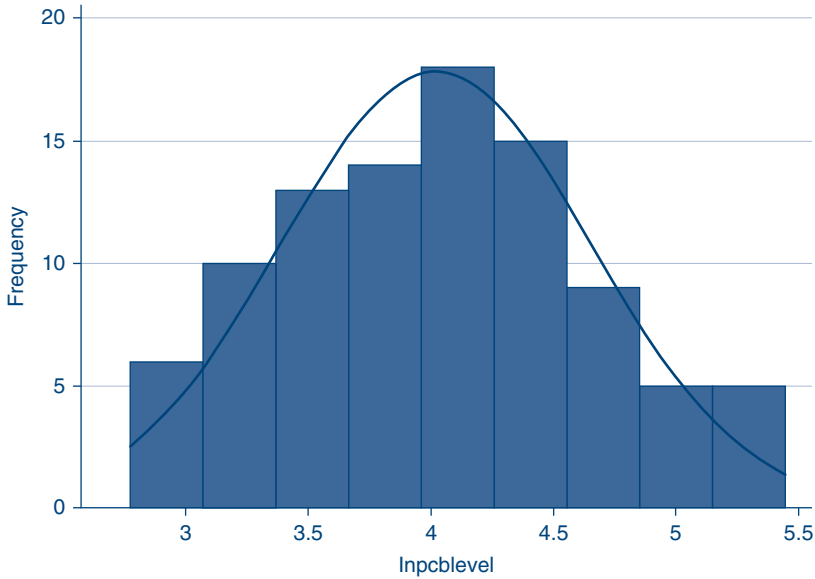


Fig. 17.3 Histogram of the natural logarithm of PCB levels in breastmilk; normal distribution curve overlaid.

Data from Albers, J.M., Kreis, I.A., Liem, A.K., and van Zoonen, P. (1996). Factors that influence the level of contamination of human milk with poly-chlorinated organic compounds. *Arch Environ Contam Toxicol* 30:285–91.

For the two maternal groups the t -statistic is as follows:

$$t = \frac{(3.65 - 4.43)}{0.495 \sqrt{\frac{1}{50} + \frac{1}{45}}} = -7.65$$

Looking at t -distribution tables with 93 ($n_1 + n_2 - 2$) degrees of freedom gives $p < 0.0001$. There is therefore strong evidence to reject the null hypothesis in favour of the alternative hypothesis: that there is a significant difference between the mean PCB-180 concentrations in two age groups.

17.4.3 Correlation and regression

Although these are interesting results, you have (somehow arbitrarily) categorized maternal age into only two groups. In doing so, a lot of information about the variable is lost. Therefore it is normally preferable to analyse maternal age as a continuous variable. The first step is descriptive analysis using a scatter plot of PCB-180 levels in breast milk against maternal age (Fig. 17.4a). Although there is quite a bit of scatter, there is a relationship with PCB-180 levels in breast milk increasing with increasing maternal age (a linear trend line is given). If you plot the natural logarithm of the PCB-180 values, the relationship now appears to be reasonably linear and the scatter approximately constant (Fig. 17.4b).

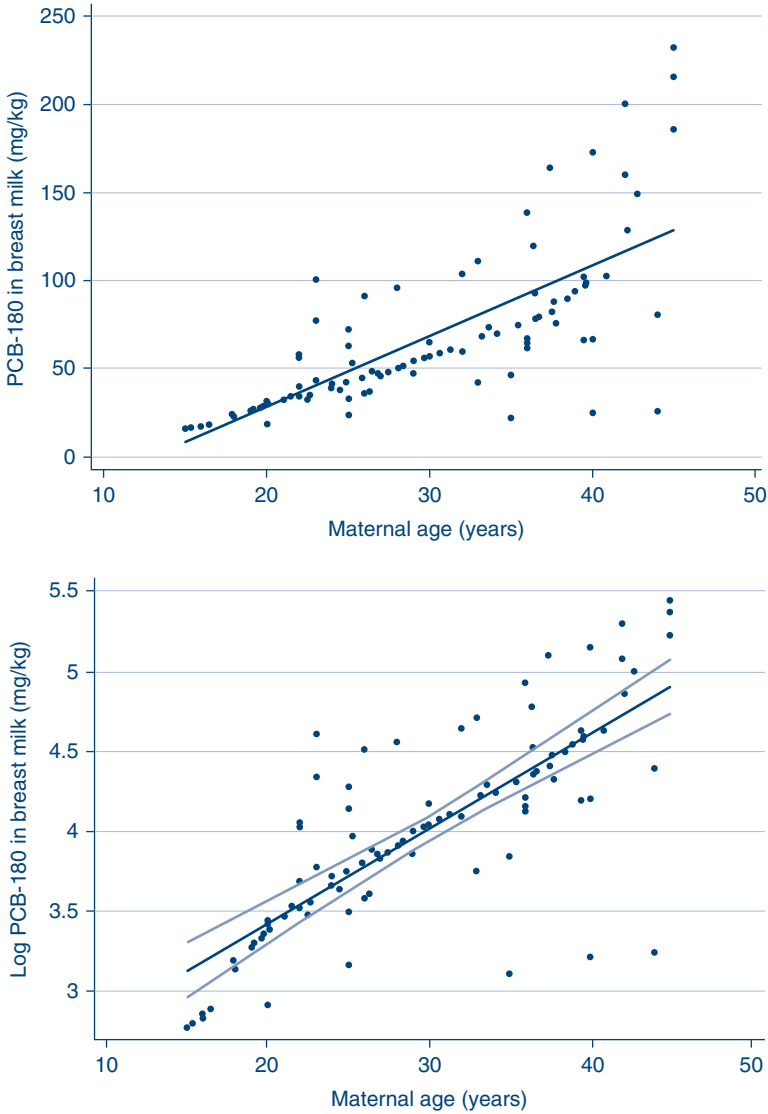


Fig. 17.4 (a) Scatter plot and best fit line of maternal age and PCB-180 concentration in breastmilk. (b) The same graph using the natural logarithm of maternal breastmilk PCB-180 concentrations (to normalize the distribution as described in the text).

Data from Alber, J.M., Kreis, I.A., Liem, A.K., and van Zoonen, P. (1996). Factors that influence the level of contamination of human milk with poly-chlorinated organic compounds, *Arch Environ Contam Toxicol* 30:285–91.

To calculate formal statistics for these data, you need to use the sample techniques of correlation and regression. The Pearson correlation coefficient (r) is a measure of how close the actual observations are to a straight line:

$$r = \frac{\sum(x - \bar{x})(y - \bar{y})}{\sqrt{\sum(x - \bar{x})^2 \sum(y - \bar{y})^2}} = 0.74 \text{ for the transformed data, graph 17.4b}$$

Here the Pearson correlation coefficient is 0.74. If you square this value ($r^2 = 0.55$), you get a measure of the proportion of the variance in log PCB-180 measurements, which is explained by this linear relationship.

The formula for linear regression is derived from calculating the properties of a straight line—effectively predicting a straight line equation. So to estimate the regression of y on x the formula would be:

$$y_i = a + bx_i + \varepsilon_i$$

where a is the intercept and b is the slope (change in the average outcome variable for a unit increasing in the exposure), and ε_i is the residual or error (that amount of the outcome observation y_i differs from the average outcome measurement $a + bx_i$ for an exposure of x_i). For the linear regression estimation to be valid, the following assumptions need to be fulfilled: the relationship between y and x must be linear (see earlier), observations need to be independent, the residuals should have a Normal distribution and there should be the same variability in the residuals for all values of y .

The fitted linear regression model of the relationship of maternal age (exposure) on $\ln(\text{PCB-180})$ levels is shown in Table 17.12. This model shows that starting at a theoretical PCB-180 level of 11.08 mg/kg when maternal age is 0 (intercept $11.08 = \exp^{2.405}$) the $\ln(\text{PCB-180})$ levels increase by 0.054 for each maternal year. On the natural scale of measurement for PCB-180 this is equivalent to a 5.5% increase in PCB-180 ($5.5 = (\exp^{0.054} - 1) * 100$) for each year of maternal age. The p -value demonstrates the slope of the relationship is significantly different from zero. The fitted line shows that $\ln \text{PCB-180}$ increases by about 0.054 for each year of maternal age. Thus PCB-180 increases from around $e^{(2.405 + 15 * 0.054)} = 24.9$ mg/kg at age 15 to $e^{(2.405 + 45 * 0.054)} = 125.8$ mg/kg at age 45.

Table 17.12 The linear regression model to analyse associations between maternal age and $\ln(\text{PCB})$ levels in breast milk

	Coefficient	Standard error	t-statistic	p-value	95% CI
Maternal age	0.054	0.005	10.57	<0.0001	0.044–0.065
Constant	2.405	0.159			2.090–2.721

Data from Albers, J.M., Kreis, I.A., Liem, A.K., and van Zoonen, P. (1996). Factors that influence the level of contamination of human milk with poly-chlorinated organic compounds. *Arch Environ Contam Toxicol* 30:285–91.

Table 17.13 Linear regression model to analyse associations between maternal age and BMI with (ln) PCB levels in breast milk

	Coefficient	Standard error	t-statistic	p-value	95% CI
Maternal age	0.033	0.005	7.08	<0.0001	0.024–0.042
BMI	0.067	0.008	8.43	<0.0001	0.051–0.083
Constant	1.350	0.173			1.006–1.694

Data from Albers, J.M., Kreis, I.A., Liem, A.K., and van Zoonen, P. (1996). Factors that influence the level of contamination of human milk with poly-chlorinated organic compounds. *Arch Environ Contam Toxicol* 30:285–91.

Maternal age may not be the only exposure variable that predicts PCB-180 levels. PCBs are lipophilic (accumulating in fatty tissue) so there may be an association with body fat. A convenient way to estimate body fat is by the body mass index (BMI). You can formulate the null hypothesis (i.e. that there is no linear relationship between BMI and PCB-180). Table 17.13 includes BMI as well as maternal age in a multiple linear regression model.

This linear regression model shows a significant ($p < 0.0001$) linear relationship between BMI and $\ln(\text{PCB-180})$. PCB-180 concentrations increase by 7% (95% CI 5–9%) for each kg/m^2 increased body mass. You can also observe that the coefficient for maternal age has changed once BMI is adjusted for. This indicates that BMI confounds the association between maternal age and $\ln(\text{PCB-180})$. The predictive ability of this model is much improved compared to the regression model with just age as a predictor and it now explains about 74.4% of the variance in $\ln(\text{PCB-180})$ measurements. You can also use the regression model to obtain more accurate predictions of the average PCB-180 levels, depending on age and BMI levels. So for 29-year-old women with a BMI of 25 kg/m^2 the calculation is:

$$\ln(\text{PCB} - 180) = 1.35 + 0.033 * 29 + 0.067 * 25 = 3.982$$

You would therefore predict an average PCB-180 level of 53.62 mg/kg in these women.

17.5 Further reading

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Ethics in environmental epidemiology

Sue Odams

Learning objectives

- ◆ Understand the role of ethics in good environmental epidemiology practice.
- ◆ Appraise the legal and professional processes involved in research ethics.
- ◆ Identify and scrutinize what ethical aspects need to be considered in different types of studies.

18.1 Introduction—case study

The British Paediatric Surveillance Unit (BPSU), in conjunction with the Health Protection Agency (HPA), is conducting a 3-year study into elevated blood lead levels in children in the UK (hereafter known as the SLIC Project). Hospital paediatricians, laboratories, and clinical toxicologists, who find an elevated blood lead in a child under 16, complete a questionnaire which is returned to the project team. The project involves the UK National Health Service (NHS), HPA, and Health Service Executive in the Republic of Ireland (ROI). What ethical issues and considerations may be involved in the conduction of this project?

There are examples in the history of health research where ethical principles have either not been used, or perverse justification given for unethical actions (e.g. the non-consented medical experiments exposed by the Nuremberg Trials). Today there is plenty of official guidance from medical and international organizations to ensure that research follows ethical principles. For example the Helsinki Declaration (World Medical Association (WMA), 2008); ethical guidelines to aid practitioners in conducting research (e.g. International Society for Environmental Epidemiology (ISEE), 2011), and national and international regulations. The UK Human Tissue Act (UK Government, 2004) is an example. Unfortunately despite this, the recent MMR research scandal has shown that ethical principles may still not be followed (Flaherty, 2011).

This chapter discusses the ethical issues involved in the SLIC Project, using the ISEE Ethical Guidelines as a framework (ISEE, 2010, 2011). It is centred around the main ethical principles relevant to research: autonomy (independent thought), non-maleficence (avoidance of wrongdoing), justice (fairness), and beneficence (doing what

is right or good) (Merlo, 2007). There other ethical approaches which are not dealt with here.

It may seem daunting at the beginning of a research project to address all relevant ethical issues and processes; however, it is highly likely that the organization conducting the research has its own guidance and policies and that someone in the organization has done something similar and can help or at least point you in the right direction. If available, the Research and Development Department can be a useful source of advice. However you decide to address the ethical issues, all decisions must be fully documented.

In the case of the SLIC Project, the key ethical issues were the use of children as subjects, informed consent, confidentiality, privacy, data protection, and data sharing. These issues will be explored in this chapter.

18.2 Beneficence

By seeking to identify children exposed to lead and monitoring mitigation of that exposure, the SLIC Project is applying the principle of beneficence (HPA, 2011). In this section we explore the beneficent requirement to protect the privacy of study participants. Beneficence also includes proper ethical management of the data generated.

18.2.1 Confidentiality and privacy

SLIC had to apply to the National Research Ethics Service (NRES), under which all UK Health Departments operate (NRES, 2011), as well as the Irish Ethics system for ethical approval of the whole project. Other countries may have similar institutions for research which may be national or multinational in nature. Maintaining confidentiality of personal identifiable data (PII) is a key feature of any research study. In the UK, the National Information Governance Board for Health and Social Care (NIGB) may also need formally to approve your protocols on PII, data storage, and data sharing, as they did for the SLIC Project. The Board is an independent statutory body which provides official advice and approval for information governance in research projects (NIGB, 2011a).

It is important that your study subjects are treated with respect and dignity at all times (NRES, 2011). One aspect of this is the maintenance of privacy in terms of their personal information, their involvement in the study, and the results of any tests or questionnaires used. Justifiable reasons for breaking privacy in a study include, for example, where a treatable health condition about which they are unaware has been identified (ISEE, 2011). However, this requires an ethics committee review prior to privacy being broken (ISEE, 2011). In occupational studies (Chapter 20), for example, the benefits of the study were considered to outweigh the privacy of the workers, and their contact details could be released to the researchers so the study could go ahead.

PII is complex for researchers to deal with, so it is wise to gauge opinion and seek advice before writing policy. The SLIC Project found that, although they had NIGB and ethics approval, not all the specialist clinicians who were asked to report cases thought this was

sufficient, and declined to participate. For practical purposes this decision was left to individual clinicians, thus resulting in the potential for reduced case ascertainment.

For the SLIC Project PII stored data is kept to a minimum in line with Caldicott Guidelines (Caldicott Committee, 1997) and only aggregate data are reported. PII is not generally required for analysis and certainly not in the final reporting but care must be taken when a study has only a small number of participants to ensure that individuals cannot be identified in reports even if not explicitly named.

18.2.2 Data storage and data sharing

You will need to store hard and soft data securely, which can be difficult in some institutions (particularly government or academic) as physical space may be limited or expensive. Hard copies of PII (e.g. paper copies of questionnaires) should be kept in locked cabinets separate from the anonymized data. The PII database must be password-protected, with access only by authorized project staff and encrypted if via laptops. Regular backups must be done and back-up files kept on tape in a locked fireproof safe. Data must be anonymized and archived for 20 years as stipulated by the Medical Research Council.

Data sharing must be justified and used only for the purposes of the study for which ethics approval has been received. In the SLIC study, although ethically it may be allowable to break privacy if it is the person's or communities' best interest (see section 18.2.1) this was not within the study protocol. Therefore, individuals identified as having high levels of blood lead could not be reported by the study to the local Health Protection Unit (HPU), which in the UK would normally investigate environmental lead exposures. Instead the study researchers encouraged the reporting clinician to report the exposure separately to the HPU.

In the UK it is also important to work with the Caldicott Guardian within your organization to help clarify any data storage or sharing issues (Department of Health (DH), 2010). The study must also comply with the relevant national law governing data and PII.

18.3 Non-maleficence

Non-maleficence is achieved by research that minimise[s] risk, disruption, and harm to both study participants and their source population (ISEE, 2011). These risks should be fully assessed, quantified and mitigated or minimized if possible.

If a risk is discovered during research that might adversely affect their well-being, it should be communicated to the individuals/populations concerned (ISEE, 2011). This may be challenging, for example, if the risk is an HIV positive status, then communicating this may be difficult if there is a stigma attached to the diagnosis. In the SLIC Project the protocol said that if the study, through the sampling methods used, discovered of a large source of lead causing harm to children this would initiate mitigation action through the relevant HPU and Environmental Health Team (E.A. Thomas, personal communication). The method of communicating the research findings to the study population should be established early in the study process, especially if there is the possibility of adverse findings. (See also Chapter 4 and 14.)

Another example of non-maleficence is the Precautionary Principle. This essentially means that: ‘When human activities may lead to . . . harm that is scientifically plausible but uncertain, actions shall be taken to avoid or diminish that harm’ (United Nations Educational, Scientific and Cultural Organization, 2005). The Precautionary Principle is enshrined in International Law (Commission of the European Communities, 2000), and is endorsed by the ISEE Guidelines (2011), though not advocated by all (e.g. Hart, 2010). However, as the harmful effects of lead are well documented, the precautionary principle is not applicable to the SLIC Project. However, there are areas of environmental epidemiology such as climate change where, due to uncertainties in the scientific evidence, it may apply so you should always consider it when planning a study.

18.4 **Autonomy (including informed consent)**

18.4.1 **The distinction between data for research and public health surveillance**

An important consideration when applying for ethics approval is to establish the research status of your project. Depending on the method used and type of information obtained, studies may be defined as research, service evaluation, clinical audit, surveillance, or usual practice (NPSA, 2010). Accurate definition may be necessary to discern the level of ethical approval required (NPSA, 2010) (but not used as a way of ‘avoiding’ an ethics committee!).

The SLIC Project was classed as surveillance (i.e. part of routine data collection) rather than research by the NIGB (NIGB 2011a). This was because the study was not trying to gain new knowledge on lead in children, but was going to be monitoring the problem and using existing mitigation methods to reduce it (NPSA, 2010). Generally projects classified as surveillance, such as SLIC, do not have to obtain individual patient consent for the use of PII (NIGB, 2011a)

18.4.2 **Institutional Review Boards/Research Ethics Boards**

There are numerous names for groups of people officially established to decide whether a research project can ethically and legally be approved, such as Institutional Review Boards, Research Ethics Boards, and Research Ethics Committees (RECs). Their constitution may differ across time and jurisdictions, with various experts brought in if required by the type of study being assessed (Merlo, 2007), but they should always contain representatives of the population involved (ISEE, 2011).

As stated previously, the SLIC Project had to go through NRES. As part of this process the study had to document robust aims and objectives for the research and a detailed study protocol (ISEE, 2011). After the study began, it was found that some individuals with elevated blood lead levels were being missed by the reporting mechanisms used by the study, as these omitted local HPU. In order to add HPUs as a reporting route, it was necessary for the project to request further ethical permission from the NRES. There may also be local or organizational ethics committees to consult (DH, 2005).

Depending on the organization conducting and funding the research, there is likely to be an internal ethical approval process to be completed before the study can apply externally for ethical approval. This is crucial to show that the primary research body has officially considered the ethical issues of the research (ISEE, 2011). The SLIC Project did this by following the HPA ethical process.

18.4.3 Informed consent

The ISEE Guidelines state that there must be full disclosure of relevant aspects of the study, such as its purpose and any potential hazards, to the study participants before explicit prior, documented informed consent is obtained. They refer to a number of sources of guidance for this and emphasize the need to use the most up-to-date documents (ISEE, 2011).

There are strong arguments for involving the community (if feasible) in the design of a study to aid in obtaining informed consent (ISEE, 2011). Other considerations include specific requirement for the consent form (NRES, 2011) as well as the need to resubmit the study to an ethics committee if the remit of consent has changed, for example, if children in a long-term study become old enough to give their own medical consent (Hens et al., 2011).

Participants have the right to self-determination or autonomy (ISEE, 2011), so they must fully understand the information given about the study and its implications. This can cause difficulties in some populations, for example, in children and people with learning disabilities. The Helsinki Declaration (WMA, 2008) states that either the participant or a legally authorized representative must give consent. In most cases this representative would be the parent(s) of the child, but it may be more difficult to define. In the SLIC Project, if informed consent *had* been needed, would an accompanying grandparent have been considered appropriate? Furthermore if representatives of a child consent to participation (i.e. a blood test in the case of SLIC) but the child refuses, whose decision is considered to take precedence (Hens et al., 2011)?

Many of the issues concerning children and informed consent also relate to those with learning difficulties or mental illness. The nature of the exposure in the SLIC Project meant that a large number of the child cases have learning difficulties. The ISEE Guidelines maintain that self-determination is usually the primary ethical concern regarding the study participants. If informed consent had had to be obtained from the SLIC Project children, then the process chosen would have had to be thoroughly justified.

There may be situations when research may be exempt from the usual rules on consent and confidentiality. In the UK there is a part of the NHS Act 2006 (Section 251) (UK Government, 2006) where the usual confidentiality and/or informed consent requirements for a research study are waived. There must be compelling reasons for this, and each part of the research process involving Section 251 must be fully justified (NIGB, 2011b); balancing between the principle of beneficence with regard to the researchers, the ethical duty of individuals to participate in studies to benefit their fellow humans and the requirement to maintain the privacy of those individuals. An example is the congenital

anomaly register discussed in Chapter 16. This was granted access to PII without consent for a variety of reasons, for example, many of their notifications come from sources such as pathology departments which have minimal contact with patients.

Even if informed consent is not required, study participants should still be protected through other means such as the right to confidentiality and discretion over the sharing of data (ISEE, 2011). The research proposal should still be reviewed by an ethics committee or internally approved in an organization.

With regard to consent of participants the key principle is that the researcher can coherently explain the reasoning behind obtaining or not obtaining individual consent. Cultural, ethnic, and religious factors also need to be considered (Merlo, 2007). It may be useful to search out past precedent or local/national experts to help.

18.5 Justice

18.5.1 Research obligations to society

Obligations to society involve ensuring objectivity in the research process and reporting of the research outcome, as well as the overarching obligation to carry out only high-quality research which will materially improve the understanding of a particular subject.

Challenges to objectivity include conflict of interest, for example, in the SLIC project if staff in the Project Team had also worked in the lead industry or an organization which removes or mitigates harmful lead exposure. Equally (and perhaps more deliberately) ‘partiality’ can arise where epidemiologists have been hired to publicly undermine research methods and results (Pearce, 2008) or allowed themselves to be influenced detrimentally by any of the organizations involved, or outside groups.

Reporting the outcome of the research does not simply mean accurate reports that draw appropriate conclusions. It also means the obligation to publish research results even where they show an outcome which does not agree with the ‘received wisdom’, is in opposition to what the sponsors or funders hoped to find (for example, a study partially funded by the waste industry which identifies an increase in health effects in the population living near waste sites) or is difficult to find a journal to accept. Clinical trials in which the drug being tested has no or a negative effect are an example as journals are known to be biased in favour of ‘publishing positive’ outcomes (see Chapter 3) but the researchers must attempt to publish all results.

Finally, environmental epidemiologists should work with people and organizations who can make a difference to environmental issues (ISEE, 2011). The SLIC Project Team worked with those who can help to mitigate lead exposure in children, such as local authorities; and GPs and hospital paediatricians to ensure cases continue to be reported.

18.5.2 Research obligations to funders/sponsors, employers, and colleagues

These obligations need to be identified early on in the research process as well as involving the population concerned at all stages of the study, from initiation to publication (ISEE, 2011). This can be difficult when there is limited time, as in the case of the Enschede firework disaster (Chapter 6).

Care must be taken to be aware of and follow the ethical policies and procedures of the organization in which your research is being conducted. Even when ethics approval has been obtained from a national committee, which should be recognized as valid for local organizations, the experience of SLIC is that medical and health service personnel may work to their own clinical ethical framework, and/or insist on local organizational approval.

It is important to acknowledge the contribution of all who have worked on any aspect of a project (ISEE, 2011), for example, in the recent published article on global lead the names of all the SLIC Project Team members were acknowledged (Thomas et al., 2011).

Finally, the ISEE guidelines state that environmental epidemiologists have an obligation to ensure that their colleagues and other relevant people have a working knowledge of ethics and their application in environmental epidemiology research (ISEE, 2011). This is why a chapter on ethics is included in this textbook.

18.6 Top tips for ethics in environmental epidemiology research

1. Get help with ethical issues and processes early in the research process, from your organization, experts, and published literature. Ensure you are adhering to the ISEE guidelines (ISEE, 2011).
2. Find out what your organization's/sponsor's internal ethical approval process is.
3. Find an appropriate work colleague/mentor to guide you through the process, preferably someone who has done a similar project.
4. Make sure legislation, guidance, and processes have not been changed or updated since your last research project.
5. Ensure that you have the full cooperation and trust of the individuals and/or community who are the subjects of your study.
6. Remember, just because you have (or think you have) official ethical approval and permission for your research processes and methods, this does not mean that your stakeholders will be of the same opinion!

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Section 4

Special topics

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Cluster investigation

Marjon Drijver, Araceli Busby, and Irene A. Kreis

Learning objectives

- ◆ Evaluate the use of a stepwise approach for the investigation of clusters and be able to apply the methodology.
- ◆ Analyse the results of cluster investigations and prepare a response for the local health authorities.
- ◆ Act as an advocate for local citizens in the investigation of environmental health concerns.
- ◆ Consider the importance of a risk communication strategy for local environmental investigations.

19.1 Introduction

Concern about health effects of exposure to local environmental factors such as waste dumps, air pollution, and electromagnetic fields may lead people to report health problems, particularly non-specific health symptoms for instance headaches, dizziness, and tiredness (Health Council of the Netherlands (HCN), 2001). Sensory observations, for instance odour and noise nuisance may play a role in this. Many complaint patterns display similarities, regardless of the different hazardous agents. Where several people report the same complaints or illnesses this may be perceived as a cluster (defined as an unusually high number of similar cases in a given area, period or population).

It is understandable that people report disease clusters, especially if they are concerned about the quality of the local environment. Concerns can increase if there is no proper response. Therefore it is good practice for public health services to respond quickly and appropriately. The main objective of the response is to assess the plausibility of any relationship with local environmental factors and hence to decide whether measures to limit exposure are needed or to proceed to a more detailed investigation.

19.2 Case study

A case study on childhood leukaemia in a horticultural community in the Netherlands (Mulder et al., 1994), will be used to illustrate the key issues in cluster investigation.

In the 1980s in Aalsmeer, a cut-flower municipality in the western part of the Netherlands, the parents of a boy who died of leukaemia the previous year reported a possible cluster of 12 similar cases living within a 1-km radius. The parents wondered if this could be related to regular swimming in a local, open air, natural swimming pool which was thought to be contaminated with pesticides and oil or living under the flight path approach for Amsterdam airport. This case study is also used in Chapter 17.

19.3 Investigating clusters

The investigation of the Aalsmeer cluster used a stepwise approach for responding to disease clusters which was developed for the public health services in the Netherlands based on American guidelines and adopted by the HCN (HCN, 2001). In this ‘triple track’ approach, it is essential to distinguish between three tracks:

- ◆ Health track (receptor): to what degree are there indications of an increased number of health events or health complaints?
- ◆ Environmental track (source): to what degree is or was there increased exposure to environmental contaminants via air, water, soil, or crops?
- ◆ Relationship track (pathway): how plausible is it that the exposure to local environmental factors brought about the identified effects on health?

These three tracks are investigated concurrently in three phases: orientation, inventory, and quantitative analysis (see Figure 19.1). The different phases cannot always be separated in practice and are not always necessary for all tracks.

Risk communication

Proper communication with those involved is important in all the phases and tracks (Drijver and Woudenberg, 1999). The discrepancies between the public’s opinion about the risk and that of the risk assessors or the authorities can create a great deal of tension. The authorities cannot rely solely on scientific explanations of the risks, but must also pay particular attention to how risks are perceived by everyone involved. The importance of proper risk communication in cluster investigation is stressed in international guidelines for cluster investigation: residents and their representatives should be involved at an early stage in considering whether further investigation is advisable and feasible (Centers for Disease Control and Prevention (CDC), 1990; Kingsley et al., 2007). Fig. 19.1 therefore includes an explicit communication section. Risk perception and communication are explored more fully in Chapter 4.

19.3.1 Phase 1: orientation

After the initial cluster report, phase 1 of the investigation involves gathering general background information in the three tracks. Gathering information from informants can be seen as preparation for personal contacts in the inventory phase. If the informant is completely satisfied after receiving information by telephone or in writing and there are

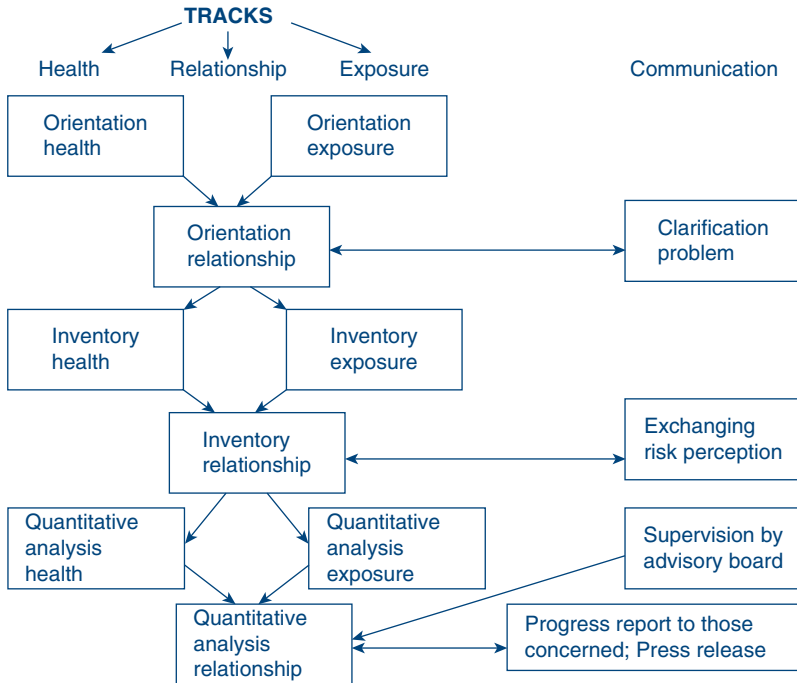


Fig. 19.1 Stepwise cluster approach, Health Council of the Netherlands.

Reproduced with permission from the Advisory Report of the Health Council of the Netherlands (HCN) (2001). *Local Environmental health concerns; risk communication, exposure assessment and cluster investigation*. The Hague: Health Council of the Netherlands, publication no. 2001/10.

no public concerns about a possible relationship to local environmental factors there may be no need to move on to the next phase.

19.3.1.1 Orientation health track

This track evaluates the normal occurrence of the health events concerned in the population.

Comparison of national data on leukaemia deaths with the population of Aalsmeer suggested that one death under the age of 40 in a 5-year period in the whole council area was within the expected range for the population. In the Netherlands, at the time of the investigation, no reliable incidence data were easily available.

19.3.1.2 Orientation exposure track

An early site visit is crucial to establish a possible exposure as well as to demonstrate that the concerns of the notifiers are being taken seriously. Whilst there may be some concern amongst public health officials that a site visit acts as confirmation for the local community that there is a problem in their environment, this risk is far less than the loss of trust generated by dismissing or playing down their fears. Loss of trust may result in the

outcome of any investigations being dismissed by the community and trust, once lost, is difficult to regain (HCN, 2001).

In Aalsmeer, local inspection identified not only glasshouses but also storage depots for pesticides and petroleum products in proximity to the natural swimming pool and recreation area. Vegetables for personal consumption were grown widely. The potential for contamination of a variety of media was therefore confirmed. The close proximity of the international airport and the potential for contamination by exhaust fumes also existed.

19.3.1.3 Orientation relationship track

This track evaluates the biological plausibility of the proposed causal relationship on the basis of a literature study.

For Aalsmeer the evidence from the literature of a biologically plausible relationship between leukaemia and (occupational) exposure to petroleum products, pesticides, and exhaust fumes was considered sufficient to warrant moving to the next phase of the investigation.

19.3.1.4 Communication in orientation phase

Risk communication begins with the first telephone call, in which the informant's problem is explored. Informal meetings were held in Aalsmeer with the people who notified the potential cluster.

19.3.2 Phase 2: inventory

In the inventory phase a face-to-face meeting is held not only to gather information on the cases but also to begin to explore the risk perception and concerns. The informants is then informed about the investigation methods, the 'normal' occurrence of disease, the possible causes of the disorder concerned, the possibility of exposure to local environmental factors, and any health risks this involves.

19.3.2.1 Inventory health track

Data on the nature and number of health complaints known to the informants or local professionals are gathered and used to derive a rough comparison with the expected number for the given population. Owing to the exploratory character of this phase, formal statistical analysis is not used here. With the aid of routinely available data it is possible to make a rough calculation comparing the reported number of cases in the population concerned with the number expected on the basis of general population characteristics such as age distribution and the number of inhabitants.

An inventory among the local general practitioners (GPs) in Aalsmeer identified eight leukaemia and seven lymphoma patients under the age of 40 years diagnosed since 1975.

19.3.2.2 Inventory exposure track

The nature of the local environmental pollution notified by the informant is sought and defined.

Examination of the records identified two relevant events in the early 1970s: an incident with a large petroleum product storage tank and a major fire in a pesticide storage

unit next to the swimming pool. The extinguishing and clean up of the fire resulted in substantial discharge to a ditch which was connected with the swimming pool. Chemical investigations showed that the soil and groundwater around the dump sites in Aalsmeer were highly contaminated with pesticides, polyaromatic hydrocarbons (PAHs), and benzene.

19.3.2.3 Inventory relationship track

This examines the time relationship between the exposure of concern and the identified health events. There may be grounds for moving to the quantitative analysis phase if there are more health problems reported in the population group than expected and/or indications of increased exposure to local environmental factors. Both were the case in Aalsmeer.

19.3.2.4 Communication in inventory phase

In Aalsmeer at this time, there was an informal meeting with the notifiers of the potential cluster to explore the problem and gain insight into their risk perception.

19.3.3 Phase 3: quantitative analysis

The third, quantitative analysis phase of the stepwise approach, where this is needed, involves the more formal analysis of the health and environmental data.

19.3.3.1 Quantitative analysis health track

The health track requires analysis of the available and often routinely collected disease and complaint records and calculating the age-standardized incidence or prevalence compared to a reference population (see section 19.5). The correct time period must be taken into account using knowledge of the latency period of the disorder concerned.

In the municipality of Aalsmeer, the mortality and hospital discharge diagnosis information for persons aged under 40 years and cancer incidence for children younger than 15 years of age were both greater than four times that observed in the Netherlands national data over the period 1980–1985. For the smaller neighbourhood concerned the observed increase was over 10 times the expected numbers. Thus the quantitative analysis of leukaemia data indicated a need for quantitative analysis of the relation between leukaemia and local exposures.

19.3.3.2 Quantitative analysis exposure track

The most suitable instrument for evaluating possible health effects of exposure to environmental factors is a risk assessment (HCN, 2001). Determining the concentrations in water, air, soil, or crops in order to estimate general exposure will generally suffice. Evaluating personal exposure (body burden) will only be necessary in exceptional cases and only if certain conditions are met, specifically the presence of an exposure indicator (biomarker) in easily accessible human tissues with a sufficiently long biological half-life. The advantages of individual measurements, such as reducing concern about possible current or future health effects have to be weighed against the disadvantages, including difficulties with interpreting individual measurement results or feasibility (time and money).

The risk assessment determines whether exposure exceeds health-based recommended limits, considering limits for at-risk groups. The transparency of the entire process is important, as both exposure and risk assessment can be fairly complex. As far as possible, the perspective and knowledge of local people must be taken into account.

If exposures are below recommended exposure limits it is unlikely that the health events are attributable to the hypothesized environmental factor. If the estimated exposure is higher than the health-based permissible level, it is advisable to recommend measures, including behaviour change, to reduce exposure, whether or not the health effects are confirmed. Rothman (Rothman, 1990) argued that measures taken at the pollution source may be more important to the public than further investigation into a possible causal relationship between the pollution and the health events. Moreover, it is easier to justify taking measures on the grounds of possible standard levels having been exceeded than it is based only on epidemiological studies.

Given that the concentrations of pesticides and PAHs in the surface water samples taken in and around the swimming pool in Aalsmeer exceeded the allowable water levels, further (causal) epidemiological investigation was considered appropriate.

19.3.3.3 Quantitative analysis relationship track

If there is a real disease cluster and if a formal risk assessment makes it plausible that local environmental exposure is or has been sufficiently high to cause health effects, further aetiological epidemiological research may be considered. Health data and exposure data are collected at the individual level to determine a possible link between personal exposure to environmental pollution and particular health effects. It is important to make clear to those involved that a causal relationship between local environmental factors and possible effects on health is hardly ever demonstrable at the local level, usually because of the relatively low number of health events.

As a rule, further study is only worthwhile under strict conditions; in particular, the number of cases has to be sufficiently high (Neutra, 1990). Other conditions include: sufficient variation in exposure, sufficient scientific or public health importance, and involvement of the local population (HCN, 2001). If these conditions are not met the disadvantages, including time, money, and resources, may outweigh the benefits, especially if the research is combined with bio-monitoring such as blood and urine analyses. From the point of view of environmental management, it is often more effective to take action on the basis of exposure assessment and associated health risks (see section 19.3.3.2).

As the result of the stepwise evaluation of the problem, in Aalsmeer it was decided that: (1) there was a cluster; (2) the numbers might be just large enough for an in-depth investigation; and (3) the possible pesticide exposures and the airport proximity gave plausible associations to be evaluated. These factors, combined with an absence of advance publicity, fulfilled the conditions for further investigation and a case-control study was considered the most appropriate method. Care was taken only to investigate the associations for which there were a priori hypotheses (formulated beforehand); the most

important being exposure to pesticides. The case–control study therefore investigated leukaemia and lymphomas and their association with pesticides, polluted water, air pollution, and related risk factors (Mulder et al., 1994).

The case–control study was conducted among patients aged under 40 years, diagnosed with leukaemia or lymphoma between 1975 and 1989 and resident in Aalsmeer at the time of diagnosis. For each patient four controls of similar age and sex and registered at the same general practice, were selected. The data were collected by interview questionnaires focused on exposure to pesticides in the (local) glasshouse horticultural industry, swimming in open water, and exposure to local air pollution. Statistical analysis consisted of the calculation of (adjusted) odds ratios (ORs) and 95% confidence intervals (CIs) using statistical software for epidemiology (Chapter 17).

Participation rates of 100% in cases and controls were achieved due to great commitment of researchers, GPs, and the community. Potential risk factors for haematological malignancies identified through literature search, such as breastfeeding, smoking, infectious diseases, and socioeconomic status, all showed expected associations (ORs <2). For the local risk factors (the a priori hypotheses) the ORs (matched for age and sex) which were statistically significantly different from unity are shown in Table 19.1.

The associations found with the air pollution indicators should be interpreted with caution due to the uncertainty in the exposure estimates. However, the identified association with indicators of exposure to pesticides was considered to be more informative given the supporting literature and the greater precision of the exposure estimates.

19.3.3.4 Communication in quantitative analysis phase

If a further (individual) epidemiological study among the local population is considered (as it was in Aalsmeer) it is vital to involve all the interested parties. It is essential to discuss the possibilities and limitations of the investigation with all those concerned beforehand to avoid creating expectations that cannot be met. Ideally an ‘advisory board’ should be formed in which the pros and cons of the various study methods can be discussed. An example of an ‘aetiological’ epidemiological study in the Netherlands in which an advisory board was formed with representatives of (organizations of) surrounding

Table 19.1 Results from the further investigation in Aalsmeer

Hypotheses	Exposure definition	OR	95% CI
Pesticides	Living short distance from glasshouses	3.5	1.1–19.6
Water sports	Swimming ≥ 1 hour per week	5.3	1.3–17.4
	Swimming ≥ 2 hour per week	4.5	1.4–14.0
Air pollution	General annoyance	5.0	1.5–28.0
	Aircraft annoyance	3.7	1.4–16.7
	Outdoor activities ≥ 10 hours per week	8.0	1.3–26.9
	Local vegetable consumption ≥ 4 times a week	3.0	1.1–11.1

Reproduced from Mulder, Y.M., Drijver, Y., and Kreis, I.A. (1994). Case-control study on the association between a cluster of childhood haematopoietic malignancies and local environmental factors in Aalsmeer, the Netherlands. *J Epidemiol Community Health* 48:161–5, with permission from BMJ Publishing Group Ltd.

residents, was the Health Impact Assessment for Amsterdam Airport (Rijksinstituut voor Volksgezondheid en Milieu (RIVM), 1993).

In Aalsmeer at this time there was an informal meeting with the notifiers, a press-release and a local press conference, a letter to all residents, and a presentation at a public meeting for residents. For the epidemiological studies in Aalsmeer, no local stakeholders participated in the (expert) advisory board, but there was regular personal feedback to the ‘notifiers’.

19.4 Outcome of the cluster investigation

Recommendations for evaluating the carcinogenic risks from the PAH contamination of swimming water, air, and vegetables have all been carried out, but concentrations did not suggest an unacceptably increased risk for the future. A follow-up among GPs showed that the incidence of haematopoietic malignancies returned to normal after 1985, so if there had been a causal relation, it would probably have been with past exposures. Education programmes on working with pesticides were started in local schools as a result of the identified risk of living near the glasshouses.

19.5 Methods for quantitative cluster investigation

19.5.1 Useful indicators and databases

When choosing health indicators, the most important criteria for cluster investigations are: low aggregation level (small area with small population), completeness of the data in the region, relevance to the exposure in question, and reliability of the records. The usefulness of the various registration systems needs to be evaluated carefully (Chapter 12). Other examples of useful population data and data on other possibly confounding factors at a low aggregation level include age composition and socioeconomic neighbourhood characteristics, such as the unemployment percentage, population density, average income, percentage of owner-occupied homes, or average number of years of education. Other national registers may be available for local environmental indicators, including data on emissions into the air and surface water, soil use, traffic intensity, drinking water quality, and housing stock. In the UK, there is a dedicated unit at Imperial College, the Imperial Rapid Enquiry Facility, looking at spatial epidemiology.

Privacy concerns prevented a quantitative analysis at postcode level in the Aalsmeer investigation. It was only possible at municipal level. The inventory phase uncovered concerns about the clustering of lymphoma (reported as leukaemia) so the investigation was broadened to encompass haematological malignancies.

19.5.2 Statistical methods

The most commonly used method for comparing a properly defined, exposed study population with a proper reference or control population is based on calculating standardized mortality or morbidity ratios (SMRs) (Goldman et al., 2000). In principle, studies of this kind can be readily conducted by public health services or by health-record administrators, such as Cancer Registries. A description of how to do these calculations also can

be found in Chapter 17. It should be noted that for small area studies when SMRs are determined at the postcode level for relatively infrequently occurring disorders, further data processing is usually necessary to correct for coincidental fluctuations. This requires spatial statistics techniques, such as Bayesian smoothing, requiring specialist expertise. Advanced cluster analysis methods are in general too complex for non-specialist use (Rothman et al., 1990). More details on options can be found in Chapter 17.

19.5.3 Limitations of quantitative cluster analysis

Exploratory (geographic) epidemiological studies are subject to various limitations, especially when conducted in connection with the occurrence of an already identified cluster, known as ‘post hoc’ cluster investigation.

19.5.3.1 Practical limitations

Owing to data protection legislation, individual disease data can not simply be supplied at an aggregated level (postcode, neighbourhood, or municipal level) matching the level of the local exposure. Also, for many locations and diseases, the numbers will be very small thus limiting statistical power to detect differences. This was one of the key reasons for conducting a case–control study in Aalsmeer. An advantage of the case–control methodology is that is a highly efficient use of the data (Rothman et al., 2008).

19.5.3.2 Methodological pitfalls

If a cluster of health events is ascertained in a particular area, it does not necessarily indicate a causal effect of local environmental exposure. From the epidemiological point of view such associations can arise out of the way in which the investigation has been conducted. Interpretation of epidemiological studies is dealt with more fully in Chapter 14; here we discuss the role of methodology with specific reference to cluster investigations such as the Aalsmeer study.

Chance

In a detected cluster, the results of a statistical test ‘post hoc’ are unreliable and investigators often incorrectly conclude that something unusual is occurring. In such cases, the conditions for a valid statistical test have not been fulfilled. After all, the occurrence of the health events was (possibly unconsciously) compared with what is normal in a particular area, after which it is particularly an increase that tends to be noticed and reported. This phenomenon, which is ‘hidden’ from the investigator, is referred to as the ‘occult multiple comparison’ problem. This means that even if a statistically significant cluster exists, it is not generally possible to draw conclusions about whether an increased incidence or prevalence is a coincidence. (Thomas, 1985)

Methods for dealing with the issue of post hoc cluster investigation include examining disease rates or clustering in alternative populations with the similar exposures (as described in Chapter 17). Additional to the issue of cluster interpretation is the general problem of multiple comparisons. Without an a priori hypothesis using a 5% level of significance, a positive association would be expected in 1 in 20 analyses purely by statistical chance.

Bias

A fundamental problem of cluster investigations is known as ‘the Texas sharpshooter’; so called because the sharpshooter positions his target *after* shots have been fired (Rothman, 1990). The phenomenon occurs because the point pattern which arises from a Poisson process (the statistical distribution for rare disease rates) in a uniform underlying population is expected to contain a number of aggregations or ‘clusters’ as a result of random variation. Whilst it is possible to compare the number in such a ‘cluster’ with the number expected on average the statistical test of how unusual this, whilst simple to perform, may be difficult to interpret. Essentially this means that where a cluster of medical conditions (cancers, congenital anomalies and so on) in a particular area has been identified it is possible that this may be based on coincidence (Neutra, 1990).

Selection *bias* is a particular problem for cluster investigations because individuals with the disease outcome have already been identified and an environmental exposure concern raised. To prevent selection bias (as well as aid the interpretation of the statistical significance as noted above) it is advisable to conduct an investigation in another comparable population (if one with a similar exposure can be found), where the boundary definition in place and time can then be chosen beforehand (a priori) on the basis of the exposure. This may need careful explanation to the concerned community who may be unhappy that their population is not being ‘properly’ investigated. In Aalsmeer it was thought that the association with the local environmental contamination had only been raised by one family (the family that initially identified the cluster) and it was not a source of generalized concern in the community. The case–control study also noted a high response rate from both cases and controls, thus reducing the likelihood of selection bias.

Information *bias* through misclassification of health effects may occur due to differences in reporting, diagnostics, registration, coding, admission and treatment policy, or availability and accessibility of health care. In Aalsmeer there was little evidence to suggest that case and control families reported exposure differently as questionnaires were initially completed before interview; the study had no advance publicity and (as noted earlier) there was no evidence of a general community concern about pollution. There may have been misclassification of exposure due to the indirect measures used; however, the researchers considered that this misclassification was not likely to differ between cases and controls. Additionally the reported measurements which could be validated against direct measures (such as distance from greenhouses) were found to be reasonable accurate.

Confounding

A confounding factor is a known risk factor which is associated with the exposure being studied, but is not an intermediary factor in the causal relationship between exposure and effect (Rothman et al., 2008). In this study the concerns about environmental risks might be seen as a possible confounder in the relationship between exposure and effect (Neutra et al., 1991). The possibility of socioeconomic confounding, because people with lower socioeconomic (and thus health) status may be more likely to live closer to pollution sources, is also a particular concern (Elliott, 1995).

The Aalsmeer study selected controls from the same GP population as cases (thus effectively using a matched case–control design) (Chapter 14) and also performed analyses stratified for neighbourhood in order to minimize the effect of local confounding factors in the study.

19.6 Value of the stepwise approach to clusters

The stepwise approach to cluster investigation is used by almost all the public health services in the Netherlands (Poll and Drijver, 2001). An evaluation study among public health services in the Netherlands between 1993 and 1997 found that the majority of cluster investigations were terminated after the inventory phase because the reported cluster was satisfactorily explained, for example because a cancer cluster could be attributed to the aging local population. Only 7% of the 120 disease clusters initially reported as being associated with environmental pollution were finally confirmed. Environmental exposure was demonstrated in fewer than 2% of the reports. Because of this, the public health services did not consider further investigation into a causal relationship between the disorders and local environmental factors to be necessary for any of the reports. Similar findings have been reported in the USA (Smith and Neutra, 1993). Although cluster reports are practically always a reflection of concerns about local environmental factors, in the USA it emerged that it was rare that an environmental factor was found to have a plausible causal role (CDC, 1990; Kingsley et al., 2007).

19.7 Importance of risk communication

Early risk communication is extremely important in managing local environmental health concerns, including an exchange of information and opinions between authorities, public, and other parties involved about the nature and extent of the risk. Proper risk communication can help ensure that the public can form a considered opinion about any risks posed by local environmental factors and can help create greater understanding and trust between parties. In this respect, the involvement of local residents is a precondition for an effective policy to address a local environmental health problem. The media can play a positive role in this area if notified in good time about research results. Guidelines for risk communication and citizen participation may be useful in the approach to local environmental health concerns, although hardly any research has been conducted into the efficacy of such guidelines. Risk communication and public participation are not only important in making a hazardous situation controllable. They could also lay the foundations for a better ongoing relationship based on trust between the authorities and the public, which may prevent unjustified concerns arising in the future and improve public health.

Descriptive epidemiological studies based on readily available health data at the geographically aggregated level are known as ‘small area health statistics’: i.e. the analysis of health data with a high spatial resolution. Descriptive epidemiological studies are often less labour intensive than aetiological epidemiological studies with data collected at the individual level. In some countries data may be available from existing records at the

Box 19.1 Key elements in cluster investigations

- ◆ Take worries about exposure to local environmental factors seriously.
- ◆ Pay attention at an early stage to risk communication and public participation.
- ◆ Perform a systematic and transparent exposure assessment.
- ◆ Consider exposure reducing measures in case of any nuisance or undesirable exposure.
- ◆ Pay attention to any possible somatic consequences of stress.
- ◆ Follow a stepwise approach to environment-related disease clusters.
- ◆ Take into account coincidence as an explanation of detected disease clusters.
- ◆ Be critical when conducting descriptive epidemiological studies.
- ◆ Explain under which conditions a further epidemiological study would be advisable.
- ◆ Involve communication specialists in epidemiological studies.

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individual level (RIVM, 1993) but for reasons of privacy, the postcode level (in the Netherlands as in the UK this is a relatively small number of houses) is usually the most suitable level for analysis. However, privacy concerns may prevent even this level of investigation.

19.8 Key elements in cluster investigations

The Health Council of the Netherlands has defined the aspects listed in Box 19.1 as important for the pragmatic approach of investigating clusters and other local environmental health concerns.

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Occupational epidemiology

Virginia Murray

Learning objectives

- ◆ Appraise the importance of occupational epidemiology to contribute to environmental epidemiology for public health and health protection, using a common cancer, bladder cancer, as the example.
- ◆ Evaluate the benefits and pitfalls of using occupational groups or studies for the evaluation of environmental risks in the general population.

20.1 Introduction

Occupational epidemiology has been described as the basis for occupational surveillance but can also be of value in monitoring the effectiveness of any intervention to minimize occupational risks (Cox et al., 2006). In 2007, the US Occupational Safety and Health Administration (OSHA) (2007) described occupational epidemiology as:

- ◆ involving the application of epidemiological methods to populations of workers
- ◆ providing methods for assessing workers exposed to a variety of chemical, biological or physical (e.g., noise, heat, radiation) agents
- ◆ determining if these exposures result in an increased risk of adverse health outcomes, and
- ◆ potentially involving evaluation of workers with a common adverse health outcome to determine if an agent or set of agents might explain their disease.

This chapter, by using a case study on the occupational investigation into bladder cancer and the source–pathway–receptor model (Chapter 9), describes how occupational epidemiology can be used to address the identification of a common cancer with occupational exposure starting from the disease in a human receptor. This case study points to lessons to help to limit future adverse health events associated with occupational exposures. This case study also points to the need to note that occupational cancers will contribute to routine geographical cancer data.

20.2 Case study

20.2.1 What is the incidence and prevalence of bladder cancer?

The UK Office for National Statistics (ONS) reports that bladder cancer is common with 6,322 new cases diagnosed in 2008 making bladder cancer the most frequently occurring tumour of the urinary system (ONS 2011).

Bladder cancer accounts for around 1 in every 46 new cases of cancer each year in the UK with 8771 new cases diagnosed in 2008 of which 6,322 were in males and 2,469 in females giving a male:female ratio of 6:2. The age standardized rate for males is 27.6 per 100,000 and for females is 9.6 per 100,000.

Bladder cancer is the fifth most commonly diagnosed cancer in men behind skin cancer at around 45,000, lung at around 18,000, prostate at around 30,000 and colon cancers at around 10,000 newly diagnosed cases in England in 2008 (ONS, 2011). Bladder cancer is the eleventh most common cancer in women.

20.2.2 Is it difficult to spot an association between bladder cancer and occupational exposure?

Such a high incidence of disease in the population has resulted in much speculation on a possible association with a common environmental cause. In particular, occupational exposure was thought to be linked to bladder cancer in men as far back as the 1890s (Bridge, 1926). The latency between exposure and the development of a bladder cancer can be considerable: first exposure to initial diagnosis lags of up to 20–40 years have been reported. Therefore the causative agent or even the industry in which the individual worked may no longer exist.

20.2.3 First published report of occupational exposure associated with bladder cancer

An occupationally-related cancer does not usually differ clinically from one occurring sporadically in the population which complicates identification of an occupational cause (Murray, 1979). Occupational tumours of the bladder were first recognized by Rehn, a surgeon in Frankfurt-on-Main in Germany, who reported four cases in 1895 in men who worked in the same factory manufacturing magenta (also known as fuchsin and rosaniline). Rehn attributed the tumours to aniline, at that time used as a starting material in the magenta process. However, in the 1890s, Leichtenstern became suspicious of naphthylamine as a possible causative agent (Bridge, 1926). A profusion of reports occurred but it was not until 1921 that the International Labour Office published a report suggesting that 2-naphthylamine and benzidine were both linked to bladder cancer. The first occupationally related cases in the UK were reported in 1926 where two cases were described in association with naphthylamine (Bridge, 1926).

20.2.4 How to determine the risk of developing cancer from occupational exposure?

The carcinogenicity of 2-naphthylamine was initially not widely accepted and the production and use of this chemical continued until the proof was obtained via Case's

classic epidemiological studies (Case and Hosker, 1954; Case and Pearson, 1954; Case et al., 1954). Case and colleagues found that of the 455 cases of bladder cancer in the British chemical industry, 311 occurred in men who had worked with 2-naphthylamine and other aromatic amines. Using cohort studies and case series, they showed that the chance of a 2-naphthylamine worker developing bladder cancer was 30 times greater than that found in the general population at that time. In addition, Case and colleagues noted that occupationally related cancers occurred at an earlier age than sporadic cases of bladder cancer. These epidemiological studies finally brought about the abandonment of manufacture and use of 2-naphthylamine in the dyestuffs, chemical, and rubber industries.

20.2.5 Can a cohort lead to relative risks assessments?

Veys (2004), in his elegant report, followed a cohort of 3,038 men employed at a large tyre factory either during the 'at-risk' period for 2-naphthylamine exposure or just after it. This study was also initiated at one of the 13 factories taking part in the British Rubber Manufacturers' Association study. This study was set up to quantify more precisely at shop floor level the extent of the hazard and risk to rubber workers employed between 1946 and 1949 when they would have been inadvertently exposed to the small quantities of 2-naphthylamine present in some chemicals used in the manufacturing process. The study reported that all requisite ethical approvals were sought for the follow-up and tracing procedures that were undertaken.

In the schematic factory plan, shown in Fig. 20.1, the at-risk departments where bladder carcinogen 2-naphthylamine was present as a contaminant (at 0.25%) in chemicals used in manufacture are shaded, while non-risk areas without exposure to 2-naphthylamine remain white. The 58 bladder tumours in at-risk men employed before December 1949 were plotted individually on the plan as black squares with white circular insets, using their relevant employment during the time period defined as at risk. The preponderance of cases occurred in the chemical stores and the mixing and mill room, i.e. the early stages in processing, where the risk of exposure to dust and fumes was greatest. Mill men had a risk rate of 4.6% for developing bladder cancer. Those men working as engineering fitters, who undertook repair and maintenance work whilst production continued, had a 3.7% risk of developing bladder cancer.

Veys (2004) also showed that the incidence of a statistically significant elevated risk of bladder cancer in tyre factory workers was reversed when the carcinogen was removed from production chemicals in October, 1949.

A report on occupational bladder cancer commissioned by the UK Health and Safety Executive (Rushton et al., 2007) notes that exposures to carcinogenic intermediates in the dyestuffs industry decreased from about 1935 and especially after 1945. The use of 1- and 2-naphthylamine in the rubber industry stopped in 1949. In 1967, the UK government prohibited the manufacture and use of this compound and even the use of substances containing less than 1% was allowed only with strict controls including mandatory medical surveillance (Verma et al., 2002). In the US, 2-naphthylamine is now used only in laboratory research.

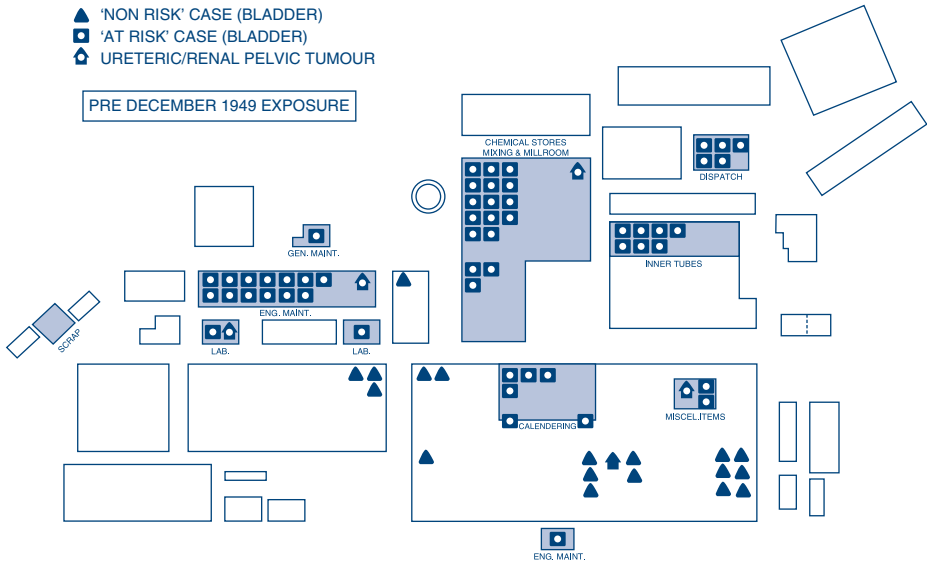


Fig. 20.1 Schematic factory plan showing bladder (urothelial tract) tumours for men employed before December 1949 in a British rubber factory with shaded showing where bladder carcinogen 2-naphthylamine was present as a contaminant (at 0.25%) in chemicals used, while non-risk areas without exposure to 2-naphthylamine remain white.

Reproduced with permission from Veys, C.A. (2004). Bladder tumours in rubber workers: a factory study 1946–1995. *Occup Med (Lond)* 54(5): 322–9, Oxford University Press, doi:10.1093/occmed/kqh010.

20.3 Examples of other occupational epidemiology investigations

A number of developments in occupational epidemiology are of note in North American and Europe. Within the UK the University of Manchester's Centre of Occupational and Environmental Health has led the way in the UK by developing a range of useful occupational epidemiology tools that may be of value to environmental epidemiology investigation. These include research networks of occupational physicians in the UK participating in health surveillance through voluntary medically certified reporting (Agius and Carder, 2011). This research fulfils the function of a national observatory on occupational disease and work-related ill health. A range of surveillance studies are undertaken looking at the determinants, incidence, and trends in incidence of work-related disease as well as the associated sickness absence burden. These can be particularly valuable as exposures in occupational settings are often greater than in other settings and thus studies are more likely to find causal links. The UK occupational disease surveillance schemes that may be useful for health protection as sources of information include:

- ◆ Occupational physicians reporting activity (OPRA)
- ◆ Surveillance of work-related and occupational respiratory disease (SWORD)

- ◆ Occupational skin surveillance (EPI-DERM)
- ◆ Musculoskeletal occupational surveillance scheme (MOSS)
- ◆ Surveillance of occupational stress and mental illness (SOSMI)
- ◆ Surveillance of infectious diseases at work (SIDAW)
- ◆ Occupational surveillance scheme for audiological physicians (OSSA)
- ◆ Occupational surveillance of otorhinolaryngological disease (THOR-ENT)
- ◆ Electronic Reporting: IRELAND
- ◆ Novel cause reporting (THOR-Extra).

20.4 Encountering occupational cluster when investigating an environmental issue

In some countries, systematic research of the spatial distribution of cancers has been conducted to evaluate the occurrence of cancer clusters. Due to the clustering of occupational exposures, bladder cancer often shows up as a geographical residence cluster. When investigating cancer clusters or potential environmental issues, occupational clustering needs to be taken into account (Jarup, 2002).

20.5 Learning points

In summary, occupational epidemiology is:

- ◆ *Valuable for:*
 - Identification of occupational risk which may also be relevant to environmental risk.
 - More likely to identify associations between health and exposure because exposure is higher.
 - May be able to monitor and reassure post exposure that there have not been health effects.
 - Providing evidence that is used to improve safety of industrial processes/occupational environment.
 - Good for following-up cohorts over a long time period if the worker population is reasonably stable (although this may be becoming harder in the current occupational and economic climate).
 - Contributing to development of safe limits and guidelines for general population.
 - Where relevant can support emergency planning.
- ◆ *Disadvantages:*
 - Unrepresentative population (those who are chronically ill, vulnerable, or disabled may be less likely to be represented in the workforce); this is also known as the 'healthy worker' effect.

- If the worker population is mobile (e.g. short-term employment practices) it may be difficult to follow them up over long time periods.
- Cohort studies are time consuming and expensive.
- There may be resistance from company owners/management to allow workers to participate.
- Extrapolation of effects at high doses to low environmental exposures may be problematic.

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Chapter 21

Radiation

Colin Muirhead and Jill Meara

Learning objectives

- ◆ Respond to enquiries about the health consequences of exposure to non-ionizing radiation.
- ◆ Understand the uncertainties in assessments of health risks and how these uncertainties are taken into account in setting exposure guidelines.

21.1 Introduction

Radiation is a general term for the passage of energy through free space as electromagnetic waves or particles. Here we are concerned with radiation in the electromagnetic spectrum. This spectrum contains ionizing and non-ionizing radiation including X-rays, visible light, radio waves, and static magnetic fields. The physical properties of these radiations depend on the energy they impart on objects, both in terms of the energy contained in the individual packets (quanta) that make up the radiation and the overall intensity (number of quanta). The quantum energy increases with frequency (or reducing wavelength), and the health effects depend on ability of the radiation to penetrate and interact with body tissues.

- ◆ *Ionizing radiation*, includes cosmic, gamma, and X-rays, as well as alpha (α) and beta (β) particles. The quantum (or particle) energy is sufficiently great to cause ionizations (stripping of electrons from atoms) in the cells and tissues of the body and consequent damage. The sources and health effects of ionizing radiation are described in standard texts and websites. Occupational and public exposure to ionizing radiation in the UK is limited by legislation including the *Ionising Radiations Regulations* (HM Government UK, 1999). There are specific regulators in place for medical uses of radiation including the *Ionising Radiation (Medical Exposure) Regulations* (Department of Health, 2000).
- ◆ *Non-ionizing radiations* include electric and magnetic fields (EMFs), radiofrequency (RF) fields, and optical (infrared, visible, ultraviolet) radiation. The energy quanta of non-ionizing radiations do not contain enough energy to produce ionizations in body tissues but the radiation can have other biological effects, such as skin cancer and

cortical cataracts (ultraviolet), excitation of retinal cells in the eye (optical frequencies), heating (radiofrequencies), electrical stimulation (low frequencies), shocks, and magnetic phenomena.

- ◆ *Radiofrequency and electrical burns* can occur as a result of concentration of electrical current in body tissues, e.g. at a point of contact with an energized conductor. Such burns have the pathophysiological characteristics of thermal burns but can sometimes penetrate deeper into the tissues than a thermal contact burn.
- ◆ A great deal of information can be found about electromagnetic fields and their health effects and it is important to identify trusted messengers. The World Health Organization (WHO) International EMF Project provides authoritative information about exposure standards/guidelines, comprehensive reviews of the literature, and factsheets. The Scientific Committee on Emerging and Newly Identified Health Risks which advises the European Commission has prepared several reports on EMFs. The Health Protection Agency (HPA) is responsible for advising on EMFs at UK level.
- ◆ Exposure guidelines containing advised restrictions on exposure are promulgated by the International Commission on Non-Ionizing Radiation Protection (ICNIRP), a body formally recognized by WHO. These guidelines prevent exposures that could cause the established health effects of electromagnetic fields such as electrical stimulation and localized or whole-body heating. The exposure guidelines are based on comprehensive published reviews of the scientific evidence. They note areas where uncertainties may suggest that precautionary measures should be considered, even though the effects concerned are not considered established.

21.2 Case study: health effects of extremely low-frequency electric and magnetic fields and radiofrequency electromagnetic fields, response to scientific uncertainty

Public health practitioners are often asked to respond to allegations of disease clusters, especially cancer clusters, in their area. Exposure to ionizing or non-ionizing radiation is often cited as a potential cause of such clusters. Are you prepared to deal with allegations of an alleged cluster of cancer cases in people who live near a mobile phone mast or a high voltage power line?

21.2.1 Power frequency electromagnetic fields

The electric power distribution system and electrical appliances produce extremely low-frequency (ELF) EMFs as separate electric and magnetic fields. There have been concerns that ELF EMFs may be associated with childhood leukaemia. Epidemiological studies have tended to focus on workers, who are easier to study and may have higher exposures. However, some information is available for adult members of the public and for children.

An epidemiological study first suggested an association between childhood cancer and electrical wiring configurations near homes in 1979. The difficulties of metrology and

dosimetry have led to uncertainties and limitations in this and the subsequent studies so they are often difficult to interpret. Research has focused on the carcinogenic potential of ELF EMFs at power frequencies (50 Hz in the UK). Surrogates for accurate personal exposure measurements, such as proximity to sources, spot measurements, or job title, are often used. The lack of consistency of reported effects between studies compounds these uncertainties.

21.2.1.1 ELF EMFs and cancer

There is evidence that exposure to power frequency magnetic fields above 0.4 μT (microtesla, a measure of magnetic flux density and hence the strength of the magnetic field) is associated with a small increase in the absolute risk of leukaemia in children, from about 1 in 20,000 to 1 in 10,000 per year. The vast majority of children are exposed to time-weighted average residential magnetic fields lower than 0.4 μT , so the hazard, even if causal, could not cause the disease in most children affected. Draper et al. (2005) suggested that proximity of residence at the time of birth to high-voltage power lines was associated with an increased risk of childhood leukaemia (by a factor of about 1.7 if born within 200 m from a power line). If causal, this would correspond to about five attributable cases of childhood leukaemia per year in the UK (about 1% of all cases). However, the distance from power lines is a poor proxy of magnetic field exposure. There is no convincing evidence linking EMFs with other cancers, and in particular with lymphoma and brain tumours in children, and with leukaemia, brain tumours, or breast cancer in adults. A review by Schüz and Ahlbom (2008) concluded that there is no biological mechanism to explain the increased risk of leukaemia in children after exposure to power frequency magnetic fields and no support for a causal link in experimental studies.

In the absence of clear evidence of a carcinogenic effect in adults, or of a plausible mechanism from experiments on animals or cells, the epidemiological evidence is currently not strong enough to justify a firm conclusion that magnetic fields cause leukaemia in children. Chance or bias cannot be ruled out as an explanation for the observed association. Nevertheless, the International Agency for Research on Cancer (IARC) judged power frequency magnetic fields (ELF-EMFs) to be ‘possibly carcinogenic’ to humans, based largely on studies of childhood leukaemia only (IARC 2002). IARC considered there was inadequate evidence for excess cancer risks of all other kinds, in children and adults. More recent studies have not changed this conclusion.

21.2.1.2 Other health outcomes

The findings from studies of health outcomes other than cancer have generally been inconsistent or difficult to interpret. There are suggestions that occupational exposure to magnetic fields may be associated with an increased risk of neurodegenerative disease (Advisory Group on Non-ionising Radiation (AGNIR), 2001). In particular, an increased risk for Alzheimer’s disease has been reported in railway workers and also in people living close to high-voltage power lines. People employed in electrical occupations may have an increased risk of developing amyotrophic lateral sclerosis; however, this could be due to effects of

electric shocks rather than any effect of chronic exposure to ELF EMFs. Studies of Parkinson's disease, multiple sclerosis, cardiovascular disease, suicide, and depressive illness show no consistent indications of increased risk with exposure to EMFs. Overall, the evidence for non cancer and reproductive effects is weaker than that for childhood leukaemia.

21.2.1.3 Response to scientific uncertainty about the health effects of ELF EMFs

In 2004, the UK's former National Radiological Protection Board (NRPB 2004a) recommended:

The government should consider the need for further precautionary measures in respect of exposure of people to EMFs. In doing so, it should note that the overall evidence for adverse effects of EMFs on health at levels of exposure normally experienced by the general public is weak. The least weak evidence is for the exposure of children to power frequency magnetic fields and childhood leukaemia.

In 2004, a stakeholder consultation process called SAGE (Stakeholder Advisory Group on ELF EMFs) was set up led by the Department of Health in England with funding from the electricity industry and a medical charity. SAGE's objective was to bring stakeholders together to identify the implications of a precautionary approach to ELF EMFs and make practical recommendations for precautionary measures which were consistent with the level of risk and uncertainty.

SAGE produced 'interim' assessments covering powerlines and property, wiring in homes, electrical equipment, and appliances in homes (SAGE, 2007). The second interim assessment covered electricity distribution networks and discussions on aspects of the scientific evidence base (SAGE, 2010). The most important finding for public policy was that prohibition of building new powerlines near (within tens of metres) of existing homes and vice versa was not justified by the magnitude and uncertainty of the hazard and cost of the intervention.

SAGE recommended that more public information be published and that the UK HPA (successor to the former NRPB) was the logical body to develop it in collaboration with the same range of SAGE stakeholders. A more intangible outcome of the work of SAGE was increased trust between groups who differ profoundly in their interpretation of the scientific evidence.

21.2.2 Radiofrequency fields

The widespread adoption of mobile telecommunication systems has caused concern about possible health effects associated RF fields, particularly in children (IEGMP, 2000; NRPB, 2004b; AGNIR, 2012).

In general, the exposures from using mobile phones are much larger, by several orders of magnitude, than those from proximity to mobile phone masts or wireless networks (Wi-Fi). Exposures from individual pieces of equipment, including mobile phones, have generally fallen over time due to improvements in the technology and the drive to use the radio spectrum as efficiently as possible. However, the number of RF devices in use has greatly increased in recent years.

21.2.2.1 Radiofrequency field exposures and cancer

Epidemiological studies have been conducted on workers and members of the public exposed to RF fields by using phones, living near television and radio transmitters, and working with RF sources. However, the quality of these studies is very variable: some studies have been limited by low statistical power or a lack of exposure measurements, while others may have been affected by bias (NRPB, 2004b).

The evidence from the more methodologically sound studies, including recent studies of mobile phone users, does not indicate that RF fields increase the risk of cancer (IEGMP, 2000; NRPB, 2004b; Ahlbom et al., 2009; AGNIR, 2012). However, the evidence is not conclusive or consistent. In particular, the studies have not been able to provide evidence about risks after around 15 years of exposure because mobile phones have only been in widespread use for about this long. Results of the INTERPHONE study, an interview-based, 13-country (including UK), five-continent case-control study using a common protocol have been influential (INTERPHONE Study Group, 2010). The study included 2708 glioma and 2409 meningioma cases and matched controls. It is the largest case-control study of mobile phone use and brain tumours so far. Overall, no increase in risk of glioma or meningioma was observed with use of mobile phones. There were suggestions of an increased risk of glioma at the highest exposure levels, in subjects who reported usual phone use on the same side of the head as their tumour. However, this finding could be attributable to recall bias which may affect the self-reported side of mobile phone use, especially in people with unilateral disease. This bias would be expected to raise risks for ipsilateral use of the phones (i.e. on the same side of the head on which the tumour arose) and reduce risks for contralateral (opposite side) use of the phones while the true risks would be around unity, which is indeed what was found in the INTERPHONE study. Selection bias is also an issue with the controls participating in the study (they used phones more than the general population) and this has led to overall apparent relative risks less than unity (protective effects) for mobile phone users versus non-users. These and other biases limit the strength of the conclusions that can be drawn from INTERPHONE and prevent a causal interpretation.

Ecological studies do not provide any substantial evidence of an association between residential exposure near television or mobile phone masts and cancer risk. Distance from the source may not be a valid proxy for exposure but is often used in such studies without regard for other more intense exposures from, for example, personal use of mobile phones or cordless phones. Other weaknesses of studies around RF broadcast transmitters include: ecological design, lack of measured field levels, lack of data on confounders, and post hoc investigations undertaken because a cluster of cases has been observed. For example, a raised risk of childhood, but not adult, leukaemia was reported with proximity to a high-power radio station near Rome. However, these findings were based on small numbers of cases and a pre-defined 'cluster'. The findings contrast with earlier UK studies around radio and television transmitters, where there was some indication of increased risk with increasing proximity for incidence of adult leukaemia but not childhood leukaemia (NRPB, 2004b; AGNIR, 2012).

Case-control studies conducted in South Korea and Germany showed no association between exposures to RF electromagnetic fields emitted from broadcast towers and childhood leukaemia risk (Schüz and Ahlbom, 2008). Also, a case-control study in Great Britain found no association between the risk of early childhood cancers and estimates of the mother's exposure to mobile phone base stations during pregnancy.

21.2.2.2 Electrical sensitivity

A number of people report a range of symptoms attributed to RF or other types of electromagnetic fields. Symptoms include dizziness, headache, nausea and fatigue, loss of memory and concentration, skin rashes, and diabetes (HPA, 2005). These symptoms are undoubtedly real and distressing. Scientific studies have failed to provide support for an effect of RF fields on self-reported symptoms, while they have provided evidence that a placebo effect (an adverse non-specific effect that is caused by expectation or belief that something is harmful) may play a role in symptom formation. WHO advises that treatment of affected individuals should focus on the health symptoms and the clinical picture, and not on the person's perceived need for reducing or eliminating EMF in the workplace or home. Behavioural approaches show promise but are not generally acceptable to sufferers who believe that such treatments are only applicable for psychological or psychogenic problems.

21.2.2.3 Mobile phones and driving

Talking on a mobile phone while driving is a distraction that impairs the driver's ability to control their vehicle and to react to changing road conditions (IEGMP, 2000; NRPB, 2004b). Mobile phone use while driving is associated with a significantly increased risk of involvement in an accident during the call and for several minutes afterwards. The risks are similar whether the phone is hand-held or hands-free.

A survey carried out in England in 2009 shows that the use of hand-held mobile phones by drivers has been gradually increasing since 2007 despite the introduction of increased penalties (Walker, 2010). The author considered that mobile phone use will become an increasingly common cause of road accidents and that there is evidence that using a mobile phone while driving has the greatest impact on young, inexperienced drivers and on older drivers.

Overall, no disease or condition has been causally linked with exposure to RF fields at levels below the internationally accepted exposure guidelines. RF fields have been classified as 'a possible carcinogen to humans' by an IARC Working Group, mainly using data on glioma (a malignant type of brain tumour) from mobile phone case-control studies (IARC, 2011). However, the existing data have limitations and some combination of chance, bias, or confounding cannot be ruled out with reasonable confidence. Further studies are required to resolve this uncertainty. The only consistent detrimental effect is associated with the use of mobile phones while driving.

21.3 Responding to queries about cancer clusters allegedly caused by non-ionizing radiation

The foregoing provides information to help respond to general public enquiries about the health effects of exposure to power frequency and RF electromagnetic fields from mains

electrical power, mobile phones, phone masts, or Wi-Fi equipment. If a cluster of disease, attributed to a particular electromagnetic cause, is alleged, as well as following the guidance in Chapter 18 the following should be considered in the response:

- ◆ Exposure guidelines have been adopted to protect people from the known adverse effects of electromagnetic fields. Guidelines are enabled practically through planning policy, health and safety legislation, and product standards.
- ◆ There are thousands of papers in the scientific literature about the health effects of electromagnetic fields. However, not all studies are of equal quality which must be taken into account before reaching conclusions based on single studies. It is possible to select papers to construct a case to support any given position. Authoritative national and international expert bodies have undertaken comprehensive reviews of the scientific literature, which have achieved a wide degree of consensus. However, there are websites and other media providing advice of variable quality which can appear contradictory, confusing, or frightening.
- ◆ Adverse health effects, if they exist at all within exposure guideline levels, are likely to confer very small relative and absolute risks, or risks that do not become apparent for longer than mobile phones have been in widespread use; otherwise they would already have been detected. Therefore small-scale underpowered investigations based around individual clusters are rarely justified, especially if overall illness rates in the locality are unremarkable.
- ◆ Epidemiological studies are often let down by poor assessments of electromagnetic field exposure. In general, residential proximity to a particular perceived electromagnetic field source may be a very poor marker of individual exposure.
- ◆ Careful explanation of how people are exposed to electromagnetic fields and the results of the most comprehensive and authoritative scientific reviews can go a long way to reassuring people. Expert national and international bodies such as the UK HPA can help in this respect.
- ◆ Common symptoms have not been linked to exposures to electromagnetic fields in double-blind studies.
- ◆ There is strong evidence that mobile phones are distracting while driving.
- ◆ The NRPB and SAGE reports have some information about precautionary measures that can be taken if people want to limit their exposures to power frequency or RF electromagnetic fields. This includes the extant precautionary advice from the HPA and UK government that children should limit their use of mobile phones to essential calls only and that precaution may be warranted to protect children from higher than average power frequency magnetic fields at home (NRPB, 2004a; 2004b).

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Heatwave plan evaluation

Catriona Carmichael and Graham Bickler

Learning objectives

- ◆ To appraise the importance of extreme events such as heatwaves for public health and health protection.
- ◆ To evaluate the role and options for policy evaluation in the context of extreme events using the rapid evaluation of the Heatwave Plan for England (Johnson and Bickler, 2007) as a case study.

22.1 Introduction

In their recent report, The Intergovernmental Panel on Climate Change (IPCC) concludes that, from their climate model projections, it is *very likely* that heatwaves will increase in frequency, duration and/or intensity over most land areas (IPCC, 2012). Although no universal definition of heatwaves exists, a heatwave is frequently described as a period during which the daily maximum temperature of more than 5 consecutive days exceeds the average maximum temperature (1961–1990 daily average) by 5°C (Frich et al., 2002). Thresholds for heatwaves will vary between geographical regions as mean temperatures differ and human adaptation to heat occurs over time (Department of Health (DH), 2011).

Heatwaves can have significant impacts on public health (DH, 2011). In the European heatwave of 2003, there were an estimated 30,000 excess deaths, of which 15,000 were in Northern France and 2000 in the UK (United Nations Environment Programme, 2003; DH, 2011). Following this heatwave, the DH launched England's first National Heatwave Plan in 2004 (DH, 2011). The plan outlines a four tiered 'Heat-Health watch' alert system based on Met Office triggered temperature forecasts. The alerts are cascaded to health service providers and those who are in contact with vulnerable groups who in turn initiate particular actions (DH, 2011). In view of the public health impact that these events can have, and the consequent development of country-specific heatwave policies and guidelines, it is essential that their effectiveness is evaluated.

22.2 Case study

Following a level 3 heatwave in July 2006, at the request of DH, the Heatwave Plan for England was evaluated by the Health Protection Agency (HPA). This chapter will give an overview of this evaluation, highlighting its importance, value, and potential application to other extreme event policy plans including cold weather and flooding.

22.3 Background to heatwaves

22.3.1 What are the potential health impacts of heatwaves?

Increases in temperature have the potential to compromise the human body's ability to maintain thermoregulation and can thus affect health (Kovats and Hajat, 2008). Heat-related health impacts range from mild heat-related illnesses to potentially severe consequences and death. Mild conditions include dehydration, heat cramps, heat oedema, heat syncope, and heat rash (DH, 2011). Severe dehydration, heat exhaustion, heat stroke, cardiovascular and respiratory disease exacerbation, and death are cited as some of the severe consequences (DH, 2011). Excessive exposure to heat can also lead to reduced productivity and impact negatively on efficiency and mental concentration which can result in an increase in accidents (World Health Organization Regional Office for Europe, 2004).

22.3.2 Who is at particular risk of heat-related illness?

Although exposure to excessive heat can affect anyone, some people are more vulnerable from exposure to heat than others (DH, 2011). Vulnerabilities include the extremes of age, residents in nursing and care homes, chronic illness, obesity, those with an inability to adapt their behaviours (including those with physical disabilities), users of certain medications, physically strenuous occupations necessitating working outside, athletes training in hot weather, and urban dwellers (World Health Organization Regional Office for Europe, 2004; DH, 2011). During the 2003 heatwave, urban areas such as London were particularly affected by the urban heat island effect which is defined as a variation between urban and rural temperatures due to atmospheric and surface impacts (Environmental Protection Agency, 2008) with temperature differences between London and the surrounding rural areas exceeding 9°C at some points (HPA, 2011).

22.4 The national heatwave plan

The Heatwave Plan for England was developed to assist organizations in the planning, preparation for, and response to heatwaves (DH, 2011). It aims to do this through publication of information and epidemiology on the impacts of heat on health, activation of a 'heat health watch system' (HHWS) (DH, 2011) and associated actions. Different temperature thresholds are in place for different areas of England because of evidence showing there are regional differences in the impacts of specific temperatures (DH, 2011). The HHWS comprises four alert levels:

- ◆ Level 1—awareness (all summer preparedness).
- ◆ Level 2—alert (60% risk of heatwave in 2–3 days).

- ◆ Level 3—heatwave (heatwave temperature reached in one or more regions).
- ◆ Level 4—emergency (heatwave for 4 or more days in two or more regions).

When threshold temperatures are forecast and/or met, alerts are generated by the Met Office (UK) and cascaded to health, social care, and voluntary organizations. The plan provides information, roles, and responsibilities specific to each of these levels (DH, 2011).

The plan is updated annually and revised following evaluation seminars and stakeholder engagement. It is published with supporting information which includes fact sheets on supporting vulnerable groups, advice for care home managers, and information for health and social care professionals (DH, 2011).

During July 2006, for the first time since the publication of the Heatwave Plan for England, a level 3 heatwave occurred and appropriate alerts were cascaded by the Met Office (Johnson and Bickler, 2007). On 4 July, the level 3 alert was issued to five regions, shortly followed by an alert to all nine English regions on 19 July (Johnson and Bickler, 2007).

22.5 Evaluation of heatwave plans

Evaluating extreme event policies, plans, and response such as those developed for heatwaves can be undertaken in a number of ways using quantitative and/or qualitative methodologies. Salisbury et al. (2011) found from a range of interviews that good evaluations shared a number of design, evaluator, and reporting characteristics (Salisbury et al., 2011). These included appropriate design, clear aims (and commitment to these aims), expertise within the evaluating team, good communication between the evaluation and policy teams, clear conclusions, good use of timetables, concise methodology, and comprehensible findings (Salisbury et al., 2011).

They also highlighted conflicting priorities and restraints in the conduction of policy evaluation, highlighting that methodological rigor as favoured by the researchers needs to be balanced with the requirement of providing users with rapid, applicable findings (Salisbury et al., 2011).

Various evaluations have been carried out on HHWS and heatwave plans demonstrating the wide range of aims, objectives and methods possible in policy evaluation. Evaluations have used methodologies which explore the attitudes, behaviours, and perceptions of key target groups, studies which aim to investigate the barriers to heatwave plan implementation experienced by health and social care services, and studies to assess HHWS value for money through economic cost–benefit analysis. Some evaluations focus on entire summers while others focus on actual heatwave events.

22.6 Health Protection Agency evaluation of the Department of Health National Heatwave Plan

The aim of this rapid evaluation was to make recommendations and improvements to the plan through a mixed methods approach focusing on three main areas (Johnson and Bickler, 2007). It aimed to provide an overview of the morbidity and mortality epidemiology over the period, assess levels of awareness and plan implementation, and identify the needs of those who use it (Johnson and Bicker, 2007).

The evaluation was split into the following three main areas:

1. Routine data study.
2. Questionnaire-based study.
3. Multiagency stakeholder seminar.

22.6.1 Routine data study

The first part of the evaluation was an epidemiological study aiming to analyse the routinely available data available on temperatures, mortality, and morbidity for the 2006 heatwave period. Temperatures, broken down into day and region, were provided by the Met Office. Mortality analysis included deaths associated with high temperatures and those associated with air pollution (Johnson and Bickler, 2007).

The Real-Time Syndromic Surveillance team within the HPA provided an analysis of NHS Direct calls (the National Health Service's telephone consultation and advice service—Chapter 11) and general practitioner consultation data (from the Qsurveillance database). NHS direct data was analysed in order to show the number of calls for heat/sun stroke as a proportion of total calls made to NHS direct (all sites). The Qsurveillance data was then used to look at clinical diagnoses known to be associated with heat.

22.6.2 Questionnaire-based study

The second section of the evaluation focused on a questionnaire-based study designed to assess awareness of the plan and the overall impacts of the plan on key organizations with roles and responsibilities at alert level 3 or above. Five sectors were targeted with telephone-based questionnaires through purposive non-random sampling: Strategic Health Authorities (SHAs), Primary Care Trusts (PCTs), Acute NHS Trusts, Health Protection Units (HPUs) of the HPA, and Commission for Social Care Inspection (CSCI) Inspectors. Questionnaires were developed that were appropriate to each setting and included both open ended and closed questions. The questions related to Heatwave Plan awareness, contacting vulnerable groups, actions taken during the heatwave and organizational capacity to disseminate heatwave alerts (Johnson and Bickler, 2007).

22.6.3 Multiagency stakeholder seminar

A seminar was organized to develop an expert consensus view. Those invited included a wide range of experts representing the voluntary sector, health and social care sector, government departments, academia, and independent organizations responsible for standards, clinical guidance, and the promotion of good health.

The seminar began with presentations of the results of the epidemiological study and questionnaires. A summary of seasonal summer weather for England and Wales during 2006 was provided by the Met Office. Attendees then worked in smaller breakout groups to explore, in a structured manner, the key issues related to heatwaves, health, and action plans (Johnson and Bickler, 2007).

22.7 Results of the case study (heatwave plan evaluation)

Results of the three-part evaluation were generally encouraging, revealing a high awareness of the 2006 summer heatwave and the plan. Responses to the plan were also very positive with many key organizations stating that the plan had assisted their response.

The routine data study showed an overall positive association between weekly temperature and weekly death counts over the summer period, with a linear regression coefficient corresponding to 75 extra deaths for each degree in temperature elevation ($p = 0.026$) in England with no time lag between the two (Leonardi et al., 2006). The feedback and analyses gained from this evaluation suggested the 2006 heatwave was less severe (both in terms of impacts and weather) than the heatwave of 2003 (Leonardi et al., 2006). However, it was not clear what proportion of the recorded mortality was attributable to other factors related to increased temperature and air pollution. High temperatures are linked to increases in small diameter air particulate matter (PM₁₀; fine particles with aerodynamic diameter <10 µm) and higher levels of ozone due to chemical reactions with sunlight (DH, 2011). These are both linked to increased cardiovascular and respiratory mortality (DH, 2011).

Four distinct peaks in heat/sun stroke calls to NHS Direct (as a proportion of total calls) were found in the syndromic surveillance analysis. Mapping the proportion of these calls against central England temperatures over the same period showed that calls increased during the periods of recorded high temperatures/activation of levels 2 and 3 of the heatwave plan. This demonstrated the sensitivity of these syndromic surveillance systems to detect the impacts of extreme events such as heatwaves. Results from these surveillance systems can be used in post-event analysis to evaluate the impact of extreme heat (Johnson and Bickler, 2007).

The questionnaire survey showed that ‘about half’ of CSCI inspectors reported that the majority of the Care Homes they had visited had made some appropriate adaptations to their plans. The majority of SHAs stated that the plan was clear and concise and also offered a number of constructive suggestions for further improvements to the plan. Awareness of the plan was high amongst PCTs with 67% satisfied that lists of vulnerable people were drawn up at practice or other local level over the heatwave period. However, from this 67%, only two-thirds were confident that the vulnerable individuals were actually contacted during level 2 alerts and above (Johnson and Bickler, 2007).

Feedback showed that alerts jumped from level 1 to 3 (missing level 2) on 75% of times a level 3 heatwave alert was met. A degree of fluctuation between levels was noted to be inevitable because they are based on forecasts. However, organizations acting on these alerts noted the challenges imposed on them when the forecasts change frequently and skip level 2. As a result, they reflected that the threshold for level 2 was possibly set too high (Johnson and Bickler, 2007).

During the seminar, the most important topics on heat and health were debated in a lively discussion on what conclusions could be drawn and what recommendations should be made (Johnson and Bickler, 2007).

22.8 Recommendations

The HPA evaluation led to a number of recommendations to improve the DH plan. These included improvements to the communication of heatwave alerts to responders, revisiting definitions of and expectations for caring for vulnerable individuals, and strengthening the out-of-hours services to ensure smooth communication of alerts. A reduction in the threshold set for a level 2 alert was therefore proposed as a response to the difficulties faced by organizations due to fluctuating alert levels over short periods of time.

Areas for further research were also highlighted, including epidemiological studies on heatwaves and associated health impacts and research to determine the most appropriate ways to evaluate interventions. The value of establishing a baseline prior to further epidemiological analysis of morbidity and mortality was also recommended for future studies (Johnson and Bickler, 2007).

It was agreed that annual heatwave seminars with stakeholders would support the regular updating and revisions of the plan. Finally, heatwave evaluations will always be difficult as extreme heat events can't be predicted. This could be overcome by producing 'ready to use' evaluation protocols and tools which could be utilised shortly after a heatwave has occurred.

22.9 Limitations

Detailed analysis of the heatwave was not possible because the evaluation team had to use weekly mortality statistics due to the lack of daily death data. Weekly data cannot be used for real-time analysis and figures are based on death registration dates which can result in delays around bank holidays. Daily mortality data would be very useful so that real-time impacts could be assessed (Johnson and Bickler, 2007). This is of particular value during heatwaves as the lag time from heat exposure to excess death is around 1–2 days (Eurosurveillance, 2005).

Qualitatively, the survey suffered from poor response rates, so the results should be handled with caution, particularly if generalizing to all organizations. Those who returned the questionnaire were probably different in some way to those who chose not to complete it, therefore biasing results. Those who returned it may already have been more aware of the plan or the effects of heat on health. Finally, stakeholder feedback is often not evidence based and expert opinion falls low on the hierarchy of evidence.

22.10 Summary

The development of heatwave plans incorporating HHWSs are important interventions designed to protect public health from increasingly frequent episodes of extreme heat. However, it is essential that their effectiveness is assessed and recommendations for improving organizational responses to a heatwave alert are garnered from those organizations who implement the plans. The rapid evaluation of the heatwave plan for England discussed here has shown how evaluation which incorporates a mixed methods approach

utilizing epidemiological and qualitative techniques can add significant value to improving the operational response of organizations that have a public health protection role.

Existing plans can be enhanced by recommendations based on frontline practice and experience of policy implementation. Heatwave plan evaluations can also strengthen the evidence base on which policy is made and improve the epidemiological evidence base of the impacts of heat and health. The techniques employed in this evaluation are transferable to other plans which have been developed to respond to the public health impacts of extreme events such as flooding and severe cold weather.

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Analysis of mental health impacts of flooding

Carla Stanke

Learning objectives

- ◆ Assess the effects of floods and their mental health impacts.
- ◆ Appraise the use of epidemiology in analysing the mental health impacts of flooding.
- ◆ Evaluate methodological complexities related to interpreting, analysing, and comparing epidemiological studies on the mental health impacts of flooding.
- ◆ Use epidemiological methods to evaluate research gaps on the mental health effects associated with flooding.

23.1 Introduction

Over the past 30 years, it has been reported that flooding killed more than 200,000 people and affected more than 2.8 billion others worldwide (Jakubicka et al., 2010). New evidence from the Intergovernmental Panel on Climate Change (IPCC) states that it is likely (66–100% probability) that the frequency of heavy precipitation will increase in the 21st century over many areas of the world, with medium confidence that projected increases of heavy rainfall would contribute to increases in local flooding in some regions (IPCC, 2012). IPCC also states that it is very likely (90–100% probability) that mean sea level rise will contribute to increases in extreme coastal high water levels in the future.

The health impacts associated with flooding can be direct or indirect. Direct health impacts are those which occur as an immediate result of exposure to flood water, and indirect health impacts are those which occur as a consequence of flooding. See Table 23.1 for a list of potential health impacts associated with flooding.

It is well recognized that flooding has negative effects on mental health (Ahern et al., 2005). Distress following disasters is common and in most cases is transient and does not require specialist mental healthcare; however, some people's distress may last longer and may require longer-term mental health services (NATO/EAPC, 2009). A recent literature

Table 23.1 Potential health effects of flooding

Direct	<ul style="list-style-type: none"> ◆ Drowning; heart attack; electrocution; injuries (e.g. from contact with debris in floodwater, hidden hazards within floodwater, moving possessions during flood) ◆ Building collapse ◆ Infectious disease (e.g. water, vector and rodent-borne diseases) ◆ Respiratory, skin and eye infections ◆ Chemical contamination (e.g. carbon monoxide poisoning) ◆ Drinking water shortages and/or contamination ◆ Mental health problems: short and long term
Indirect	<ul style="list-style-type: none"> ◆ Loss of access to or interrupted health care; loss of essential drug access ◆ Damage to healthcare infrastructure ◆ Damage to water and sanitation infrastructure ◆ Damage to crops; disrupted food supply ◆ Disruption to livelihoods and income ◆ Population displacement ◆ Continuing or exacerbated mental health problems due to 'secondary stressors' (e.g. dealing with insurance claims, builders, displacement)

Data from World Health Organization Regional Office for Europe (2002). *Flooding: Health Effects and Preventative Measures, Fact sheet 05/02*. Copenhagen/Rome: WHO and Ahern, M., Kovats, S. (2006). The health impacts of floods: Responding to present and future risks. In Few, R. and Matthies, F. (Eds.) *Flood hazards and health: Responding to present and future risks*, pp. 28–53. London: Earthscan.

review found that flooding can have significant effects on people's mental health, including depression, anxiety, and post-traumatic stress disorder (PTSD), both in the short and longer terms (Murray et al., 2011).

While all populations are at risk of the direct and indirect health impacts associated with flooding, certain groups are at higher risk of morbidity and mortality. Those who are already vulnerable, including children, the elderly, people with chronic illness who may require continuing care (i.e. dialysis patients), the disabled, ethnic minorities, and those with low incomes, may require special consideration during the flood response and recovery periods (World Health Organization Regional Office for Europe, 2002; Edkins et al., 2010).

23.2 Case study: UK floods of 2007

In 2007 the UK experienced extensive flooding which resulted in the deaths of 13 people; this event has been called the biggest civil emergency in British history (Pitt, 2008). The floods of 2007 were the worst ever recorded in the UK and the impacts on health were wide-ranging. The combined rainfall of 24–25 June and 19–20 July 2007 in England and Wales was unprecedented; the affected areas registered over three times as much rain as the average for the same period in the previous year. Exceptional flooding occurred in many regions: South Yorkshire and Hull were worst affected in June 2007, followed in July by Worcestershire, Gloucestershire, and the Thames Valley. The events were characterized by both fluvial (riverine) and pluvial (rainfall on water-logged ground) flooding. Box 23.1 contains a summary of the main impacts of the 2007 UK floods.

Box 23.1 The main impacts of the 2007 UK floods

- ◆ Population affected: 55,000 properties were flooded; 7000 people were rescued from the flood waters by emergency services.
- ◆ Mortality: 13 people died.
- ◆ School closures: 400,000 pupil school days were lost.
- ◆ Impacts on critical infrastructure: 350,000 people lost mains water supply for 17 days; 42,000 people were without electricity for up to 24 hours, 10,000 people were trapped on the M5, and 500 people were stranded at Gloucester railway station.
- ◆ Impacts on health care infrastructure: Tewkesbury hospital was evacuated and 20 patients were transferred to other hospitals.
- ◆ Economic impacts: the economic cost of the flooding was estimated at £3.2 billion, based on infrastructure damage (health and social costs were not included in this estimate).

23.2.1 Epidemiological study: psychosocial impact of the summer 2007 floods in England

A research team from the Health Protection Agency, Cardiff University, King's College London, and the NHS in affected areas conducted a cross-sectional study comparing the prevalence of four mental health symptoms (psychological distress, generalized anxiety disorder, depression, and PTSD) between flooded and non-flooded populations following the floods of 2007 in South Yorkshire (3 months post-flood) and Worcestershire (6 months post-flood) (Paranjothy et al., 2011).

23.2.1.1 Methods

In South Yorkshire the sampling frame included all addresses in one housing estate ($n = 347$), all addresses in one village ($n = 436$), all addresses on the local authority flooded properties register in one town ($n = 626$), and a random selection of 1252 addresses that were not on the flooded properties register.

In Worcestershire the sampling frame included all addresses in two villages ($n = 460$), all addresses on the local authority flooded properties register in two towns ($n = 533$), and a random selection of 7995 addresses that were not on the registers. As the towns had much larger population sizes than the villages, the research team sampled 15 properties not on the flooded register for every property that was on the flooded register. Non-affected households were used as controls in both areas.

Letters of invitation to participate in the survey were sent to households identified through sampling. Three methods were offered for completing the survey: telephone (via free phone number), online, or post (using a freepost envelope that was provided). Due to a low response rate in South Yorkshire, the decision was made to conduct face-to-face interviews in the two villages in Worcestershire.

Exposure variables recorded include flooding (presence of flood water in or near the home and damage to property), psychological exposure (perceived impact of the floods), and incident management variables (including disruption to essential services and evacuation).

Standard validated instruments were used to assess the prevalence of mental health symptoms. Symptoms measured include psychological distress (using the General Health Questionnaire GHQ-12, score of 3 or more), probable generalized anxiety (Generalized Anxiety Disorder GAD-7, score of 10 or more), probable depression (Patient Health Questionnaire PHQ-9, score of 10 or more), and probable PTSD (PTSD checklist-short form, score of 14 or more).

Data analyses were carried out using STATA version 10. Researchers first examined the univariate relationship between all the exposure variables and mental health symptoms; they then used multivariate logistic regression to describe the association between water levels in the home and mental health symptoms, adjusted for the following potential confounding variables: age, sex, presence of an existing medical condition, employment status, area (defined as South Yorkshire or Worcestershire; there is a difference in socio-economic status between the two areas), and method of data collection.

23.2.1.2 Results

A total of 2265 people responded to the invitation to participate in the study (38% from South Yorkshire and 14% from Worcestershire). The mean age of responders was 50 years in South Yorkshire and 57 years in Worcestershire; people under 36 years were under-represented and people over 50 years were over-represented. A higher proportion of females responded to the survey, and at least half of respondents reported that they had lived in their area for at least 15 years.

People who reported flood water in the home had a significantly higher prevalence of mental health symptoms (psychological distress 69%, probable anxiety 48%, probable depression 43% and probable PTSD 22%) compared to individuals who did not have flood water in the home (psychological distress 14%, probable anxiety 5%, probable depression 7%, and probable PTSD 2%) ($p < 0.01$ for difference in proportions for each outcome).

There was a strong association between the presence of flood water above floor level in the home and each mental health measure. This association changed little after adjusting for age, sex, employment, prior health status, area of residence, and data collection method. Symptoms of psychological distress, probable anxiety, probable depression, and probable PTSD were three to five times higher in South Yorkshire compared to Worcestershire in univariate analysis; these symptoms were significantly higher among women, unemployed people, and those with prior medical conditions.

After adjusting for the perceived impact of the floods and evacuation variables, odds ratios for 'water above floor level in the home' were reported as 5.0 for psychological distress (95% confidence interval (CI) 3.4, 7.3), 4.8 for probable anxiety (95% CI 3.0, 7.8), 2.6 for probable depression (95% CI 1.6, 4.3), and 3.9 for probable PTSD (95% CI 1.9, 7.8). Following adjustment for explanatory variables, concern that the floods would affect

people's health was associated with an odds ratio of 3.0–4.7 for the mental health symptoms; disruption to essential services was associated with odds ratios of 1.8–3.1. Evacuation was associated with psychological distress (odds ratio 1.7; 95% CI 1.2, 2.5) but not significantly with the other three mental health symptoms in the adjusted analysis.

23.2.1.3 Discussion

The results from this study contribute to a growing body of epidemiological evidence on the health impacts of flooding, specifically the effects on mental health. Findings are consistent with other UK studies examining the impact of flooding on mental health. Mason et al. (2010) report that among flood-affected adults, 27.9% met criteria for symptoms associated with PTSD, 24.5% for anxiety, and 35.1% for depression. Another study found a fourfold increase in psychological distress following flooding among flooded households compared to non-flooded households (Reacher et al., 2004) and another found that 'problems with insurers' were a predictor of psychological distress and PTSD following flooding (Department for Environment, Food and Rural Affairs/Environmental Agency, 2004). A longitudinal study (follow-up of persons affected by the 1998 flood in Oxfordshire) found participants reported continuing psychological effects that they attributed to the experience of being flooded (Tapsell and Turnstall, 2008).

23.2.1.4 Limitations

Limitations of the study include heterogeneity in population profile (South Yorkshire is more deprived than Worcestershire), timing of the survey following flooding (3 months for South Yorkshire versus 6 months for Worcestershire), different methods of data collection, low response rates, and lack of ascertainment of how pre-flood mental health affected post-flood mental health.

23.3 Methodological complexities

Flood definitions are useful for triggering the activation of an emergency response and for assessing the impacts of floods, including health-related impacts, yet there is no universal definition of what constitutes a flood. While the definition of flooding was not addressed in the Paranjothy et al. (2011) study, it is worth noting this deficiency. Flooding in different contexts, measured and defined in different ways, with different triggers for emergency response, can influence the design and outcomes of epidemiological research, and this should be considered when comparing studies of similar design and intent.

In their review of the literature on the mental health effects of flooding, Murray et al. (2011) report a number of methodological complexities in conducting research and analysing and comparing data. Challenges to interpreting and comparing data include:

- ◆ The lack of universally agreed statements about the definitions used when researching disasters; the authors found that people may use different terms to describe people's experiences, responses, and mental disorders.
- ◆ Varying methodologies used across the studies that were reviewed.
- ◆ The broad range of mental disorders that are described and assessed in the literature.

- ◆ Diversity in the covariants that different researchers have assessed.
- ◆ The use of a variety of different diagnostic measurement tools.
- ◆ Complexity when classifying the nature of each flood and the exposed population.

The authors found no consistent association between risk factors and covariants with poorer mental health across the reviewed studies; this could be due to methodological differences and the unique characteristics of each flood. Lack of baseline information on the mental health morbidities of a given population makes comparison before and after flood events difficult.

These methodological complexities are relevant for the Paranjothy et al. study when considering the results within a wider context of other epidemiological studies which examine the effects of flooding on mental health. While the results showed significantly higher levels of mental health symptoms (recorded by validated measurement tools) amongst people whose homes had been flooded, other studies, conducted in different contexts (i.e. with different flood characteristics, different populations, using different measurement tools with different lengths of time following the event, and perhaps different definitions of mental health symptoms), may show similar results, yet careful consideration is needed when comparing studies and generalizing the conclusions.

23.4 Knowledge and research gaps

There are a number of gaps in knowledge. More studies are needed on the short- and long-term impacts of flooding on mental health, and studies which distinguish normal distress from symptoms of mental disorders following flooding disasters. Further research should emphasize the use of internationally agreed definitions of mental health and mental ill health and consistently used methods for comparing research findings (Murray et al., 2011).

23.5 Learning points

- ◆ Epidemiological studies have created a growing evidence base on the health impacts of flooding, including the effects on mental health. Evidence has demonstrated that flooding has detrimental effects on people's mental health, both in the short- and longer-terms.
- ◆ Despite a number of studies which have quantified the impact of flooding on mental health, a number of methodological challenges exist. This makes comparison of studies difficult.
- ◆ Further research should utilize internationally agreed definitions of mental disorders and standardized tools for assessing mental health symptoms.

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Chemical incidents

Virginia Murray

Learning objectives

- ◆ Synthesize the key issues in identifying and defining chemical incidents.
- ◆ Synthesize the main issues in response to chemical incidents.
- ◆ Discuss methods of environmental epidemiology used in chemical incident response.
- ◆ Assess the epidemiological evidence for the health effects of chemical incidents.

24.1 Introduction

Every day, serious chemical incidents occur which threaten the health of the population (World Health Organization (WHO), 2009). A chemical incident is the unexpected release of a substance that is (potentially) hazardous either to humans, other animals, or the environment. Chemical releases arise from technological incidents, the impact of natural hazards, and from conflict and terrorism. Examples include chemical fires such as burning tyres which release clouds of toxic smoke; acid leaking out of a tanker creating noxious gas leading to chemical contamination of the environment; the deliberate release of chemicals and poisons; or an explosion at an industrial plant.

The International Federation of the Red Cross has estimated that between 1998 and 2007, there were nearly 3200 technological disasters, including chemical incidents, with approximately 100,000 people killed and nearly 2 million people affected (WHO, 2009). Severe incidents have the potential to disrupt the lives of affected people through injury, bereavement, loss of property or employment, and societal disruption.

Chemical incident response requires assessment of risks and impacts to determine what type of response may be required and if an emergency response may be required. The first task is hazard identification—identification of the chemicals involved in the incident and potential health hazards summarized from published information. Consideration of dose–response (Chapter 9) and environmental exposure assessment (Chapter 8) information is then needed to define how people could come into contact with chemical(s) (pathway). Information on health effects reported amongst those exposed leads to emergency response management choices. The management of chemical incidents requires a

multidisciplinary and multisectoral approach—the health sector may play a supporting or a leadership role at different stages.

Chemical incidents can cause injury through four basic injury mechanisms which may coexist in a single incident:

- ◆ Fire produces injuries through heat and exposure to toxic substances (including combustion products).
- ◆ Explosion produces traumatic (mechanical) injuries through the resulting shockwave (blast), fragments and projectiles.
- ◆ People may come into direct contact with a chemical released from its containment be it from storage or in transport, or as reaction or combustion products. Chemicals cause harm by a range of toxic mechanisms, including chemical burns, asphyxiation, and neurotoxicity.
- ◆ Mental health effects are not only determined by exposure to the chemical, fire, or explosion but also by ‘exposure to the event’ itself and may be independent of toxicological effects.

24.2 Case study: the Buncefield explosion and fire, UK, 11 December 2005

The explosion at the Buncefield Oil Storage Depot in Hertfordshire, UK caused what was reported to have been the largest fire in Europe since the Second World War. The incident began with a major explosion on Sunday 11 December at 06.01.32 UT, triggered by the ignition of approximately 300 tonnes of unleaded petrol which had overspilled from a storage tank (Mather et al., 2007). A number of explosions occurred with at least one of the initial explosions being of massive proportions. A large fire engulfed a high proportion of the site and by the end of the incident 21 storage tanks had been damaged or destroyed. The chronology and details of the incident have been summarized in progress and final reports of the Buncefield Major Incident Investigation Board (BMIIB) (2008a, 2008b, 2008c).

24.3 Chemical incident response planning

Preplanning is key to preparing the response to a chemical incident. At country level it is important to have in place a national ‘all hazards’ emergency management coordinating group, with plans and trained staff. Planning should be meticulous. These structures need to be mirrored at local level to ensure adequate technical response. It provides an opportunity to understand and integrate the roles and responsibilities of health professionals, agencies, and organizations that are part of the response. The Civil Contingencies Act, 2004, with its accompanying non-legislative measures, delivers a single framework for civil protection in the United Kingdom which is aimed at making us capable of meeting the challenges of the 21st century. Local needs and logistics can heavily influence the organization of major incident strategies and plans. The development and use of emergency plans should be assessed by regular emergency planning meetings. Many of these

activities can be facilitated by local emergency planning officers in the health services, local authority, or industry.

Plans can be divided into the following areas: anticipation, assessment, prevention, preparedness, response, and recovery. The last four are briefly described here.

Prevention: this section of the plans allows for improved incident documentation and response audit to identify strategies to reduce future incidents. It should also include hazard prevention, surveillance, and identification of incidents, and the development of strategies to reduce hazards, including education.

Preparedness: plans for chemical incidents should include active preparation in a number of areas, e.g. arrangements for patient decontamination. Health and safety issues for responders and personal protective clothing provision should be included in plans and documented by availability and location. Other areas that should be considered include general biological and environmental sampling requirements that may be needed during incidents.

Response: chemical incident plans should include all the documentation likely to be needed during the response including incident logs; check lists and material related to generic and specific sampling; public safety and clean-up measures. Health system emergency capacities need to include facilities to decontaminate, if necessary, and to treat casualties whilst organizing chemical incident surveillance if required.

In summary during emergency response it is important to include the following:

- ◆ Terminate the release as soon as possible.
- ◆ Prevent spread of contamination and limit human exposure.
- ◆ Activate the incident management system, including the public health response.
- ◆ Provide initial assessment and advice, and alert the health care services.
- ◆ Ensure coordination and integration of the public health response.
- ◆ Conduct a best outcome assessment for both immediate and long-term actions.
- ◆ Disseminate information and advice to responders, the public, and the media.
- ◆ Register all exposed individuals and consider if an environmental epidemiology study may be required and how this will be done.

Recovery: recovery is about getting back to 'business as usual' in the shortest time and at least cost. Recovery also includes reviewing the incident and auditing the response, legal proceedings, and feedback on processes (lessons identified).

Implementation of command and control mechanisms: for major (or any) chemical incident response, health protection and public health professionals act as the interface between clinical health care and the overall incident management. In the UK, it is health protection professionals may attend (Fig. 24.1) the operational, tactical, or strategic incident meetings, the Science and Technical Advice Cell, or even the Cabinet Office Briefing Rooms (UK HM Government, 2010).

Risk assessment for a chemical incident: an incident risk assessment starts as soon as the first information about the incident becomes available. It is not a one-off exercise but a continuing process and is updated as the situation unfolds and as more information

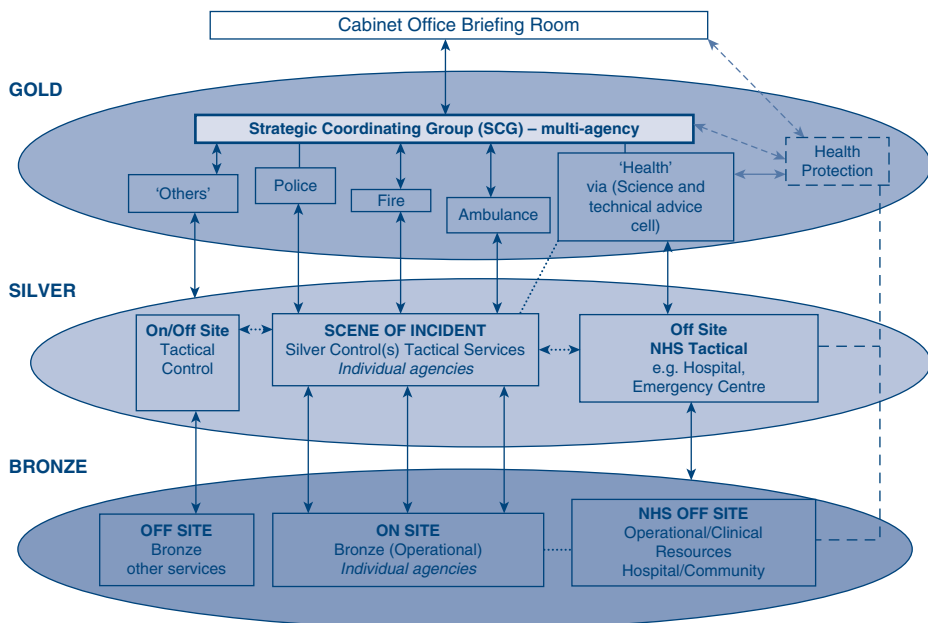


Fig. 24.1 Command and control at operational, tactical, and strategic meetings with the role of the Health Protection Agency summarized. NHS = National Health Service; PCT = primary care trust.

Adapted with permission from *Chemical Hazards and Poisons Report*. From the Chemical Hazards and Poisons Division, June 2006 Issue 7. Available from http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1194947315694.

about the incident and hazards become available. The potential hazard of a chemical is a function of its toxicity and exposure (Baker et al., 2012). The latter is a function of both the chemical bio-available concentration and time. Circumstances and environmental factors can affect any or all of these factors, making a risk assessment a complex process (Baker et al., 2012).

Once an incident has occurred and been recognized, a preliminary evaluation of risks and assessment of hazards, using the source–pathway–receptor model, must take place in conjunction with the health protection professionals. The circumstances surrounding an incident are crucial to making an informed evaluation. The key details are the nature and amount of the chemical or toxin involved, its toxicity (known human acute and chronic effects), transmissibility, storage, degradation, and persistence factors (dilution, dispersion, diffusion) (Chapter 9).

Details concerning mixtures of chemicals are also important because they can lead to unexpected effects, making an assessment more complex (Baker et al., 2012). The incident type is also part of the assessment, e.g. was the incident a fire, explosion, transport accident, spill or leak, malicious act, air, water, or land pollution, waste, food, or medicine contamination? Another important factor is the timescale of the incident and whether it is acute or chronic.

Other information needed includes any reactions observed between the released material and the environment, as well as the number of exposed or symptomatic casualties, any relevant clinical details, and the route or routes of exposure (contact and cutaneous absorption, inhalation, or ingestion).

Data about potentially hazardous chemical processes, which are part of routine operation at the site, are highly valuable (e.g. information about manufacturing, storage, transport, or waste disposal). Other useful information includes where required the exposure conditions and site details, including location, meteorological conditions (atmospheric and temperature conditions, rivers, and tides), topography (housing, schools, hospitals, nursing homes), agriculture and food chain factors, industry and transport, population factors (susceptible groups), and any sentinel cases or clusters.

Finally, information on environmental or biological assays, specific antidotes, and treatments can be important. All this information is used to formulate an assessment and extrapolate the probability of short- and long-term toxicity for the hazard exposure.

24.4 **Buncefield explosion and fire incident response**

At Buncefield, the first of a series of explosions occurred at the oil depot early on Sunday 11 December 2005, which resulted in a huge fire producing a massive smoke plume that could clearly be seen over London and the south-east of England. The explosions were felt in the local area, causing widespread structural damage to commercial and residential buildings, and were reported to have been heard as far away as the Netherlands. Indeed Mather et al. (2007) reported that impulsive waves from the explosion were recorded by British Geological Survey seismometers up to 300 km away.

A major incident was declared by 09.00 hours on the Sunday and the command centre (Strategic Co-ordinating Group, SCG) set up (HPA, 2006). This SCG took the decision to evacuate people with damaged homes and workplaces, and to tell everyone under the plume to shelter, 'go in, stay in, tune in' (Kinra et al., 2005). The fire burned for several days, destroying most of the site and emitting large clouds of black smoke into the atmosphere that travelled over the south of England and towards Europe.

During the incident the SCG called on many organizations and government agencies to help the emergency services in the response. During the first 48 hours or so further explosions occurred and the fire continued until it was finally under control by the evening of Wednesday 14 December (HPA, 2006).

At the time of the fire the Met Office provided details of the plume direction and spread through visual observations, satellite images, and computer modelling. The weather conditions were stable which allowed the smoke to rise to the higher levels of the atmosphere and be trapped there. Information on air quality both around the site and throughout southern England was collected by a number of agencies, including fire brigades, local authorities, and the Health and Safety Laboratory. Soil and grass samples were also collected and analysed to support the air quality data by identifying whether any chemicals from the smoke had fallen onto the ground. Fortunately, due to the heat generated by the

fire and the favourable local wind and weather conditions, the impact of the fire on the local population outside the evacuation zone was minimal (HAP, 2006).

The HPA provided local staff to support the incident and national experts in chemical hazards and emergency response. This team worked very closely with the local Primary Care Trusts to provide advice and help on any potential health impact of the incident and to monitor this. The immediate concern was to assess the risk to health and provide advice on how to reduce any threat to people in the vicinity. The health impact during the incident was monitored by using reports from hospital Emergency Departments (EDs), general practitioners (GPs), and NHS Direct to identify people suffering from breathing problems or any other symptoms associated with the fire (HPA, 2006). A relatively small number of people attended EDs. Of the 244 patients who attended three-quarters were emergency services staff and of all those attending, 90% were sent home without needing follow-up; most of the others had minor injuries, and although over 40 people were injured, there were no fatalities.

24.5 Occupational health surveillance after the Buncefield Oil Depot fire, UK, December 2005

It was apparent that because of ongoing local anxiety about potential toxic hazards from exposure, it would be important to set up a register of emergency service personnel responding to the fire. The emergency services in Hertfordshire with Hertfordshire County Council and the HPA East of England Regional Epidemiology Unit established an Occupational Health Working Group to set up a register following the fire (Eastern Region Public Health Observatory, 2007). HPA facilitated the work of the group, the development of an occupational health exposure and illness questionnaire, the establishment of a Buncefield Fire Occupational Health Register database and epidemiological analysis of the data.

The case definition for individuals to be included in the register was that they were occupationally deployed to or near the Buncefield Oil Depot fire site between 11 December 2005 and 5 January 2006, covering the burn phase from 11–14 December and the clean-up and recovery phase from 15 December to 5 January. All the occupational health departments who looked after staff deployed to the Buncefield fire site were thus identified. A register questionnaire was distributed by each occupational health department and an anonymous copy of each completed questionnaire was sent to the HPA East of England Regional Epidemiology Unit for entry into a database.

A total of 51 organizations deployed staff to the incident site: 35 fire services, 10 public sector organizations, three voluntary organizations, and three private companies. Of the 1834 eligible individuals from participating organizations, 815 (44%) returned the study questionnaire. Of these, 660 individuals were deployed during the burn phase (11–14 December 2005) with almost three-quarters deployed inside the inner safety cordon. Three-quarters of respondents reported inhalation of smoke, fumes, or particles, 85% smelled smoke and/or chemicals, with about two-fifths reported using respiratory protective equipment. During the burn phase, 41% of 660 individuals reported at least

one symptom: irritation to the nose (20%, 130), throat (26%, 174) and eye (21%, 139), coughing (21%, 138), and headaches (16%, 105).

Twenty-six ED attendances were reported in the cohort (3%) and a further 12 (1.5%) consulted their GP after the fire. An occupational health review was provided for 22 individuals (3%). Reassuringly, only 2% (18) individuals took time off work, 2% (15) noted any subsequent ill effects, and 4% (32) reported feeling anxious about their health.

In conclusion the proportion of respondents on the occupational register reporting health symptoms was higher during the burn phase than the control and clean-up phase. Compared with the general public, reports of eye irritation, coughing, and headaches were more common during the burn phase, but there was no difference between the general public and individuals deployed only during the control and clean-up phase. Few individuals sought health care as a result of their deployment. As a result the findings from the Occupational Health Register suggest that deployment to the Buncefield fire was not associated with major acute health symptoms. Follow-up of individuals included in the Buncefield Occupational Health Register was not recommended because of the mild nature of their acute symptoms.

From these findings as well as other investigations, it was concluded that there was no evidence of a public health risk from the plume either when airborne or as a ground deposit. Local population surveys showed a drop in the level of anxiety amongst the public from approximately 50% at the time of the incident to 13% about 7 weeks after the event.

A wide range of organizations and resources are required to support the response and recovery from major chemical incidents such as Buncefield. Following the court case the Judge Sir David Calvert-Smith said: 'Had the explosion happened during a working day, the loss of life may have been measured in tens or even hundreds.' (BBC, 2010). The cost of this event has been put at UK £1 billion.

24.6 Conclusions

Chemical incidents happen daily, The International Federation of the Red Cross has estimated that between 1998 and 2007, there were nearly 3200 technological disasters, including chemical incidents, with approximately 100,000 people killed and nearly 2 million people affected (WHO, 2009).

Effective planning, routine response framing and exercising, as well as command and control are essential for successful incident response. Timely communications and specialist health protection support are also important. The scale of the response may differ between incidents but public and worker safety together with advice to speed recovery remains at its heart.

Environmental epidemiology is an invaluable tool in helping to determine health impacts. The occupational health surveillance following the Buncefield explosions and fire demonstrated the feasibility and usefulness of large-scale, harmonized, anonymous occupational health follow-up after major incidents in the UK. Similar approaches should be considered in the future and mechanisms set up to facilitate them.

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Odour incidents and epidemiology

Helen Smethurst

Learning objectives

- ◆ Appraise the importance of odour incidents for public health protection.
- ◆ Evaluate the use of the Odour Complaints Checklist in analysing the health impacts of exposure to odours using an incident case study.
- ◆ Assess the use of epidemiology in analysing exposure to odours.

25.1 Introduction

Complaints concerning odour are common and have been reported in association with regulated activities such as waste disposal, waste water treatment, and industrial installations. The presence of odours can also be an early warning indicator of incidents such as spills, leaks, and accidents or be a sign of the deliberate release of chemicals into the environment.

Environmental odours can be unpleasant and may cause a reduction in the quality of life of those who experience exposure. In some cases, no serious health effects occur because of exposure to odours, whilst in other situations, odours may represent a proxy for exposure to a serious hazard to health. The human nose is very sensitive to odorants and responds to the presence of odorous chemicals in the air at extremely low concentrations and within about a second (Jacob, 2006). Odour thresholds, i.e. levels at which perception occurs, may lie at concentrations that are orders of magnitude lower than levels that produce adverse health effects, yet symptoms are often reported at these low levels (Shusterman, 1999; Schiffman, 2005). Furthermore, humans vary considerably in their sensitivity and objectivity to odour, hence introducing a wide range of possible perception scenarios. The health protection issues relating to odour complaints and incidents are therefore undeniably difficult to address.

Studies on populations and individuals have demonstrated that exposure to environmental odours can result in varying degrees of annoyance or odour nuisance and frequently include reports of health effects, such as headaches, nausea, and respiratory complaints (Shusterman, 1991; Schiffman, 2004). In the most extreme and tragic examples, exposure to odorous chemicals can cause human deaths, with the toxic properties

causing fatalities rather than the odour itself (e.g. the inhalation of the pungent smelling toxic chemical methyl isocyanate in the Bhopal tragedy).

In order to assist with the early investigation of odour complaints and to inform any subsequent epidemiology studies, an ‘Odour Complaints Checklist’ has been developed by the UK’s Health Protection Agency (HPA). The checklist is primarily intended for staff in the HPA; public health practitioners at Health Protection Units and Local Health Boards; Public Health Bodies in the Devolved Administrations; and Environmental Health Officers who may be asked to deal with local odour-related health complaints.

25.2 The Odour Complaints Checklist

The underlying philosophy of the checklist is to assess exposure to odours and to evaluate public health outcomes. The checklist can be used as an aid to determine the location of an odour source, to establish the nature of the odour and to estimate exposure via a robust risk assessment process. Information collected in the checklist allows management decisions to be made, defines the appropriate level of response, and can support communication of the assessments made. The checklist can also be used as a tool to collect data which has the potential to be used for subsequent epidemiological studies.

The checklist is available as an online resource consisting of a list of structured questions and associated guiding information (HPA, 2011). The checklist is broken down into six sections:

- ◆ Sections 1–3 contain a list of pre-defined questions.
- ◆ Section 4 offers recommendations for the acute phase of odour incident response.
- ◆ Section 5 details the legislative requirements for odour control and provides information on the roles of the regulators (the Environment Agency and/or local authority).
- ◆ Section 6 offers recommendations for post-incident investigation.

The checklist also contains two appendices:

- ◆ Appendix 1 contains information regarding odour characteristics and detection thresholds for a number of common chemicals.
- ◆ Appendix 2 details the sensory effects of odour and gives the guideline values based on annoyance reactions, as set by the World Health Organization (WHO) (2000).

The question sections of the checklist (Sections 1–3) are phrased to act as an aide-memoire and guide the health practitioner in extracting the necessary information from the person reporting the incident. This is important as odour incidents are complex and varied, requiring specific information to allow an appropriate risk assessment to be made. The questions were devised in order to obtain sufficient information to populate the source–pathway–receptor conceptual model (Chapter 9). The checklist questions are structured into sections:

- ◆ Section 1—to identify the hazard(s) by ascertaining the nature and source of the odour.
- ◆ Section 2—to identify and consider the pathways for potential exposure.
- ◆ Section 3—to gain information regarding receptors in order to characterize the risk.

The questions are used to focus incident data on being descriptive in a way that can help to find the source and the location of the odour. This is an important feature of the checklist, as odour may be an indicator of a more serious threat to public health. Knowing, at the earliest stage of the investigation, the origin of the odour and/or what the actual odour is, can be extremely important information for preventing further exposure and harm.

Odour incidents are multifaceted and the specific questions are used to determine the exact characterization of the odours involved. Questions regarding the odour intensity, pleasantness or unpleasantness, and descriptions are designed to tease out the different characteristics of the odour being investigated. Odours are unique entities and therefore these data should allow categorization of the risks.

The connection with the source–pathway–receptor model, Sections 1–3 of the checklist, act as an intrinsic standard that allows future analysis of the odour incident with the completed answers being recorded onto a database. By ticking the check boxes on the list, the health practitioner dealing with the incident knows that a minimum amount of sufficient information has been gathered. Depending on the answers given to the questions posed, the health practitioner is guided to additional information that is provided in the checklist (Sections 4–6).

25.3 Case study: strange odours in south-east England

This incident case study started on the morning of Friday, 18 April 2008, as people were making their way to work, and led to numerous reports of unusual odours/smells being made to the HPA, Guys & St Thomas' Poisons Unit, the UK Met Office, and the BBC. The reports came from many locations in London and the south-east, suggesting that there had potentially been a wide-scale pollution event. No casualties were being reported at this time although the general public were 'concerned' as to the cause of the unpleasant smells. Several individuals who reported the smell initially speculated that the origin was local but began to become anxious when the smell remained even after they had travelled some distance from the place of initial detection.

25.3.1 Early investigations

During the early investigations of the incident the Odour Complaints Checklist was used to gather information to try to identify the source and the cause of the odour and hence determine the risk to public health. The checklist was used to collect incident-specific data regarding receptors, i.e. the various reports of odour perception and the potential pathway, i.e. the prevailing meteorological conditions, in an attempt to determine a likely source.

25.3.1.1 Meteorological conditions

Due to the high volume of calls received, the Met Office carried out analysis into the potential source of the smell. A press release was issued stating 'over the last few days, we've had fresh, strong winds from an easterly direction. As a result some of our air is coming from continental Europe'. The press release concluded 'that the likely explanation

was either agricultural or industrial works in western Europe' (BBC, 2008). The National Farmers Union (NFU) also issued a press release (18 April 2008), in which they stated that the odour was caused by Dutch farmers slurry spreading en masse at the end of the winter no-spread period (NFU, 2008). Surface pressure charts for 17 April 2008 shows relatively tight near-surface isobars over southern England, indicating that wind speeds were relatively high which implies that any polluted air would have been transported quite rapidly from the continent to the UK.

As odours were reported simultaneously from other areas of the UK, it is natural to look for a large source region where some common and concurrent activity could have generated the odorant. For example, the Met Office back trajectory maps for London (Fig. 25.1) identify the general regions within Europe from which air reached this area. This reveals that there was a large source region over northern Germany favouring the hypothesis of an emission from northern Germany as a whole, probably with additional contributions from the Benelux countries.

25.3.1.2 Potential sources

Different potential causes, other than slurry spreading, were considered based on answers given to the Odour Complaints Checklist questions, including major chemical incidents or accidents. Investigating the plume pathway for excessive pollution via observations from the UK's Automatic Urban and Rural monitoring Network (AURN) showed no major increases in any concentrations of monitored pollutants (i.e. the main regulated species). Enquiries undertaken regarding reports of odour from receptors outside the UK also proved to be negative.

25.3.1.3 Health surveillance

Health surveillance by the Local Health Protection Units of the HPA and NHS Direct showed that there were no reported clinical health effects attributed to the incident. In addition, the presence of the 'odour' in the atmosphere did not lead to an increased incidence of health complaints for 'nausea' or 'breathing difficulties' at the time of the incident (NHS Direct, personal communication).

25.3.2 Results

The evidence for slurry spreading on the continent being the cause of this incident was initially considered circumstantial. Therefore a more detailed examination of the event has taken place (Smethurst et al., 2012).

The perception of odour in areas of southern and eastern England and beyond ruled out a localized source or set of sources. Although the precise source of the odour was not determined and probably will never be, the evidence strongly suggested that the cause was widespread agricultural slurry spreading in Belgium, the Netherlands, and, in particular, northern Germany. Odorous emissions associated with these activities were transported by converging air flow over Germany and relatively strong and steady easterly winds to the south-east of the UK, where their arrival coincided with thousands of people who commuted to work on the morning of 18 April 2008. No reports or evidence of any other

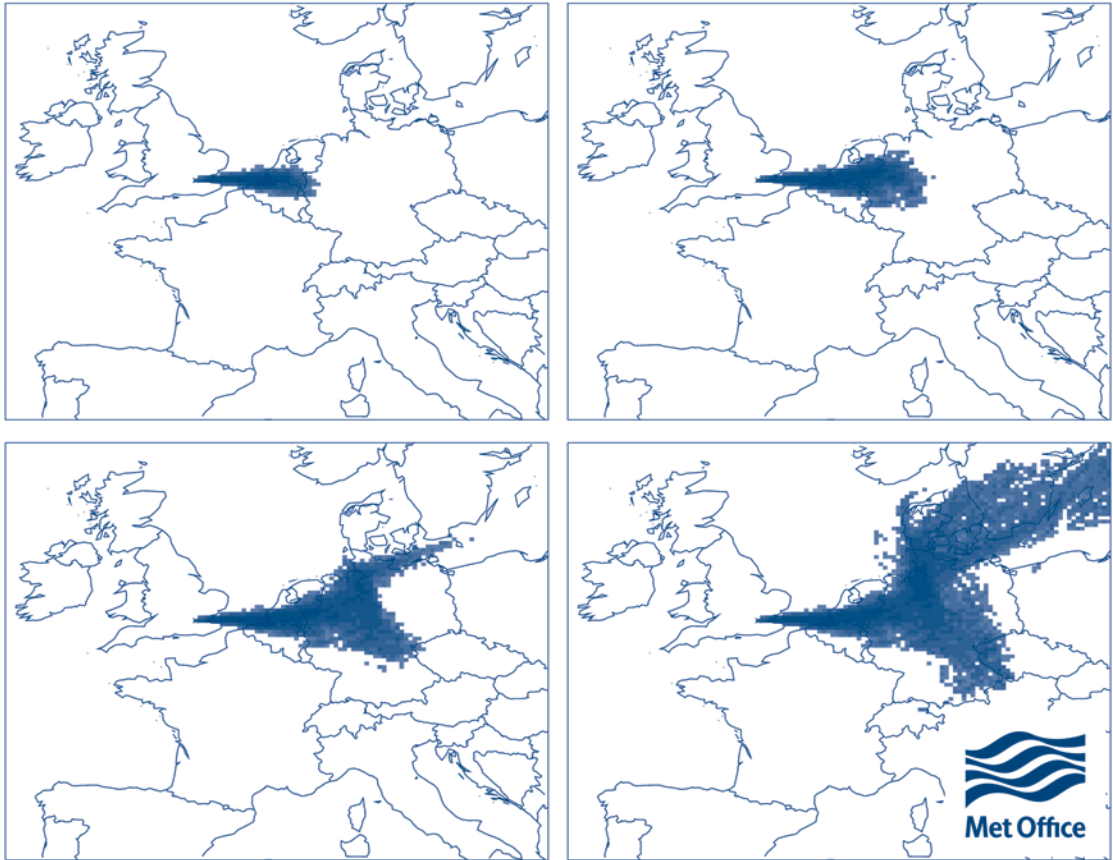


Fig. 25.1 Maps of the source regions of air contributing to London within the (a) 6, (b) 12, (c) 24, and (d) 48 hours leading up to 08:00 UTC 18 April 2008. Maps produced by the Met Office using the Numerical Atmospheric dispersion Modelling Environment NAME.

pollution incident or causal mechanism were found and the more detailed analysis supported the conclusions reached at the time. This was that favourable weather conditions during mid April 2008 encouraged mass slurry spreading in north-west Europe and this was the likely source of the odour plume. The analysis showed that with a combination of the wind conditions at the time, plausible levels of slurry spreading activities, and resulting emissions would explain the event. However, the variability in many of the parameters that were involved in determining the source terms is such that similar events are by no means certain whenever similar meteorological conditions arise.

The detailed analysis illustrates how a combination of Met Office data and the geographical distribution of odour complaint reports can be used to back track pollutant plumes to identify likely source areas. It also illustrates how forward modelling can be applied using both complex and simple models to explore the veracity of the conclusions from the back trajectory study and identify the uncertainties in source–pathway–receptor modelling. This approach will assist in attaining an accelerated response should similar events arise in the future and help in the management of such events.

25.4 Discussion and lessons identified

The philosophy of the source–pathway–receptor conceptual model used in the odour checklist was extremely important for this case study. The initial evidence populating the model was focused towards the receptor, with numerous reports of odour perception without health symptoms. Gathering data about the locations of the receptors suggested that the area affected was large. Whereas the timing of the odour reports indicated that the complaints were connected, reports featuring different odour descriptions conflicted with this assumption.

An important finding for the HPA during this event was that collating evidence from all sources helped to resolve some of the initial uncertainty regarding the cause and facilitated the provision of timely advice. Analysis of the pathway via dispersion modelling was invaluable in this event, substantiating the odour reports and suggesting possible sources. The results of the initial modelling implied that the odour emission must have been concentrated at source in order for perception at distance. It was safe to say that the levels of odour in the atmosphere would have been sufficiently diluted so as not to cause health effects. Therefore, from this point onwards the public were informed that threats to health were minimal.

25.5 Summary

The rational principle of the Odour Complaints Checklist was tested in the incident of strange odours in the south-east of England, where detailed investigations were undertaken in order to ascertain the source, or potential source, of the odours, the pathway, and the impact at exposed receptors and has been found to be very useful. The investigation at the acute stage of the incident was focused towards early assessment and determination of the public health risk and making informed decisions based on the available information. Whilst the general public were not at risk during this incident and the event

was short lived, there was a clear need to investigate further. Additional and more comprehensive investigations have revealed a source for the odours and modelling of the pathway has revealed a plausible dispersion mechanism. The investigation has also shown that similar events may have occurred previously, although have not been examined, and that comparable circumstances could occur in the future.

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Decision model for an investigation

Irene A. Kreis and David A. Griffiths

Learning objectives

- ◆ Identify the key players, including the public stakeholders, in determining a public health concern, who will be involved in the decision-making process and any communication needs.
- ◆ Break down the public health concerns into relevant stages for investigation:
 - To formulate the questions that need answering at each stage of the investigation.
 - To determine if the investigation needs to continue or can be stopped.
- ◆ Define the methods, as described in other parts of this book, which would be needed to tackle a practical local health protection problem.

26.1 Introduction

The most difficult problem in environmental epidemiology and public health in general is to decide when and how much to investigate a public health concern. Most of the previous chapters describe public health responses after the decision to investigate has been made. This case study illustrates how to make the decision to investigate. This is a complex and therefore difficult process.

Various techniques and frameworks have been proposed to aid the process of the ‘need to investigate or not’ decision. All these methods divide problems into stages. One such tree, designed for the investigation of clusters, is described in Chapter 19 (Health Council of the Netherlands, 2001) but others have been described for non-cluster situations (e.g. Connor, 1999).

To make a decision the following process, summarized in Fig. 26.1 with clear yes/no determinants, can be valuable:

- ◆ Orientation stage—this asks the questions: what is the problem, who has identified it, where is it, why is it there, is it still going on? Review the health and exposure signals using background research from the literature and the target illnesses occurrence in the population of interest. Ensure the exposure pathways are also assessed. Talk to those concerned, particularly the public, to clarify the issue. Specific data collection is not required at this stage.

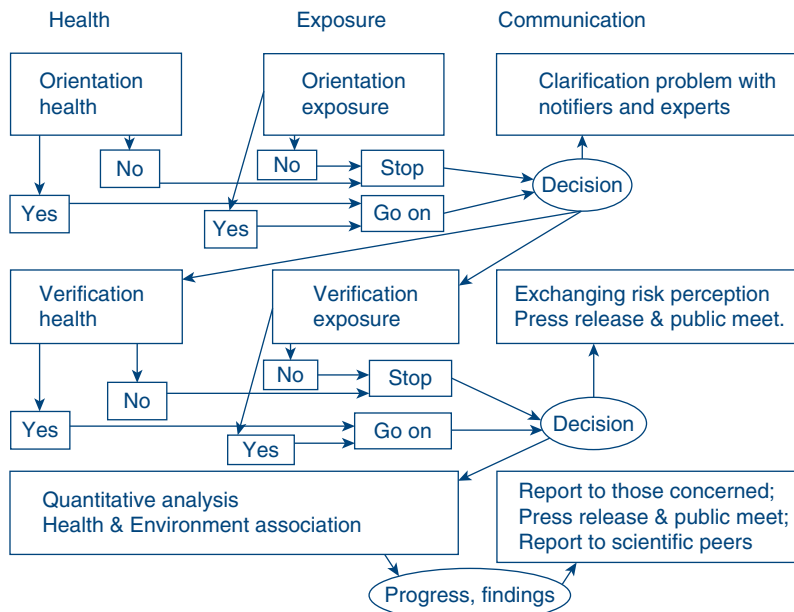


Fig. 26.1 Decision tree or step-wise staged approach to investigating a public health concern.

- ◆ Verification stage—this focuses on the evaluation of any appropriate routinely collected data, recognizing that both health and exposure information should be taken into account. Data verification is required at this stage.
- ◆ Quantification stage—this phase is intended to address the specific question raised in the verification stage and as agreed to being important by the stakeholders. This phase also can be separated into environmental and epidemiological components but the balance depends on the problem identified.

Of vital importance is the need to maintain communication channels with those who raised the concern as well as all other stakeholders, who would routinely include local health, environment, and civil authorities. This communication must run in parallel to the listed stages and be open and transparent (Fig. 26.1).

26.2 Case study

A health issue occurring around heavy industry in a small community is used to illustrate a common type of problem faced by a local public health practitioner. The location is Corrimal, part of the city of Wollongong, which is approximately 80 km south of Sydney, Australia. The neighbourhood has grown up around a coke works, a traditional beehive set of ovens which has been there for 100 years. Improvements have been made to the operations of the works over time, generally having the effect of reducing pollution. As the coke works used to generate electricity as a by-product, houses were built in relatively close proximity. The neighbourhood expanded around the coke works. Nowadays, the process is automated so very few people work there.

Coke works are dusty enterprises at each stage of the process: with the transfer of coal from the mines into the ovens, transfer of coke from the ovens into stockpiles, and transport out of the factory. The process uses the fumes generated by heating the coal as a fuel source but some emissions are inevitable. When the coke works are operating effectively, the main emissions are due to filling and emptying the ovens and to quenching (dowsing the coke with water). Besides (fine) particulates (dust) and depending on the amount of sulphur in the coal, hydrogen sulphide (H_2S) can be emitted which is odorous (smelling like ‘rotten eggs’). Although unpleasant, at low concentrations H_2S is not generally regarded as a danger to health.

As with most heavy industry, there are rail and road links for the transport of goods (especially coal). This transport of goods, often fuelled by diesel, generates fine particulates.

The main public health problem was frequent complaints from neighbouring communities about smell and dust. A local primary school directly adjacent to the works had repeatedly been a source of complaints.

Heightened concern arose after a particular incident at this primary school when, during morning assembly in the school yard, a steam cloud which had formed during quenching dipped (as a result of an unusual weather situation ‘inversion’), and ‘landed’ on the students. Whilst not a common occurrence, this could not be regarded as a unique event. A few students ‘fainted’ and were briefly admitted to the emergency ward of a local hospital. Until then, the local health authorities were aware of issues with the coke works but not involved as complaints had been handled by the local Environmental Protection Agency (EPA). The EPA was working with the coke works to improve the situation and reduce emissions and were legally mandated to deal with all complaints (including health). However, they had not investigated health issues because they felt that they were unequipped to do so.

26.3 Orientation to the problem

The key orientation question can be subdivided into:

- ◆ What are the characteristics of the health issue posed?
- ◆ Is this a recognized disease or syndrome?
- ◆ What are the main environmental issues in the region?
- ◆ What are the specific issues with coke works?
- ◆ What is known about health effects on workers and ambient populations?

And also:

- ◆ Who has already done what in relation to this problem?
- ◆ Who are the key stakeholders?
- ◆ Who is complaining about what?
- ◆ What communications channels are already in use?

The techniques involved in addressing these issues are predominantly described in the ‘Identifying the problem’ part of this book (Chapters 1–6) and is summarized in the rest of this section.

26.3.1 Environment and health

During the orientation phase, it became apparent that coke works have historically been recognized as work sites which are potentially occupationally hazardous but effects on local populations had also been recognized (Bhopal et al., 1994). Emissions of dust and H₂S are well defined; particularly from beehive oven coke works. Dust emissions, specifically in the form of (fine, diesel) particulates from rail and road freight traffic are typically high.

The adverse health effects of fine particulates including respiratory and cardiovascular health are well established (Sacks et al., 2011). Fine particulates generated by diesel fuels are more hazardous than those from petrol fuels. Health effects of H₂S, are also well documented by dose and duration of exposure (Morii et al., 2010).

26.3.2 Communication

At this stage monthly public meetings at the primary school adjacent to the coke works had already been organized by the city council. The meetings were attended by representatives of the coke works and the EPA. The meetings were very well attended by local residents. Some of these residents were very vocal and some organized lobby groups were engaged in the process. After the incident when school students went to the hospital emergency ward, public health professionals investigating the health impacts became essential too.

26.3.3 Decision

The conclusion from the orientation phase was that the investigations needed to be intensified. If there had not been a known or likely environmental problem or there had not been any indication of a possible health effect, the process would have stopped here. Note that the health arm and the exposure arm are present at the same time and had ‘equal’ weight. In this situation, there were indications of a problem on both the health and exposure sides.

26.4 Verification

The main question posed here is: is there an exposure and/or a health effect of relevance? The scientific literature reported adverse health effects occurring from coke works. The questions to address were the following:

- ◆ What is known about the emissions?
- ◆ What information is available from routinely collected data?
- ◆ How does this relate to accepted standards?

For the local health effects:

- ◆ Where are the complaints arising from geographically?
- ◆ How often do they occur?
- ◆ What are the complaints about?

In the verification phase, it is generally expected that only already available data (Chapter 12) are used. However, identifying such data often requires knowledge of local data resources and how these can best be used. This stage of the case study on assessing and scoping the problem uses information from this book, including the chapters on environmental measures, exposure assessment, toxicology, and risk assessment (Chapters 7, 8, 9 and 10 respectively) as well as the routine data analysis and geographic information systems chapters (Chapters 12 and 13).

26.4.1 Environment

Coke works, like all heavy industries, are heavily regulated, with obligatory self-monitoring of emissions using a sampling programme measuring particulate matter as total suspended particulates (TSP) continually for 24 hours (midnight to midnight) every sixth day. However loading and unloading of the coke ovens with accompanying quenching, occurs on average approximately four days every week. Thus the coke works are an ongoing source of emissions, not a continuous source. Analysis of the available data indicated that there were occasional breaches of the national standards. Additionally the local residents had expressed concerns about the validity of the monitoring process as it was conducted by the works themselves.

26.4.2 Health

For the health assessment, the use of routine data was not possible because:

- ◆ mortality increases were deemed unlikely
- ◆ monitoring morbidity through family doctors would have required evaluation from a large number of practitioners, each with only a few patients from the relevant location, and
- ◆ monitoring medication use (as a proxy for morbidity) through pharmacies would have required a large number of pharmacies and extraction of data relevant to the relevant population.

Sadly, a form of syndromic surveillance (Chapter 11) where routine health data collection can be modified and targeted, was not available either. However, the EPA routinely monitored complaints as it had long been recognized that Corrimal was a major source of complaints in the Wollongong area. However, the records contained little important information about the complaint event itself, e.g. the number of people affected and the reported health impacts were not noted. After the incident with the school students, the public health unit's environmental health officer requested EPA complaint records be forwarded on a routine basis. This allowed ascertainment of additional information.

The EPA complaint data were analysed over a full year, even though the complaints had existed for much longer. It was found that about 6% of the local population complained

at least once a year, which was considered to be of note. The complaints included eye and throat irritations (around 12% of complaints each), coughs, headaches, and breathing difficulties (around 10% each), and many others at much lower rates. The quenching plume was labelled by the residents as ‘acid rain’ and the complaints were attributed by the complainants to the coke works operations. The affected members of the population were largely those living to the east and north of the coke works, and consisted of about 565 households as well as schools and local businesses (Willison et al., 1996).

26.4.3 Communication

The results of the data collection in the verification stage were discussed in the public meeting. The local population and the local media were well represented at the meeting. Local residents were happy with the actions taken thus far but wanted more information.

The health authority and the EPA had been provided with limited funds to do the quantification that the population wanted. The coke works committed to support in kind.

26.5 Quantification

Remembering what the community and authorities needed to know, the main question to pose in the quantification stage is:

- ◆ What should be investigated?
When this question is formulated, decide
- ◆ What is the optimal strategy to investigate the question?
- ◆ How should this stage of the investigation relate to the previous findings?

This part of the case study relates to the ‘designing and interpreting’ part of the book (Chapters 14–18). It addresses issues of the choices in study design, population selection, logistics, sampling options, quality control, as well as budget control. Analysis of the data to be collected needs to be considered at the planning stage. Also considered are the management of expectations and effective consultation with experts (Chapter 4). The assumptions made in the process (Chapter 8) and about the ethics (Chapter 18) of various options and processes should be addressed.

Having chosen the specific research question it was important to consider the possible outcomes of the investigation if a positive or negative association between exposure and health effects was identified, and what actions would follow. These considerations were discussed at one of the routine public meetings to ensure the population understood the strengths and limitations of the planned investigation.

26.5.1 Design

The coke works investigation was a practical 6-week limited time-series study such as is classically used in air pollution epidemiology. Adult residents and school children were included in the study population. A control population was identified in a suburb to the north which was of similar socioeconomic composition, had the same train line and main road, but no heavy industry.

26.5.1.1 Health

The basic design allowed participants to complete a questionnaire about general health, normal residential/travel patterns and a daily health diary. The population were sampled in three parts:

1. The general population was contacted using a letter box drop and visit for all households. All local residents in the defined exposed and control populations were eligible and all were eventually contacted. Staggering of participation occurred because people were deliberately not contacted at the same time due to logistics. For those who agreed to participate, each kept a diary for 2 weeks during the 6-week period of investigation.
2. School children at the primary and high schools in both the exposed and control population were also enrolled. For the primary school, teachers kept daily diaries about health complaints. For the high schools, individual school pupils from year 11 (typically aged 16–17 years) were asked to keep diaries. A 6-week diary was requested from these participants.
3. The (limited) number of workers at the local train stations in both the exposed and control areas were also asked to keep a diary for the full 6-week period (Kreis and Willison, 1997).

26.5.1.2 Environment

Air pollution data for fine particulates with subsampling for polycyclic aromatic hydrocarbons (PAHs) were collected at three sites. As the coke works operate (charge, empty, and quench) between 08.00 and 12.00 in on some days of the week, air pollution sampling was conducted with a 24-hour window from 18.00 to 18.00 hours so that clean and affected days could be clearly differentiated. One air pollution monitor was very near the works to the east (less than 1 km), one a bit further way to the north (less than 2 km) and one in the control population, a few kilometres to the north. The air pollution sampling started a week before the population sampling to sort out technical issues and allow for lag-times in exposure effects.

The coke works continued to collect routine monitoring data every sixth day a short distance north-west of the coke works (about 0.5 km). They also collected weather data and information about operational matters on site. These data were made available for the study.

26.5.2 Results

The analysis was designed to compare working days at the coke works with non-working days, taking into account actual air pollution levels and rates of complaints. In practice, some effects on the upper airways of residents and particularly primary school children of extremely high pollution days were seen, but the identified associations were weak. The air pollution levels were too influenced by other (e.g. transport) air pollution sources as well as (probably) re-emissions from the stockpiles and other dust sources. Response rates were low but for this intensive requirement acceptable (ca. 45% collected in both

areas and an additional ca. 10% of residents contacted and agreed but not collected in both areas) (Kreis and Willison, 1997).

The results showed weak association between health effects and environmental exposures associated with the coke works. When these results were shared with the stakeholders, the community felt that they had been taken seriously and the people at the coke works felt included in the team trying to deal with the issues. This was a positive outcome of the study, despite weak statistical findings.

As a result of the process, the management of the coke works became more willing to accept that there was a potential health issue. Previously they had been convinced that complaints reflected a mild form of ‘mass-hysteria’. As a result of this study and the associated review, the coke works investigated the quenching plume and found that it contained measurable levels of H₂S. Prior to this the coke-works staff thought it was ‘pure’ steam. Following the study the quenching water was treated continuously and the sulphur smell became markedly less noticeable. The manager even noted that he could now enjoy wine which he ‘never could before’. Thus the environment was improved even though the study did not demonstrate an association.

26.5.3 Communication

A specific public meeting was held when the study was launched with the details discussed in this meeting. It was decided at that time by those present that, if the levels of complaints were not found to be significantly raised or if no pattern in the health complaints could be related to the exposure data, then these results would demonstrate a limited health issue, and the investigation would be terminated.

When the results became available, they were also presented to the public meeting. They were accepted as informative and the progress of the management of situation by the coke works was discussed. As the limitations of the investigation had always been presented honestly, the lack of a clear result did not come as a surprise. The effort taken and the information gathered were still seen as useful.

26.6 Conclusion

The case study used here illustrates the steps that can be taken in response to an environmental public health issue and related them to the methods described elsewhere in this handbook. Usually, not all investigative steps are needed, but clear recording of the reasons for decisions is vital. Investigations, even to the level of a full-flung epidemiological study, often have useful community spin-offs, particularly if communication channels are kept open in the course of the investigation. If all involved are learning about what can and what cannot be proven, what the real issues are, and what remedial actions are possible/necessary then a widely acceptable solution is achievable.

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