International Archives of
Occupational and Environmental Health
Supplement

Peter N. Lee

Misclassification of Smoking Habits and Passive Smoking

A Review of the Evidence

With 14 Tables

Springer-Verlag
Berlin Heidelberg New York
London Paris Tokyo

Peter N. Lee
17 Cedar Road
Sutton, Surrey SM2 5DA, United Kingdom

ISBN-13:978-3-540-19425-5 e-ISBN-13:978-3-642-73822-7
DOI:10.1007/978-3-642-73822-7

Library of Congress Cataloging-in-Publication Data. Lee, Peter N., 1943- Misclassification of smoking habits and passive smoking: a review of the evidence / Peter N. Lee.
p. cm.
ISBN-13:978-3-540-19425-5 (U.S.)
1. Lungs - Cancer - Etiology - Research - Evaluation. 2. Passive smoking - Health aspects - Research - Evaluation. 3. Tobacco habit - Health aspects Research - Evaluation. I. Title. RC280.L8L43 1988 616.99'424071 - dc19 88-22442

2119/3140-543210 - Printed on acid-free paper

Summary

Based on the observation in some studies that non-smokers have a higher incidence of lung cancer if they are married to smokers, it has been claimed that passive smoking increases lung cancer risk. Considering the very low exposure to smoke constituents received by non-smokers, the increase in lung cancer risk seems implausibly high and possibilities of bias have to be considered. One theoretically important source of bias is misclassification of smoking habits, but scientific opinion has disagreed about its practical importance.

This monograph reviews this issue by bringing together relevant information from a number of sources.

The monograph starts by looking at the relative effects that different types of smoking habit misclassification have on biassing the association between lung cancer and passive smoking. It is shown that random misclassification of non-smoking subjects as smokers and of their spouse's smoking habits are relatively unimportant sources of bias, but that misclassification of smoking subjects as non-smokers is a potential source of major bias. It is important to quantify not only the extent of this type of misclassification, but also whether its magnitude depends on the amount smoked by the subject and on whether the spouse smokes.

The monograph considers ways in which information on the accuracy of smoking habits can be collected, factors which might affect reported smoking habits, and general and specific problems related to the use of various objective markers of smoke uptake.

The main part of the monograph consists of a detailed literature review on the evidence of misclassification. Studies involving objective markers, based on determination of carbon monoxide, thiocyanate, nicotine and cotinine levels are considered, as well as those involving multiple subjective smoking habit reports on the same individual.

In all, some 100 different studies have been reviewed. Despite the various study designs and populations involved a number of clear conclusions can be reached.

(a) Even in circumstances that are apparently similar quite a wide variation in the extent of misclassification can be found.

(b) The proportion of "non-smokers" subsequently found actually to be smokers is markedly higher in smoking cessation studies than in studies where the respondent is under no special pressure not to smoke.
(c) The proportion of "non-smokers" subsequently found actually to be smokers is also markedly higher in lung cancer patients than in the general population. This is not surprising in view of the overall a priori expectation that a lung cancer patient actually is a smoker.
(d) Studies of "non-smokers" without lung cancer and under no special pressure not to smoke suggest that around 4% are likely actually to be current smokers. While not all studies provide information on the extent to which such misclassified smokers smoke, and those that do indicate many of them are occasional smokers, it seems that 1 to 2% of self-reported non-smokers are regular smokers.
(e) In addition to these misclassified current smokers there are a somewhat larger number of ex-smokers misclassified as never smokers. Available information suggests that these tend to have smoked less and a longer time ago than average ex-smokers.
(f) None of the studies have investigated whether the extent to which smokers deny smoking depends on whether their spouse happens to smoke.

In attempting to relate these findings to the specific epidemiological studies in which the association between passive smoking and lung cancer has been investigated, a number of points are evident.

(a) The strongest associations were seen in those studies reported earliest, in Japan and Greece, but even now there is virtually no information on the extent which smoking habits might be misclassified in these populations.
(b) Generally the papers describing the studies reviewed in this monograph provide insufficient detail for the reader to assess fully the circumstances under which the smoking habit data were collected. However, it is notable that the smoking data appeared to be collected in a less detailed manner in the Japanese and Greek studies than in most of the other studies.
(c) No study of passive smoking and lung cancer has used an objective marker of smoke exposure (e.g. cotinine in saliva). Many studies have made no attempt to assess the validity of statements made, despite the fact that the information often came from a next-of-kin whose answers might have been affected by knowledge of the subject's disease, by difficulties of recall or by never having known the subject's smoking history in full.

(d) Two authors have attempted to assess the likely extent of bias caused by misclassification of active smoking habits. In Appendix B I concluded that it could explain all or virtually all of the epidemiological association between passive smoking and lung cancer. Wald et al. (1986), in contrast, concluded that it could explain only a minor part of it. Both papers were based on estimates of misclassification from a limited (and different) set of studies. The review of evidence considered here indicates the estimates used by Wald, particularly of the frequency of misclassified current regular smokers, were too low but that those I has used were consistent with the overall literature.

Overall it seems reasonable to conclude that bias due to misclassification of smoking habits provides an explanation for the association observed between passive smoke exposure and lung cancer.

Contents

Glossary of Terms

2×2 table — Where a population can be subdivided according to presence or absence of two attributes A and B, the data are often laid out in the form of a 2×2 table as follows

	Attribute B	
Attribute A	Absent	Present
Absent	a	b
Present	c	d

bias — systematic tendency for an observed value to differ from its true value.

"bogus pipeline" — technique whereby subjects are asked questions in the false knowledge that their answers are later going to be checked up on by objective means.

CO — carbon monoxide.

COHb — carboxyhaemoglobin.

concordance ratio — as used in this report, the cross product ratio for a 2×2 table where a data item is a married couple and attributes A and B are the same, one measured for the husband and the other for the wife.

cross product ratio — see odds ratio.

odds ratio — for a 2×2 table, the odds of having attribute B given attribute A is present (d/c) divided by the odds of having attribute B given attribute A is absent (b/a). This ratio can be calculated by the cross-product ratio ad/bc.

passive smoking — the inhalation of tobacco smoke other than by puffing on a cigarette, cigar or pipe. In this report passive smoking refers to passive smoking by non-smokers.

relative risk — risk of disease when factor present divided by risk when factor absent. For a 2×2 table where attribute A is risk factor and attribute B is disease, the relative risk can be estimated by the odds ratio.

RR — relative risk.

SCN — thiocyanate.

1 Introduction

1.1 Objectives

The main purpose of this monograph is to present the results of a comprehensive look at information available relating to accuracy of statements made about smoking habits, in particular about the frequency with which smokers are misclassified as non-smokers, and to illustrate the effects such misclassification can have on epidemiological studies of passive smoking and lung cancer and their interpretation.

1.2 Reasons for Study of Inaccuracy of Smoking Habits

In any epidemiological study, possible effects of inaccuracy in the recorded data should be borne in mind. This applies to the diagnosis of disease, to the assessment of exposure to the main agent of interest and also to potential confounding factors. Over the years, attention has been given to the accuracy of recorded smoking habit data for a number of reasons. These are related to doubts about whether:

(a) information obtained from a next-of-kin or other surrogate is valid,
(b) the subject himself can remember past smoking habits accurately, especially in relation to more subtle aspects such as brand smoked,
(c) subjects admit to all the cigarettes they smoked, bearing in mind the shortfall often found when estimate of total cigarettes claimed to be smoked are compared to those actually sold (Todd 1978),
(d) people attending anti-smoking clinics claiming subsequently to have given up smoking are actually telling the truth, and
(e) those who claimed never to have smoked are actually telling the truth.

1.3 Epidemiological Evidence of an Association of Passive Smoking and Lung Cancer

In recent years, the relationship of so-called passive smoking to lung cancer has received increasing attention. Following virtually simultaneous publication of studies in Japan (Hirayama 1981) and Greece (Trichopoulos et al. 1981), showing an increased risk of lung cancer among non-smokers if they are married to smokers, results from a further 13 studies have become available. These studies are described in Appendix A, and Table 1 summarises the findings.

Table 1. Summary of results from published studies of passive smoking and lung cancer

Authors	Study location	Sex	Number of lung cancers[a]	Relative risk	Significance[b]	Source of smoking habit data of subject
Prospective studies						
Hirayama (1981, 1984)	Japan	F	163	1.63	Yes	Short at-home interview with subject
		M	64	2.25	Yes	
Garfinkel (1981)	USA	F	153	1.18	No	Detailed at home self-completion questionnaire by subject
Gillis et al. (1984)	Scotland	F	8	1.00	No	Detailed self-completion questionnaire by subject during screening
		M	6	3.25	No	
Case-control studies						
Trichopoulos (1981, 1983)	Greece	F	77	2.11	Yes	In-hospital interview with subject
Chan and Fung (1982)	Hong Kong	F	84	0.75	No	Detailed in-hospital interview with subject
Correa et al. (1983)	USA	F	22	2.07	No	Detailed at-home interview with subject or next-of-kin
		M	8	2.00	No	
Buffler et al. (1984)	USA	F	41	0.78	No	Detailed at-home interview with subject or next-of-kin
		M	11	0.52	No	
Kabat and Wynder (1984)	USA	F	24	0.79	No	Detailed in-hospital interview with subject
		M	12	1.00	No	
Koo et al. (1984, 1987)	Hong Kong	F	88	1.64	No	In-depth in-hospital interview with subject
Garfinkel et al. (1985)	USA	F	134	1.31	No	Interview at hospital with subject or next-of-kin
Wu et al. (1985)	USA	F	<29	1.2	No	Detailed telephone interview with subject
Akiba et al. (1986)	Japan	F	94	1.5	No	At-home interview with subject or next-of-kin
		M	19	1.8	No	
Lee et al. (1986a)	England	F	32	1.00	No	Detailed in-hospital interview with subject
		M	15	1.30	No	
Ziegler (in Dalager et al. 1986)	USA	M		<1	No	Detailed at-home interview with subject or next-of-kin
Pershagen et al. (1987)	Sweden	F	67	1.20	No	Mailed questionnaire to subject in 1961/63 and to subjects or next-of-kin in 1984

[a] In never smoking subjects.

[b] At 95% confidence limit for exposed vs non-exposed direct comparison.

There seems to be an overall tendency for non-smokers married to smokers to have a higher risk of lung cancer than non-smokers married to non-smokers. A number of attempts have been made to combine the results from the various studies. These have given overall relative risk estimates (based on differing combinations of studies) of 1.30 (Lee 1984), 1.41 (Wells 1986), 1.2 to 1.5 (Doll 1986) or 1.35 (Wald et al. 1986), the last author finding the association to be statistically significant.

1.4 Possible Explanations for the Association

This positive association does not of course necessarily indicate a causal effect of exposure to passive smoking and, in a paper published in Human Toxicology in 1987, reproduced for convenience as Appendix B, I argued that the association might essentially be an artefact.

I pointed out in Appendix B that the epidemiologically based estimates of risk in relation to spouse smoking are much higher, perhaps by as much as 2 orders of magnitude, than would be expected based on extrapolation of results from epidemiological studies of active smoking and lung cancer using estimates of the relative levels of smoke constituents to which passive and active smokers are exposed. Because of this apparent discrepancy, and because it is well-known that the epidemiological techniques currently available are unreliable when used to assess the magnitude of weak associations (see e.g. Alderson 1983), I looked at various possible sources of bias.

1.4.1 Non-Reporting Bias

One possibility (Mantel 1987) was failure to publish studies which showed no association, the so-called "file drawer problem" described by Rosenthal (1979). Evidence that this is a real problem for randomized controlled trials has been provided by Chalmers et al. (1987), who cite results from a comparison of published and completed unpublished randomised controlled trials. Of the former, 55% showed a significant ($p < 0.05$) advantage to the new therapy and only 22% showed no difference between the therapies. Of the latter, only 15% showed a significant advantage to the new therapy and 44% showed no difference. The difference between the reporting rates for trials which showed treatment effects and those that did not was very highly significant. It is clear that the problem of non-reporting bias is likely to be as great, if not greater, for epidemiological associations, where scientists often have access to large data bases with the potential for studying numerous associations without reporting all their findings.

1.4.2 Passive Smoke Exposure Recall Bias

A second possibility of bias considered, relevant only to case-control studies, was that knowledge of disease may result in passive smoke exposure being recalled more readily by cases than controls (Kilpatrick 1987).

1.4.3 Misclassification of Active Smoking Habits

In Appendix B, I paid particular attention to a third, and more generally relevant, source of potential bias. This is caused by random misclassification of smokers as non-smokers, coupled with a tendency for smokers to marry smokers. Table 2 illustrates this bias. It was constructed using the following assumptions:

Table 2. An example of bias caused by misclassification of the subject's smoking habits

Smoking habits		Assumed data		True effects	Observed data			Apparent effects
Subject	Spouse	N	RR		N	D	RR	
Non-smoker	Non-smoker	65	1	Passive	$65+\underline{1.75}=66.75$	100	1.50	Passive
	Smoker	35	1	1.00	$35+\underline{3.25}=38.25$	100	2.61	1.75
Smoker	Non-smoker	35	20		$\underline{35}-\underline{1.75}=33.25$	665	20	
	Smoker	65	20		$\underline{65}-\underline{3.25}=61.75$	1235	20	
Non-smoker	Total	100	1	Active	105	200	1.90	Active
Smoker	Total	100	20	20.00	95	1900	20	10.50

Concordance ratio assumed $=65\times65/35\times35=3.45$
Concordance ratio observed $=66.75\times61.75/38.25\times33.25=3.24$

N = relative numbers of subjects
RR = risk of lung cancer relative to true non-smokers
D = relative numbers of lung cancer deaths (Observed N × True RR, e.g. in line 1 $100=65\times1+\underline{1.75}\times20$)
Underlined numbers are true smokers

(a) 5% misclassification of smoking by subjects,
(b) no misclassification of smoking by spouses,
(c) a relative risk (RR) of 20 in relation to active smoking,
(d) no true effect of passive smoking, and
(e) a between spouse smoking concordance of 3.45.

The misclassification has 4 consequences

(1) creation of an apparent passive smoking effect when no true effect exists ("passive smoking bias"),
(2) underestimation of the active smoking effect,
(3) slight underestimation of the concordance,
(4) the creation, among self-reported non-smokers with lung cancer, of a large proportion (50%) of true smokers.

As will be shown later, the size of this passive smoking bias depends critically on the assumed RR for active smoking, the degree of concordance and on the level of misclassification of subject smokers as non-smokers.

Many researchers assume that the general effect of random misclassification is to dilute an observed association. While true for a simple 2×2 table, the example demonstrates this is not necessarily so in more complex situations. Random misclassification may artefactually cause associations to appear stronger than they really are or to appear present when they are really absent.

1.5 First Attempts to Estimate Misclassification Bias

In Appendix B I presented findings from a number of studies aimed at estimating the size of the passive smoking bias, from which I concluded that the bias was large enough to "explain the unexpectedly high lung cancer risk associated with spouse smoking in epidemiological studies of self-reported never smokers." The most important of these studies (all of which will be referred to again in more detail in subsequent sections) was one in which a nationally representative sample of 1537 British men and women who had earlier answered questions about their smoking habits provided saliva for cotinine analysis. Of the 808 self-reported non-users of cigarettes or other tobacco products, 20 (2.5%) had cotinine levels indicative of misreporting, with 11 (1.4%) having levels typical of regular smokers.

Wald et al. (1986), in their review of the evidence of passive smoking and lung cancer, also considered the possibility of bias due to misclassification of active smoking habits, but concluded its effects were relatively minor, adjusting their overall relative risk estimates in relation to spouse smoking down only slightly (from 1.35 to 1.30) to take account of it.

1.6 Difference in Conclusions and Need for More Data

There were a number of other differences between the procedures of Wald et al. (1986) and myself (Appendix B) which might partly explain the very different conclusions. The main reason for the discrepancy, however, clearly lay in the markedly different level of misclassification inferred from the different studies, in particular in respect of misclassified current regular smoking. For this purpose, Wald used information from 4 relatively small studies, involving a total of 690 self-reported non-smokers, in which cotinine or nicotine levels had been related to statements made about smoking habits. While the overall proportion of self-reported non-smokers having cotinine or nicotine levels considered indicative of smoking (1.6% based on 11 cases) was not so different from that I had reported, Wald found only 1 subject (0.14%) with a level over 50% of that seen in average smokers.

This 10-fold difference between Wald and myself in the proportion of misclassified current regular smokers, with consequent completely contrasting

conclusions concerning the likely true effects of passive smoking, clearly shows that more data are required to resolve the issue. While I cited some other studies which had levels of misclassification as high or higher than those found in my own specially designed study, this by no means represented a full literature survey. The need to collect together information available relating to accuracy of statements made about smoking habits (in particular about the frequency with which smokers are misclassified as non-smokers) is clear, and is the main purpose of this monograph.

1.7 Misclassification Not the Only Issue

It should be remembered that misclassification is only one of a number of problems in the whole passive smoking/lung cancer issue that require more attention before any clear view of the relevance of the epidemiological association can be reached. Some of these have been referred to briefly above. Among these, accurate quantification of "dose" to the non-smoker is particularly important. While it is beyond the scope of this monograph to look at this issue, the reader is referred to Lee (Appendix B) for critical comment on Wald et al.'s (1986) view that "the magnitude of the excess (risk of lung cancer in relation to spouse smoking) seems reasonable in view of the extent of exposure."

1.8 Structure of the Monograph

The monograph is divided into 3 further sections. Section 2 considers a number of general issues, starting with a look at the major and minor sources of misclassification bias in passive smoking studies and the types of study which supply information on misclassification, and then going on to the various sources of error in determining smoking habits and the difficulties of obtaining objective data. Section 3, the main part of the monograph, summarises all relevant papers on level of misclassification, and contains the overall conclusions. For convenience, this section is subdivided into studies of various types, e.g. studies based on the use of objective markers such as cotinine, and those involving multiple reports on smoking habits for the same individual. The monograph ends, in Sect. 4, with an overview in which the relevance of the studies reviewed in Sect. 3 to the passive smoking studies summarised in Appendix A is discussed. Section 4 also highlights questions that remain unanswered concerning the misclassification problem.

2 General Considerations

2.1 Major and Minor Sources of Misclassification Bias in Passive Smoking Studies

In Appendix C the mathematical theory behind misclassification in passive smoking is discussed in some detail. Two situations are considered. The first is the 2×2 table, where the true proportional division by smoking habits of the subjects and their spouses is as follows:

Subject	Spouse	
	Non-smoker	Smoker
Non-smoker	N_1	N_2
Smoker	N_3	N_4

and the between-spouse smoking habit concordance is defined as $C = N_1 N_4 / N_2 N_3$.

The second is the $2 \times k$ table, where the true data are assumed to be:

Subject	Spouse	
	Non-smoker	Smoker
Non-smoker	U_0	V_0
Smoker - level 1	U_1	V_1
...		
Smoker - level k	U_k	V_k

and the concordance for level i is defined as $C_i = U_0 V_i / U_i V_0$.

Appendix C first considers the 2×2 table situation where the subject's smoking multiplies risk of lung cancer by a factor S in the absence of spouse smoking and where the spouse's smoking multiplies risk of lung cancer by a factor P in the absence of subject smoking.

For a multiplicative model of risk, the relative risks in the 4 cells of the table will be $1, P, S$ and SP, while for an additive model they will be $1, P, S$ and $P + S - 1$. Defining p_1 as the proportion of non-smokers misclassified as smokers and p_2 as the proportion of smokers misclassified as non-smokers, Appen-

dix C looks at the effect on the relative passive smoking bias, defined as (Observed P – True P)/True P, of variation in S, P, p_1, p_2, C and N_i for a multiplicative model in which S and C are assumed > 1. Within the usual range of p_1 and p_2, the following general conclusions are reached:

(a) the observed relative risk in relation to passive smoking always exceeds the true relative risk,
(b) the relative bias increases markedly with increasing misclassification of smokers as non-smokers,
(c) the relative bias is little affected by the reverse misclassification, of non-smokers as smokers,
(d) the relative bias is increased markedly by increasing concordance,
(e) the relative bias is affected much more by an increase in the overall percentage of subjects who smoke than by an increase in the overall percentage of spouses who smoke,
(f) the larger the relative risk in relation to active smoking, the greater the effect of misclassification, and
(g) given the relative risk in relation to active smoking, variation in the passive smoking effect has little influence on the relative bias.

For an additive model, the last conclusion does not hold, the relative bias decreasing with increasing true passive smoking effect. Where the true passive smoking effect is large with respect to the true active smoking effect, the bias can in fact become negative, so that the first conclusion also does not hold strictly. In practice, however, it will be correct for realistic true passive smoking effects.

It can be concluded that, for practical purposes, useful results can be obtained by considering the much simpler situation in which it is assumed that:

(a) no non-smokers are misclassified as smokers,
(b) there is no true passive smoking effect, and
(c) misclassification of spouse's smoking habits is ignored.

Using this "simpler scenario", formulae for estimating the passive smoking bias in the $2 \times n$ table situation are derived in Appendix C. For a given level of smoking, the contribution to the passive smoking bias depends both on the true excess risk due to smoking at that level and on the proportion of observed non-smokers who are actually smokers at that level. For this reason, ignoring amount smoked can result in substantial overcorrection for bias if smokers misclassified as non-smokers are light smokers.

All the above is based on the assumption that the rate of misclassification of a subject's smoking habits is independent of whether or not his or her spouse smokes. In theory, this might not be so. If a smoker denies smoking more readily when married to a non-smoker, the bias will be reduced and indeed in extreme circumstances, for example when the subject denies smoking only if the spouse does not smoke, it would reverse to produce a negative bias. As shown in Appendix C, such a reversal will not occur in most circumstances. Usually misclassification of the subject's smoking will cause upward bias when attempting to estimate the effect of passive smoking.

2.2 Types of Information on Misclassification of Smoking Habit

2.2.1 Information from 2 Sources at the Individual Level

Where individual information is available from 2 sources on the presence (+) or absence (−) of an attribute on a number of subjects, the relevant data in a 2×2 table can be laid out as follows:

Source 2	Source 1		
	−	+	Total
−	A	B	A+B
+	C	D	C+D
Total	A+C	B+D	N

Interpretation of the data and statistics commonly derived from this table depend on whether:

(a) one source can be assumed to provide correct data and interest is in the accuracy of source 2 data or
(b) neither source can be assumed accurate.

2.2.2 One Source of Information Assumed Correct

If source 1 is assumed to be correct and if, for the sake of illustration, the attribute in question is smoking, there are a number of statistics which it may be useful to calculate:

Total misclassification rate - the proportion of all the subjects misclassified by source 2 - which equals

$(B+C)/N$

Sensitivity - the proportion of true smokers who are classified as such by source 2 - which equals

$D/(B+D)$

Specificity - the proportion of true non-smokers who are classified as such by source 2 - which equals

$A/(A+C)$

In regard to misclassification of non-smokers, two statistics may be of interest. Firstly, the proportion of true non-smokers who are classified as smokers by source 2 -

$C/(A+C)$

which is equal to

(1 - specificity)

or alternatively the proportion of source 2 classified non-smokers who are actually smokers -

$B/(A+B)$

2.2.3 Neither Source of Information Necessarily Correct

If neither source of information can necessarily be considered correct, the true data cannot be estimated correctly. $(B+C)/N$ is an estimate of *inconsistency*, but theoretically at least the accuracy of any one specific source might vary from 0 to 100%, even with perfect consistency.

For such data, consistency is often measured by the *kappa statistic* (Horwitz and Yu, 1975). This is calculated by the formula

$$\kappa = (p_0 - p_c)/(1 - p_c)$$

where p_0 is the observed proportion of agreement and p_c is the proportion expected by chance. The value of kappa can vary from $+1$, indicating perfect agreement, to 0 indicating agreement no better than chance, and to -1 where agreement is less than expected by chance. Horwitz and Yu (1985) consider a value of greater than 0.75 excellent, 0.60–0.75 good, 0.40–0.59 fair and <0.4 poor, though it must be noted that what might be considered good in some contexts would not be so good in others. In the above formula p_0 and p_c are calculated by

$$p_0 = (A+D)/N$$

and

$$p_c = [(A+B)(A+C)+(B+D)(C+D)]/N^2$$

Although misclassification cannot in general be measured where neither source of information can be relied upon, progress can be made by assuming that, if misclassification exists, it is in one direction. There are many reasons why a smoker may be recorded as a non-smoker, but, at least in some situa-

tions, the possibility that a non-smoker may be recorded as a smoker may be so small that it can be ignored for practical purposes.

Under this assumption it is easy to see that for subjects classified as non-smokers by source 1, the proportion who are actually smokers must be at least $C/(A+C)$; the C subjects classified as smokers by source 2 must all be smokers while there may be further subjects who are actually smokers but who are reported to be non-smokers on both occasions.

Given the further assumption that misclassifications by the two sources are independent, the proportion of subjects classified as non-smokers by source 1 who are actually smokers can be calculated exactly by the expression

$$(C+CB/D)/(A+C)$$

In practice, of course, the reason which causes a smoker to be misclassified as a non-smoker may apply to both sources of data. In this case the above expression will underestimate the proportion of source 1 non-smokers who are actually smokers, perhaps substantially.

2.2.4 Types of Situation Where Two Sources of Information are Available

One main type of situation where information from two sources concerning smoking habits is available is in studies using objective biological markers based on carbon monoxide, cyanide, nicotine, or their metabolites. Typically the subject is asked whether or not he or she smokes and a sample of blood, urine or saliva is taken and the level of marker determined.

The other main type of situation is where no objective information is recorded, but where questions regarding the subject's smoking habits are asked twice. Typically the subject him or herself is asked twice, or the subject is asked on one occasion and a next-of-kin or other informant is asked on the other. Often the two questions are separated in time, sometimes by many years. This need not necessarily be the case, however, in studies where one is looking directly at the effect of the type of question or type of respondent on the response.

2.2.5 Information from 2 Sources at the Group Level

The most useful studies are those where response in the two situations is recorded at the individual level, as they allow direct estimates of misclassification and/or inconsistency rates to be calculated. However, information on validity can also be obtained from studies where results are only recorded at the group level. For example, a study of a single group of subjects which showed that in one situation x% were classified as smokers, but in another (using a different questionnaire and/or a different respondent) y% were, with y materially different from x, would allow a direct inference that the situation had an effect on response. In a comparison of two separate groups of subjects the

inference would be less direct, but it could still be made provided the groups were otherwise similar.

2.3 Factors Which Might Affect Reported Smoking Habits

There are a number of factors which might affect the extent to which valid (or consistent) answers are given to questions on smoking habits. Many of these factors are common to survey questions generally, and the reader is referred to Belson (1981) and Belson (1986) for a detailed discussion of general issues. The most important are considered below:

(a) the respondent may not have understood the question or may have ignored relevant parts of it e.g. the respondent might say yes to the question "have you ever smoked as much as one cigarette a day for as long as a year?" if he had ever smoked, ignoring the remainder of the question.
(b) the respondent may have interpreted the question in a way not intended by the researcher. For example, people who smoked daily except in Lent would be expected to say "yes" to the question above but it could be argued "no" is a technically correct answer.
(c) the question may be badly or incorrectly worded. To some extent this overlaps (i) and (ii) above.
(d) the interviewer may not ask the question as intended e.g. by leaving out "as much as one cigarette a day for as long as a year" to save time.
(e) the respondent may not know or be able to remember the answer to the question. This may particularly apply to surrogate answers and in relation to past smoking history.
(f) the respondent may not admit he or she (or in the case of surrogate answers, the subject) smoked or had smoked in the past. Possible reasons for this are:
    (1) to avoid having to answer a whole lot of further detailed questions on smoking history,
    (2) because the respondent decided that the few years he smoked in his youth were irrelevant,
    (3) because he or she did not want to admit to what some may deem an unsociable or unhealthy habit.

On general principles, denial of smoking is likely to vary according to a number of factors – e.g. honesty of the respondent; presence of others thought likely to disapprove; whether the accuracy of the answer is going to be verified later by an objective test; whether the respondent considers the question relevant and the questionnaire helpful to his interests; whether the answers are given anonymously (e.g. unsigned self-completion questionnaire); fear of punishment (in studies in children); the manner of the interviewer; the intensity of the questions.

Even when the right answer has been given to the question, the interviewer may enter it wrongly on the questionnaire or the data processors perhaps misread or mispunch it.

2.4 Use of Objective Markers

2.4.1 General Problems

Because of the possible unreliability of smoking habit information collected by self-report or by the report of next-of-kin or other surrogates, attention has been drawn in recent years to the use of objective markers, such as smoke constituents measured typically in blood, urine or saliva. In considering the advantages or disadvantages of any one of these markers, a number of factors are relevant.

a. Time of Smoking Period Detected
The level of some markers increases rapidly on smoking a single cigarette and then decreases rapidly so that it is critically dependent on when the last cigarette was smoked. Such markers are of limited value since they fail to detect a smoker who has not smoked for a few hours. For this reason preference is given to chemicals with a longer half-life. Even then these typically only indicate smoking in the last few days and are therefore markers of current smoking habits. Currently there is no objective marker that measures long term smoking behaviour.

b. Other Sources of the Marker Chemical
Subjects might wrongly be considered smokers simply because of exposure to another source of the marker chemical (false positives). Although, ideally, the marker would be derived specifically from tobacco smoke, it might still be of practical use if levels from the other sources are consistently much lower than seen in smokers or if exposure to the other sources is very rare. To some extent false positives can be reduced by asking questions regarding these potential other sources.

c. Adequacy of Chemical Method
The method used should be reliable, accurate and specific to the chemical of interest.

Some objective markers are more expensive to use than others, not only because of direct assay costs, but because of other considerations such as ease of sample collection. Using 24-hour urine samples, for example, will involve costs in man-hours in collecting and storing the samples and possibly in payment to the subject as an inducement to participate.

The 3 groups of markers most commonly used are considered briefly below. Those based on carbon monoxide and thiocyanate were popular in the 1970's and early 1980's while those based on the more tobacco-specific nicotine have recently become widely used as analytical methods have become available. In the discussion, attention is given mainly to the first 2 of the points considered above.

2.4.2 Carbon Monoxide and Carboxyhaemoglobin

Frederiksen and Martin (1979) have reviewed the evidence on carbon monoxide and smoking behaviour and the reader is referred to that paper as reference for a number of the statements made below.

Carbon monoxide (CO) is an odourless, colourless, asphyxiant gas commonly resulting from incomplete combustion of organic matter. Carbon monoxide can be assessed by measuring the concentration of CO in blood directly, expressed as percent carboxyhaemoglobin (%COHb). Alternatively CO levels can be assessed through obtaining expired (alveolar) air samples, the CO concentration in the analysed air being expressed as parts per million (ppm). Ambient (environmental) air samples have also been found to be highly correlated with blood COHb. Two similar regression equations relating COHb to CO have been derived from experimental data: (1) %COHb = 0.6 + 0.3 (CO ppm) (Cohen et al. 1971); (2) %COHb = 0.5 + 0.2 (CO ppm) (Ringold et al. 1962).

The level of CO in the body in the form of COHb is affected by at least five factors:

a. Environmental Exposure
The major source of CO in the environment is car exhaust, accounting for approximately 60% of the yearly total CO emissions (Stewart, 1975). Concentrations depend on time, place and weather, and those with occupations such as bus drivers or traffic wardens may be particularly affected.

b. Elimination Rate
The half-life of COHb is estimated to be between 1 and 4 hours, depending on activity level, the elimination rate being affected by pulmonary ventilation and cardiac activity.

c. Constitutional Factors
This is less clearly understood, but is a possible determinant of CO level.

d. Drug Therapy
CO is produced endogenously and this can be affected by phenobarbital and disphenylhydantoin.

e. Smoking
Smoking is the major determinant of the variation in CO levels between individuals (Wald and Howard, 1975).

Non-smokers typically have COHb levels of between 0.5 and 2.0%, whereas smokers have levels above this range. 2.0% COHb is equivalent to about 8 ppm CO. Even under experimental conditions in a room with a virtually intolerable level of cigarette smoke, where ambient CO was 38 ppm (close to the 50 ppm levels at which air pollution emergencies are called), non-smokers' COHb levels rose only from 1.6 to 2.6%, far lower than typical smokers' levels. In well-ventilated rooms containing smokers, in which CO levels are as low as 5 ppm, non-smokers' COHb levels have been shown to increase from 1.1 to 1.6%.

When the evidence from studies using CO as a marker is considered, there is some variation in the cut-off point above which non-smokers are reclassified smokers. This is reasonable, given the variation in analytical methods and in the general level of background CO exposure.

2.4.3 Thiocyanate

Bliss and O'Connell (1984) have critically reviewed thiocyanate (SCN) as an index of smoking status, the reader being referred to that paper for reference to a number of statement made below.

SCN level is affected by a variety of exogenous sources of cyanide, including cigarette smoke, as well as some exogenous sources of SCN. There are a number of dietary sources of SCN. Almonds, bamboo shoots and tapioca contain cyanide-producing compounds, while vegetables in the Brassica genus, such as cabbage, broccoli and cauliflower contain SCN. While it has been experimentally demonstrated that eating extremely large quantities of these vegetables can increase non-smokers SCN to levels typical of smokers (Pechacek et al. 1982), the effect of eating normal amounts of SCN-containing foods is probably small. Other exogenous sources of cyanide include workplace exposure (e.g. in electroplating, precious metal refining, case hardening of steel and gas manufacturing), non-tobacco substances such as marijuana, and possibly inhalation of sidestream smoke which contains acetonitrile, a cyanide precursor.

The half-life of thiocyanate has been reported to be 10 to 14 days by a number of publications, but as Bliss and O'Connell (1984) point out, many of these citations derive from a single study of a single smoker by Pettigrew and Fell (1972). Bliss and O'Connell considered data from several other studies, which presented rather a conflicting picture, with estimates from studies of giving up smoking appearing to vary from 1 day to over 2 weeks. They point out that it is difficult to estimate half-life exactly because exposure to non-tobacco sources is never cut off so that this baseline is not known exactly. A more recent estimate of half-life of 6 days has been provided by Junge (1985).

Bliss and O'Connell (1984) reviewed evidence from 19 studies which assayed SCN in smokers and non-smokers. Plasma or serum SCN levels were estimated to be 156 μmol/l in smokers and 60 μmol/l in non-smokers. While the overall estimate of standard deviation for non-smokers was calculated as 41 μmol/l, this was dominated by results from one large study (Neaton et al. 1981), MRFIT, where it was known that there was a high level of misreporting of smoking habits. Many studies reported rather lower means and standard deviations of around 20 μmol/l suggesting that around 100 μmol/l SCN may be a reasonable cut-off point for detecting up "deceivers".

Levels of SCN in saliva were much higher, 2724 μmol/l in smokers ankd 1219 μmol/l in non-smokers, although the smoker/non-smoker ratio is similar. SCN in μmol/l can be converted to μg/ml by multiplying by 0.058. Thus typical levels of SCN in non-smokers can be calculated as 3.5 μg/ml for plasma and serum and 71 μg/ml for saliva.

Compared with CO, SCN has the adventage of measuring longer term exposure. However, it has the disadvantage that the ratio of levels in typical smokers and typical non-smokers is much smaller (around 2 or 3 rather than around 10), with no corresponding reduction in variability. Vogt et al. (1977) have suggested using a combination of CO and SCN for detecting subjects who falsely report their smoking status.

2.4.4 Nicotine and Cotinine

Contrary to most reports nicotine is not entirely specific to tobacco smoke, suggesting that detection of nicotine or its metabolite cotinine need not necessarily indicate active or passive smoking. Castro and Monji (1986) have detected nicotine in various *Solanaceae* (tomato, pepper and eggplant) confirming earlier literature (cf. Dawson et al. 1960). However concentrations are very low. Lee (Appendix B) has estimated that someone would have to eat 25 kg of eggplant or 60 kg of green tomatoes in a single day (!) to have cotinine levels similar to those seen in typical smokers.

Nicotine has an average half-life of 2 h in regular smokers (Benowitz et al. 1982), and is only useful as an indicator of very recent smoking status, the level being highly dependent on when the last cigarette was smoked. Nicotine "boost" from a single cigarette can be determined by taking measurements shortly before and after smoking it.

Cotinine has a much longer half-life, with estimates for smokers ranging from 7 to 37 h (Bliss and O'Connell, 1984) with typical values between 15 and 20 h (Curvall and Enzell, 1986). Because of the much higher levels in smokers than non-smokers, the average smoker will still have cotinine concentrations above those of non-smokers for up to 4 days after cessation (Wilcox et al. 1979). It has been reported that the half-life for cotinine is longer in non-smokers (49.7 h) than in smokers (18.5 h) (Sepkovic et al. 1986).

Levels of cotinine in serum and saliva are typically of the order of 300 ng/ml in smokers, though occasionally levels as high as 1000 ng/ml are found. In non-smokers median levels are generally below 1 ng/ml. Heavy passive smoke exposure rarely results in levels above 10 ng/ml, and a level above 30 ng/ml can be taken to indicate active smoking with confidence. Urinary cotinine levels are markedly higher than levels in serum and saliva, by a factor of about 5.

3 Evidence on Misclassification

3.1 Studies Using Carbon Monoxide and Thiocyanate as Objective Markers

3.1.1 Overview

In Sect. 3.1.2 each paper relevant to the use of CO and SCN as an objective marker of smoking status is considered approximately chronologically, with a paragraph or two describing the study and giving the key results. Table 3 summarises the data from each study, giving the percentage of self-reported non-smokers considered to be true smokers, together with relevant factors of the study, in particular whether it concerned adults or children and whether the subjects were or were not specifically advised to give up smoking.

A number of points are evident from Table 3 or from the detail of the studies summarised below.

(a) Most studies based on CO have used a cut-off point of around 1.6%–2% COHb, or 5–12 ppm CO, which is not dissimilar (see Sect. 2.4.2). One study, by Jones et al. (1972), did not reject non-smokers with 3% COHb as smokers, only considering a self-reported non-smoker with a 6.6% COHb as clearly a smoker. This may reflect the fact that this was a study of taxi drivers who have high occupational CO exposure. Three studies, 2 in Sweden and 1 in Canada, used cut-offs which were distinctly lower, 0.8% or 1% COHb, or 2.5 ppm CO. Whether this reflects lower CO exposure in the study areas is not clear, but in the study by Ohlin et al. (1976), as many as 13 of the 35 originally self-reported ex-smokers with levels above 0.8% COHb admitted still being smokers on requestioning.

(b) Studies based on SCN have used cut off points ranging from 50–100 μmol/l for serum/plasma or 85–100 g/ml for saliva. The only study based on urinary SCN used 11 mg/ml.

(c) Table 3 highlights an obvious difference between the false claim rates in smoking cessation studies (where one is validating statements made by self-reported ex-smokers) and in observational studies (where one is validating statements made by self-reported non-smokers).
Table 3 give details for 23 smoking cessation studies. Of these, 7 gave false claim rates in the range 19–41%, 6 gave false claim rates in the range 8–18%, with the remaining 10 giving lower figures, zero in 6 cases. It was evident from the papers that the high false claim rates typically come from large general population studies given relatively limited advice to stop smoking, followed up only once or twice and not aware that their statements were going to be validated. In contrast the zero false claim rates

Table 3. Evidence from studies using carbon monoxide and thiocyanate as a marker

Paper	Study: population and groups	Told to give up smoking?	Criterion for false report	% (n/N) false claims	Time after advice	Comment
Jones et al. (1972)	London taxi drivers	No	6.6% COHb	4.8% (1/21)	–	Highest other non-smoker 3% COHb
Delarue (1973)	Canadians attending voluntary antismoking clinic	Yes	2% COHb 4% COHb 6% COHb	20.6% (22/107) 9.3% (10/107) 4.7% (5/107)	1 year 1 year 1 year	No fixed criterion given. 8 admitted smoking on challenge
Ohlin et al. (1976)	Swedish patients with smoking related diseases attending antismoking clinic and given nicotine gum	Yes	0.8% COHb	19.2% (25/130) 32.1% (35/109)	1 week 6 months	13 of the 35 admitted smoking at 6 months
Isacsson and Janzon (1976)	Swedish heavy smokers in quit-smoking research project	Yes	1% COHb	8.8% (3/34)	8–9 weeks	–
Farquhar et al. (1977)	Californian trial of community health education	Some groups	Based on SCN in plasma	About 4%	Varies	No details given of criterion or variation in false claims by test group
Lando (1977)	US smokers in multigroup smoking cessation study	Yes	Based on CO	0.0% (0/22 to 60)	1 week to 1 year	Abstinence also confirmed by friends of subject
Vogt et al. (1977)	Californian part of Multiple Risk Factor Intervention Trial (MRFIT)	Yes	8 ppm CO and 100 μmol/l SCN in serum	2.4% (1/41)	Not stated	–
Pederson et al. (1977)	Canadian schoolchildren	No	2.5 ppm CO	6.3% (7/111)	–	–
Sillett et al. (1978)	UK study in 2 groups: A: Survivors of myocardial infarction B: Volunteers in nicotine gum trial	 Yes Yes	1.7% COHb	 A: 21.6% (11/51) B: 40.2% (33/82)	Varied	–
Hjermann (1980)	Norwegian randomized intervention trial of men with high coronary risk	Test group	Based on SCN in serum	Some	After some years	No estimate made

Kirk et al. (1980)	London trial of advice to give up in arterial disease patients	Yes	70 μmol/l SCN in serum	10.5% (2/19)	2–19 months	–
Malcolm et al. (1980)	UK trial of nicotine chewing gum	Yes	1.6% COHb	41.6% (47/113)	1 month	May be same group as B in Sillett et al. (1978)
Raw et al. (1980) Raw and Russell (1980)	UK smokers attending a smokers' clinic in comparison of psychological treatment and use of nicotine gum	Yes	Based on CO or COHb	0.0% (0/33)	1 year	–
Lando (1981)	US smokers in multigroup smoking cessation study	Yes	Based on CO	Between 1.4% (1/74) and 4.2% (1/42)	1 week to 1 year	Friends of subject also supplied data on smoking
Luepker et al. (1981)	US children given anonymous questionnaire after providing saliva and being told why it was collected	No	85 μg/ml SCN 100 μg/ml SCN 120 μg/ml SCN in saliva	4.7% (55/1163) 3.3% (38/1163) 2.1% (21/1163)	–	Of children reported not smoking in last week
Petitti et al. (1981)	Californians having health checkups, 176 female twins and 91 males	No	8 ppm CO and 100 μmol/l SCN in serum	0.6% (1/181)	–	–
Neaton et al. (1981) and Ockene et al. (1982)	US Multiple Risk Factor Intervention Trial	Yes	Based on SCN in serum	[16%]	Varied	Estimated indirectly
Ronan et al. (1981)	Irish post MI patients	Yes	1.6% COHb	8.8% (5/57)	Varied	Authors note low level of deception due to rapport with staff
Jarvis et al. (1982)	UK smokers attending a smokers' clinic in trial of nicotine gum	Yes	Based on CO or COHb	0.0% (0/27)	1 year	–
Powell and Arnold (1982)	New York smokers at high risk of coronary disease	Yes	50 μmol/l SCN in serum	0.0% (0/11)	1 year	–
Research Committee British Thoracic Society (1983)	UK patients with smoking related diseases in 4 group intervention trial involving advice, booklet, placebo and nicotine gum	All groups	1.6% COHb and 73 μmol/l SCN in plasma	27% 25%	6 months 1 months	Similar rates in 4 groups
Russell et al. (1983)	UK smokers attending general practitioners	Some groups	7 ppm CO	About 15%	4 months and 1 year	–

Table 3 (continued)

Paper	Study: population and groups	Told to give up smoking?	Criterion for false report	% (n/N) false claims	Time after advice	Comment
Glasgow et al. (1984)	US worksite smoking control study	Yes	10 ppm CO	0.0% (0/4)	6 months	-
Hall et al. (1984)	US smokers recruited for cessation study	Yes	10 ppm CO and 85 μg/ml SCN in plasma	Some	Varied	Four time points. Max of 3 deceivers out of 46 to 111 reported ex-smokers
Jamrozik et al. (1984)	UK smokers in trial of nicotine gum	Yes	12 ppm CO	28.0% (7/25)	6 months	-
Li et al. (1984)	US asbestos exposed smokers receiving 1: behavioural counselling or 2: minimal warning	Yes	9 ppm CO	1: 22.2% (4/18) 2: 23.1% (3/13)	11 months	-
Williams and Gillies (1984)	Nottingham adolescents	No	100 μg/ml SCN 85 μg/ml SCN in saliva	6.6% (16/242) 10.0% (24/242)	-	No fixed criterion
Aaronson et al. (1985)	Californian trial of advice not to smoke in pregnant smokers and ex-smokers	Yes	11 μg/ml SCN in urine	12.9% (4/31)	3 months	-
Clavel et al. (1985)	French trial of acupuncture and nicotine gum	Yes	5 ppm CO	0.0% (0/24)	1 year	Base is "half of 47"
Lando and McGovern (1985)	US subjects undergoing various treatments for eliminating smoking	Yes	Based on CO	2 cases out of at most 90	Up to 2 months	Number tested not stated
Richmond and Webster (1985)	Australian smokers in a general practice. Randomised trial of effects of advice to give up	Test group	Based on COHb, SCN and cotinine in plasma	5.7% (2/35)	6 months	Criterion not stated
Robertson et al. (1987)	Birmingham office workers who completed a questionnaire given by a doctor	No	70 μmol/l SCN in serum	9.0% (14/155)	-	3 of the 14 admitted smoking on requestioning

typically come from small studies in which the experimenters have considerable contact with the subjects over an extended period of time and in many of which the subjects are well aware they are going to be checked up on. For the 6 studies in which no attempt had been made to alter the subject's smoking habits, none of the estimates were over 10%. Three of the studies (Pederson et al. 1977; Luepker et al. 1981; Williams and Gillies, 1984) were of children or adolescents. These all give false claim rates of the order of 5%, the exact value depending on the cut-off point used. The remainder are theoretically of more relevance to the passive smoking/lung cancer situation. Unfortunately here the information is rather sparse and conflicting. One of the 3 studies (Jones et al. 1972) is of only 21 non-smoking taxi drivers, with a derived estimate of 4.8%, based on only 1 apparent deceiver. Of the other 2 studies, both of 150–200 self-reported non-smokers, one (Pettiti et al. 1981) gave an estimate of 0.6% based on 1 deceiver, while the other (Robertson et al. 1987) gave a much higher estimate of 9.0%, based on 14. The extent to which this reflects difference in the situation (Californians having health check ups, as against Birmingham office workers completing a questionnaire given by a doctor) or the criterion used (8 ppm CO and 100 μmol/l SCN in serum, as against 70 μmol/l SCN in serum) is not clear.

(d) Although subjects with high CO and SCN levels might be non-smokers, having high exposure from other sources and be telling the truth about non-smoking, the marked difference in false claim rates according to the study situations suggests strongly that the majority of those with SCN or COHb levels above the cut-offs, are deceivers.

(e) The studies provide some information on the proportion of self-reported non-smokers who have COHb or SCN levels typical of avarage smokers. This is summarised in the table below.

Study	Criterion used	% (n/N)
Jones et al. (1972)	6.6% COHb	4.8% (1/21)
Delarue (1973)	6% COHb	4.7% (5/107)
Sillett et al. (1978) A	5% COHb	3.9% (2/51)
Sillett et al. (1978) B	5% COHb	2.4% (2/82)
Ronan et al. (1981)	5% COHb	0.0% (0/57)
Robertson et al. (1987)	120 μmol/l SCN	1.9% (3/155)

While the information is limited, especially in non-cessation studies, it is consistent with the notion that it is not only the light or occasional smokers that deny smoking in interview.

3.1.2 The Studies

Jones et al. (1972) described a study of blood lead and carboxyhaemoglobin levels in 50 London taxi drivers. Of 21 self-reported non-smokers, 1 was ex-

cluded from consideration because he claimed to have recently given up smoking but had 6.6% COHb in his blood. The range of COHb values for the remaining men was 0.4–3.0%.

Delarue (1973) interviewed subjects about their smoking habits one year after attending an anti-smoking clinic, and measured their COHb. Of 107 who reported they were then totally abstinent, 22 had COHb above 2% (2–4% 12, 4–6% 5, >6% 5). On direct challenge, eight of these, including all those with levels above 6%, admitted they had smoked.

Ohlin et al. (1976) describe a study in which 285 consecutive Swedish patients with smoking-related diseases were advised to stop smoking and given nicotine chewing gum and in which self-reported smoking habits were recorded and a blood sample taken for COHb measurement (by gas chromatographic methods) after 1 week and 6 months. Of the 130 who reported no smoking in the last 7 days in the follow-up after 1 week, 25 (19%) had COHb values over 0.8%. None of these reported being a non-smoker at 6 months, compared with 58% of the remaining 105 with normal COHb. The authors consider these results suggest the 25 patients might have been smoking during the first week.

35 (of 109) patients who at 6 months reported no smoking during the previous month had COHb levels above 0.8%. On being telephoned by the secretary who stated there was an apparent error in their records, 13 stated they had actually smoked, 12 stated they had not and provided a further COHb sample (11 of which were normal), 7 stated they had not but refused to supply a further sample and 3 could not be contacted. The authors consider the 7 were likely in fact to be smokers and it seems possible some of the 12 might have been too, only stopping before the additional sample. The authors state that "our results, if correct, indicate that a surprisingly large number of persons give inaccurate information as to their ability to abstain entirely from smoking, when attending an anti-smoking clinic", though they noted that "it is likely that this phenomenon will vary considerably in different circumstances".

Isacsson and Janzon (1976) describe a study in which 51 heavy smokers agreed to take part in a quit-smoking research project. After 8–9 weeks, 34 of the men claimed to have given up. Three of these were found to have COHb values of more than 1% and it was regarded as unsafe to assume that they had given up smoking.

Farquhar et al. (1977) carried out a study of whether community health education can reduce the risk of cardiovascular disease in three Californian towns. One town, Tracy, was selected as a control town, while people in Watsonville and Gilroy received health education over 2 years through a mass-media campaign. Additionally, in Watsonville, two-thirds of high risk people received intensive instruction. A random sample of 35–59 year old men and women provided data on smoking habits, while plasma was taken for thiocyanate assay by the method of Butts et al. (1974). The authors noted that "plasma thiocyanate assay indicated that only about 4% of those reporting abstinence may have given inaccurate reports" but gave no detailed figures nor any indication of whether this percentage varied according to type of health education received.

Lando (1977) randomly assigned 73 US smokers to 7 different conditions designed to elimate smoking. Subjects were required to name 3 informants who were familiar with their smoking patters and who could verify reported abstinence and to submit CO breath samples as another check upon self-reported smoking status. Follow-up continued for a year. Numbers reporting abstinence ranged from 60 at week 1 to 22 after a year. The author reports that "in no instance was self-reported abstinence called into question by either informants or by suspicious CO samples" but no cut-off point is mentioned.

Vogt et al. (1977) measured expired air CO by Ecolyzer and serum thiocyanate by the method of Butts et al. (1974) in 45 subjects who claimed to be non-smokers and 94 who claimed to smoke only cigarettes. The subjects were men aged 35–57 who were enrolled at the San Francisco clinic of the Multiple Risk Factor Intervention Trial. 16 of the smokers were considered atypical in that they reported <9 cigarettes a day and/or no inhaling or they reported no cigarettes for the last 24 hours. Using >8 ppm CO (measured by Ecolyzer) as an indicator of smoking correctly classified 43 (95.6%) of self-reported non-smokers and 77 (98.7%) of typical self-reported smokers. Using >100 μmol/l thiocyanate (measured by the method of Butts et al. 1974) as an indicator correctly classified 42 (93.3%) non-smokers and 71 (91.0%) typical smokers. The authors recommended using both indicators simultaneously. Among the 45 non-smokers, 41 (91.1%) were below the cut-off on both criteria, 3 (6.7%) were below on only one, while 1 (2.2%) was above on both.

Pederson et al. (1977) reported a study of Grade 4 to 6 Canadian schoolchildren who first completed a health questionnaire including a yes-no question on whether they smoked cigarettes and then provided a sample of air for assessment of CO concentration (measured by Ecolyzer), the situation being presented as a technique for determining the effect of air pollution on the respiratory system. Using 2.5 ppm CO as a critical value classified 7 out of 111 (6.3%) self-reported non or ex-smokers as smokers. Six of the 7 children who reported non or ex-smoking at the health questionnaire but had high CO levels also reported non smoking at a previous questionnaire 4 months earlier, "apparently lying twice".

Sillett et al. (1978) compared COHb in 2 groups advised to stop smoking (see table below). The first group (A) were taking part in a secondary prevention trial having survived a myocardial infarction. They were given routine advice on stopping smoking at hospital and at outpatients clinic, and were followed up for a year after infarct. Group B came from a trial of nicotine chewing gum as an aid to stop smoking. They attended the clinic weekly for a month and received advice and encouragement to stop smoking. Using a critical COHb value of 1.7% for smoking, based on a control group of non-smoking hospital staff whose concentrations ranged from 0.3 to 1.6%, 11 out of 51 subjects in group A (22%) and 33 out of 89 subjects in group B (40%) who claimed to have given up smoking were considered to be true smokers. The possibility that COHb levels may be raised by another factor was considered not to have influenced the results, patients confronted with a raised COHb result often remembering smoking the cigarettes they had "forgotten". The authors concluded "deception appears to be common in people trying to stop smoking".

Relationship between COHb Level and Subjects' Statements that they had given up Smoking

COHb level[a]	Subject's statement			
	Stopped smoking		Still smoking	
	A[b]	B	A	B
≤1.6	40	49	3	2
1.7–2.9	8	21	4	6
3.0–5.9	1	11	15	20
6.0–8.9	0	1	4	23
≥9.0	2	0	2	7

[a] Estimates based on bar chart in paper
[b] See text for definition of A and B

Hjermann (1980) reported on a randomized intervention trial in Oslo. From an initial 16000 men aged 40–49 screened during 1972–73, 1232 healthy men with above average coronary risk were randomly allocated to an intervention group of 604 men and a control group of 628. Intervention involved advice by the doctor to stop smoking and to change dietary habits. Follow-up was carried out every 6 months in the intervention group and every 12 months in the control group during which questions on smoking were asked. Towards the end of the follow up period serum thiocyanate, measured colorimetrically by the method of Pettigrew and Fell (1972), was analysed as a measure of smoking. At the start of the study almost 80% of the men in both groups were daily smokers. This percentage reduced during the trial to about 55% and 65% in the intervention and control group respectively. The authors quote that when serum thiocyanate is used as an indicator of the degree of smoking, the difference between the 2 groups reduced, "i.e. it is likely that some men in the intervention group who said they had stopped smoking, in fact were still smokers". However, no estimate of this proportion was made, other than to state that this reduced the "real" difference between the groups by about one cigarette a day.

Kirk et al. (1980) strongly advised 39 London arterial disease patients to give up smoking and followed them up for 2–19 months. 19 claimed to have given up smoking by the end of the trial, but 2 of those (10.5%) had serum SCN levels (measured according to the method of Butts et al. 1974) that exceeded 70 μmol/l.

Malcolm et al. (1980) carried out a trial of nicotine chewing gum as an aid to stopping smoking, comparing 73 smokers on nicotine gum, 63 on placebo gum and 74 in a control group. At 1 month rather more subjects in the nicotine group (66%) claimed to have stopped smoking than the placebo (47%) or control (47%) groups. Using 1.6% COHb to validate statements, as measured by a CO-Oximeter, the proportions confirmed as having stopped smoking reduced to 34%, 37% and 24% respectively. For all groups it can be estimated that of 113 subjects who reported stopping smoking, as many as 47 (42%) continued to smoke. This may be the same study as Group B in Sillett et al. (1978).

Raw et al. (1980) compared 49 UK smokers attending a smokers' clinic given psychological treatment during 1974–6 with 69 receiving nicotine chewing gum

during 1977–9. Respectively 7 and 26 reported abstinence from smoking after one year, claims being stated to be "validated by measuring COHb concentrations or expired air CO". However, it is not stated what the cut off points were. Further results for the first group of smokers are given in Raw and Russell (1980).

Lando (1981) gave a variety of different types of anti-smoking advice to 100 US smokers. Subjects were required to name 3 informants who were familiar with their smoking patterns and who could verify reported abstinence and to submit CO breath samples as another check upon self-reported smoking status. Follow-up continued for a year. Numbers reporting abstinence ranged from 74 at week 1 to 24 after a year. The author reports only one case where there was a "suspicious" CO sample, smoking being confirmed by checks with the informants.

Luepker et al. (1981) measured salivary thiocyanate (SCN) by the method of Denson et al. (1967) in 1419 Minnesota children aged 12–14, following presentation of a film demonstrating how recent cigarette use is readily detected from such samples. Immediately following the saliva collection, all students were given an anonymous questionnaire about general health knowledge, attitude to smoking and smoking behaviour of themselves, parents, siblings and friends. Of those 1163 children who reported they had smoked no cigarettes in the last week, 4.7% had SCN levels (Measured spectrophotometrically) above 85 μg/ml, 3.3% had SCN levels above 100 μg/ml, 1.8% had SCN levels above 120 μg/ml and 0.4% had SCN levels above 160 μg/ml. No attempt was made in this study to record intake of cyanogen containing foods.

Petitti et al. (1981) described a study of 267 Californian subjects aged 18–72, 176 female twins having a health check-up for a special study of twins and 91 men recruited from those receiving a routine health check-up. Subjects completed a research questionnaire on smoking habits and another questionnaire on current health status which included questions on smoking. After completion of the questionnaires, serum thiocyanate and expired air CO were measured using methods as described by Vogt et al. (1977), subjects not being informed that blood tests indicative of smoking were to be done. Of the 181 subjects who reported no current tobacco use on the questionnaire (which questionnaire not stated!) and who had SCN and CO measurements available, only 1 (0.6%) had SCN $>$ 100 μmol/l and CO $>$ 8 ppm which was considered indicative of smoking. In contrast, 62 of the 87 subjects (71.3%) who reported smoking had blood measurements above these levels.

In the Multiple Risk Factor Intervention Trial (MRFIT), Neaton et al. (1981) correlated SCN levels, determined by the method of Pettigrew and Fell (1972), measured at the second screening visit with the number of cigarettes reported to be smoked at the last screening visit. There was a clear dose relationship, with non-smokers having the lowest level of 65.9 μmol/l and smokers having values ranging from 113.6 μmol/l (1–15 cigs/day) to 186.8 μmol/l ($>$55 cigs/day). There was an obvious tendency for those in either the special intervention (SI) or the usual care (UC) groups who claimed to have given up smoking during the study to have SCN levels greater than this, values varying from 100.8 μmol/l at 12 months to 82.5 μmol/l at 48 months in the SI group and from 84.2 μmol/l at 12 months to 68.7 μmol/l at 48 months in the UC group.

The authors describe a statistical method for adjusting downwards reported rates of giving up smoking by taking account of SCN levels. The adjustment varied by number of cigarettes reported to be smoked at screen 1, by treatment group and by month of follow-up, but averaged 16%.

Results similar to thoose presented by Neaton et al. (1981) were also described in Ockene et al. (1982).

Ronan et al. (1981) estimated the accuracy of self-reported abstinence among 117 Irish post-myocardial infarction patients by measuring COHb (using a CO-oximeter). Of the 57 who claimed to have quit smoking after MI, 5 had COHb levels between 1.6 and 2.3% considered possibly indicative of smoking, an estimated deception rate of at most 8.8%. These authors suggested that the relatively low level of deception found in their study may have been due to "a high degree of rapport achieved between patients and medical staff during an exceptionally long and regular follow-up period".

Jarvis et al. (1982) randomised 116 UK smokers attending a smokers' clinic to receive either advice or placebo nicotine chewing gum. Of 27 subjects claiming to be abstinent after 1 year for whom expired air CO (Jarvis et al. 1980) or COHb (Russell et al. 1973) values were available, there were stated to be no cases of deception. Cut-off points for this decision were not given.

Powell and Arnold (1982) carried out a multiple treatment smoking cessation program on 22 New York men with an elevated risk of coronary heart disease classified as "hard core" smokers because of failure to quit despite 5 years continual smoking cessation effects. One year after treatment, 11 of the men had given up, all confirmed as being non-smokers by serum SCN levels less than 50 μmol/l.

The Research Committee of the British Thoracic Society (1983) described a multicentre study of outpatients or inpatients aged between 18 and 65 who smoked cigarettes and who had a condition related to or aggravated by smoking. Patients were randomly allocated to four groups, each of size about 400; (1) advice to stop smoking by the physician and oral instructions to stop; (2) as (1) but a booklet on the dangers of smoking and advice to stop; (3) as (2) but supplemented by placebo chewing gum with instructions to substitute it for a cigarette when the urge was felt to smoke; (4) as (2) but nicotine chewing gum. Patients were seen 1, 3, 6 or 12 months after entering the study with blood

Treatment	After 6 months		After 12 months	
	Claimed non smokers having blood test	Claims not validated (%)	Claimed non smokers having blood test	Claims not validated (%)
1	59	27	54	20
2	61	26	51	22
3	73	26	68	22
4	67	30	59	34
Total	260	27	232	25

taken for COHb and SCN estimation (measured by CO-Oximeter (Jarvis et al. 1980) and the Aldridge technique (Casapieri et al. 1970) respectively) taken at 6 and 12 months from self-reported non-smokers. As shown in the table above, about a quarter of those patients who denied smoking had COHb and SCN concentrations typical of smokers, with the proportions not markedly different in the treatment groups.

Claims were taken as invalid based on critical values of 1.6% for COHb and 73 μmol/l for thiocyanate.

In a study reported by Russell et al. (1983), 1938 UK cigarette smokers attending the surgeries of 34 general practitioners' were assigned to one of three groups: (a) non-intervention controls, (b) advice plus booklet, and (c) advice plus booklet plus the offer of nicotine gum. Two thirds of those who claimed to be off cigarettes at 4 months and 1 year were checked by measurement of expired air CO, (Jarvis et al. 1980) levels above 7 ppm being attributed to smoking. Among those who reporting having given up at 4 months (287) and at 1 year (261), an estimated average of 7.4% were smoking a pipe or cigars, but 22% failed biochemical validation. This suggests about 15% of self-reported non-smokers of cigarettes were still actually smoking.

Glasgow et al. (1984) describe a study in which 36 employees of a US telephone company were randomly assigned to 3 procedure aimed at controlling smoking. After 6 months, 4 claimed to have given up smoking, all having CO readings of less than 10 ppm.

Hall et al. (1984) describe a study in San Francisco in which 135 subjects were recruited and divided into 4 groups assigned to different cessation techniques. At 3 and 6 weeks, smoking status was verified by expired air CO (measured by the Ecolyzer). At 26 and 52 weeks, a subject was considered abstinent if four measures indicated abstinence: self-report, significant other report, CO (<10 ppm) and thiocyanate (<85 ng/ml measured by GLC from a blood sample). The total classified as abstinent reduced from 111 at week 3 to 46 at week 52. It was noted that the number of subjects exceeding the biochemical cut point for abstinence did not exceed 3 at any one assessment.

Jamrozik et al. (1948 a) recruited 2110 UK adult cigarette smokers to a study of the effect of antismoking advice in general practice. Of 429 who reported at 1 year follow-up they were still smoking, 200 took part in a double blind study comparing the effectiveness of nicotine or placebo gum. After 6 months, 25 claimed to have given up smoking, but 7 of these (28%) exhaled levels of CO (as measured by Ecolyzer) more than 12 ppm, indicating that they were probably still smoking.

Li et al. (1984) described a US study in which asbestos-exposed smoking men undergoing screening in a program for naval shipyard workers were categorised as having normal or abnormal pulmonary status on the basis of chest X-ray and pulmonary function tests (PFT). They were than randomly assigned within PFT categories to receive either a simple warning or lengthier advice from a doctor to give up smoking. Subjects' smoking status was evaluated after 3 and 11 months with expired air CO measured with an ecolyzer at the 11 month follow-up. A value of <9 ppm CO was defined as consistent with non-smoking status. 31 of the 579 study subjects reported having given up smoking

after 11 months. 3 of the 13 subjects receiving minimal warning (23.1%) and 2 of the 18 receiving behavioural counselling (22.2%) had CO levels indicative of still being smokers. The authors note that exposure to high levels of ambient CO at work might explain some of these high CO levels.

Williams and Gillies (1984) determined salivary thiocyanate concentrations by the method of Densen et al. (1967) in 300 adolescents aged 11–16 from Nottingham, and obtained information about smoking by a self-completed questionnaire administered in the classroom. Using cut-off levels of 100 μg/ml and 85 μg/ml respectively, 16 (6.6%) and 24 (10.0%) of 242 non-smokers were classified as smokers.

In a section assessing the efficiency of worksite smoking cessation programs, the U.S. Surgeon-General (1985) summarised results from 13 uncontrolled studies without objective measures of smoking status and from 13 controlled studies where there was biochemical verification of smoking status by CO and/or SCN in all but 3. The report notes that one of the more striking differences to emerge is that the results of the better controlled studies, with a median post-test cessation rate of 28 to 31%, are generally lower than those of the uncontrolled studies, with a median post-test cessation rate of 60%. "The most obvious explanation for this finding" is said to be "that most of the controlled studies included objective biochemical indices of treatment outcome and subjects in these studies may have more accurately reported their smoking status".

Burling et al. (1984) in a critical review of the literature on smoking following myocardial infarction, also noted that rates of giving up smoking tended to be lower in studies where CO samples are collected concurrently with the self-report, suggesting that knowing they are being checked up may reduce the tendency for deception. Although they noted a consistent pattern in that those who gave up smoking following myocardial infarction had much lower mortality or reinfarction rates than those who did not, the review was strongly critical of the methodology used. In particular they noted a number of general shortcomings of the studies reviewed including failure to define properly criteria for abstinence, an almost total reliance on patient self-report of smoking habit, and failure to give adequate definition of the level and type of anti-smoking advice given to the patient.

Aaronson et al. (1985) gave advice not to smoke to 58 Californian pregnant women attending a prenatal clinic, 35 of whom reported being currently smokers and 23 of whom reported having quit at pregnancy onset. At follow-up 3 months later, all the latter group and 10 of the former reported not smoking. Urine samples were available for 31 of the 33 women, and 4 (12.9%) were found to exceed a threshold value of 11 mg/ml urinary SCN.

Clavel et al. (1985) enrolled 651 French participants in a randomised controlled trial of acupuncture and nicotine chewing gum as an aid to giving up smoking. After 1 year 47 of the participants claimed to have given up smoking in the test and control groups. Half of these were visited at home to give an expired air sample. None of the CO values exceeded 5 ppm.

Lando and McGovern (1985) randomly assigned 130 US subjects to various treatments for eliminating smoking. Subjects were required to name 3 informants who were familiar with their smoking patterns and who could verify

reported abstinence and to submit CO breath samples at initial follow-ups (up to 2 months) as a further check upon self-reported smoking. Numbers reporting abstinence varied from 90 at 1 week to 65 at 2 months and to 43 after 1 year. The authors note that in 2 cases, self-reported abstinence appeared inconsistent with either CO readings or with informant reports, though no denominator is given, it being noted that attendance at follow-ups dropped off rather sharply after 2 weeks. Nor is the cut-off point used to indicate inconsistency given.

Richmond and Webster (1985) randomized 200 smokers attending a General practice in Sydney into 2 groups of 100, one receiving detailed advice to assist giving up smoking. After 6 months, 35 of the intervention group claimed to have given up smoking, but evidence from blood tests for cotinine, carboxyhaemoglobin and thiocyanate using respectively the methods of Thompson et al. (1982), Zwart et al. (1981) and Lundquist et al. (1979) but with no cut-off points stated, showed that 2 were in fact still smokers, confirmed by further questioning.

Turner et al. (1986) measured COHb (by CO Oximeter) in 3,487 subjects at the Central Middlesex Hospital, patients and staff, over a 5 year period and a detailed smoking history was taken at the time of blood sampling. Mean COHb was reported as 0.91% for the 1,255 non-smokers with a range of 0.1–1.7%. The fact that they refer to 1.7% as being the value previously found to be the upper limit of normal in their laboratory suggests that self-reported non-smokers with values above 1.7% had been excluded from the analysis or had been reallocated as smokers.

Robertson et al. (1987) used a serum thiocyanate assay based on the method of Bowler (1944), to validate smoking histories in 206 Birmingham office workers who completed a smoking questionnaire administered by a doctor. 14 of 155 (9.0%) self-reported non-smokers or ex-smokers had a SCN of >70 μmol/l, which was still raised on a repeat sample. Questionnaires were repeated on 11 and on this occasion, 2 admitted to having been smoking at the time of the previous sample. Expired carbon monoxide measurements on the remaining nine showed one person with a level of 22 ppm who subsequently admitted to smoking. The remaining eight who said they were non-smokers had a mean level of 7 ppm. The authors note that all people found to have raised SCN concentrations and who say that they are non-smokers cannot be deemed to be giving invalid replies, since they may have eaten food high in thiocyanate precursors. A comparison of dietary history was made between the 9 subjects who had expired CO measurements and 10 control non-smokers with low SCN. Eight of the former (89%), as against 5 of the latter (50%), reported more than average consumption of brassicas, pips from soft fruit, radishes, nuts and green bananas, whilst 4 of the former (44%) as against 0 of the latter reported taking vitamin preparations.

3.2 Studies Using Nicotine or Cotinine as Objective Markers

3.2.1 Overview

Section 3.2.2 considers papers relating to the use of cotinine or nicotine as an objective marker of smoking status. Table 4 summarises these data in a manner similar to Table 3 for CO and SCN studies.

Table 4. Evidence from studies using nicotine and cotinine as a marker

Paper	Study: population and groups	Told to give up smoking?	Criterion for false report	% (n/N) false claims	Time after advice	Comment
Russell and Feyerabend (1975)	London smokers, non-smokers and heavy passive smokers	No	Based on urinary nicotine	0.0% (0/27)	-	No overlap of smoker and non-smoker distributions
Russell et al. (1979)	London smokers attending general practices in intervention trial	Yes	Based on salivary nicotine	7.1% (1/14)	Not stated	Criterion not given
Wilcox et al. (1979)	Nottingham myocardial infarct patients	Yes	2 μg/100 ml urinary nicotine 10 μg/100 ml urinary cotinine	16.3% (8/49)	Not stated	Further 5 with detectable levels
Paxton (1980)	UK smokers assigned to various stop smoking treatments	Yes	Based on urinary nicotine	n=2 N<60	Up to 6 months	60 subjects in trial. Numbers of non-smokers supplying urine not given
Feyerabend et al. (1982)	London hospital staff and out-patients	No	Saliva and urine nicotine 10% of smokers level	0.0% (0/56)	-	Perhaps 10% of non-smokers with nicotine 5% of smokers level
Haley et al. (1983)	New York volunteers	No	Cotinine	0.0% (0/18)	-	No cotinine detected
Jamrozik et al. (1984b)	UK smokers attending general practitioners in trial of various antismoking interventions	Some Groups	100 ng/ml urinary cotinine	23.9% (11/46) to 39.7% (23/58)	1 year	Subjects who denied smoking in postal questionnaire and again at interview
Wald et al. (1984)	Non-smokers attending BUPA, and Oxford colleagues	No	256 ng/ml urinary cotinine	0.9% (2/221)	-	-
Pojer et al. (1984)	Australian non-smokers attending clinic and smokers taking part in voluntary smoking-reduction program	Some	Blood cotinine 10% of smokers level	3.3% (6/181)	-	-

Jarvis et al. (1984) Jarvis et al. (1987)	London cardiology and vascular out-patients	Yes	20 ng/ml plasma cotinine	17.4% (21/121)	-	-
Jarvis et al. (1984)	British schoolchildren	No	11 ng/ml salivary cotinine	1.0% (6/575)	-	Told their statement would be checked on by saliva
Haddow et al. (1986)	US women attending well women screening	No	30 ng/ml serum cotinine	1.3% (3/232)	-	-
			10 ng/ml serum cotinine	2.6% (6/232)		
Coultas et al. (1987)	New Mexico Hispanic children and adults in household survey	No	50 ng/ml salivary cotinine	3.2% (43/1360)	-	Users of other tobacco products excluded
			20 ng/ml salivary cotinine	4.6% (63/1360)	-	
Haddow et al. (1987)	US pregnant women in screening for neural tube defects	No	10 ng/ml serum cotinine	4.9% (142/2871)	-	Unpublished
Lee (1987)	Representative UK sample providing saliva, without prior warning, after smoking data	No	30 ng/ml salivary cotinine	2.5% (20/808)	-	Questions on other nicotine sources included
			10 ng/ml salivary cotinine	4.2% (34/808)		
Russell et al. (1987)	UK smokers attending general practitioners in trial of effects of brief intervention and support of a smokers' clinic	Some Groups	50 μg/l urinary cotinine	38.8% (57/47)	1 year	-
McNeill et al. (1987)	London schoolgirls aged 11-16 in survey on smoking	No	20 ng/ml	1.5% (5/335)	-	Told their statements would be checked on by saliva

Table 4 shows wide variation in the proportion of non-smokers having levels of blood, urine and saliva nicotine of cotinine considered inconsistent with non-smoking status (estimates varying from zero to almost 40%). The highest two values were in studies of smokers attending general practitioners for trials of various antismoking interventions (38.8% from Russell et al. (1987) and 23.9% to 39.7% from Jamrozik et al. (1984b)) where contact with the subject was relatively minimal and the subject was unaware their statements were going to be checked up on. The next highest values (17.4% from Jarvis et al. (1984) and 16.3% from Wilcox et al. (1979) were from studies of cardiovascular disease patients likely to have been strongly advised not to smoke, with the highest value after that (7.1% from Russell et al. (1979)) also from an intervention trial of advice against smoking. All the remaining studies in Table 4 (except that of Pojer et al. (1984) where some subjects received advice to stop smoking and a 3.3% false claim rate was seen) did not involve specific advice to give up smoking and it is notable that here none of the false claim rates exceeded 5%. It is interesting to note, however, that the highest false claim rate in these observational studies was from a study of pregnant women (4.9% from Haddow et al. (1987)), a group more likely than average to have received material recently advising them not to smoke.

In their review Wald et al. (1986) cite results from Feyerabend et al. (1982), Wald et al. (1984), Pojer et al. (1984) and Haddow et al. (1986). Overall this gave a proportion of non-smokers with marker concentrations $>10\%$ of the smokers concentrations of 1.6% (11/690). For the total data in Table 4 (using the lower of alternative figures where appropriate, the rate is 4.6% (325/7061). Excluding the studies of advice to give up smoking, the large Haddow et al. (1987) study of pregnant women and the McNeill et al. (1987) study of schoolgirls, gives a reduced rate of 2.2% (74/3297).

Perhaps more important than the overall misclassification rate is the rate at which self-reported non-smokers are typical smokers rather than occasional smokers. Few studies address this issue but this is one of the main differences between the 4 studies cited by Wald et al. (1986) and the study of Lee (Appendix B). Only 1 of the 11 deceiving smokers in the 4 former studies had a nicotine or cotinine level more than 50% of a typical smoker. Eleven of the 20 in the latter study were considered to have levels typical of smokers. The difference between the proportions of typical smokers amongst self-reported non-smokers in the two situations is substantial ($1/690 = 0.1\%$ and $11/808 = 1.4\%$, $p < 0.05$). Coultas et al. (1987), in their recent large study, do not give their results in this form. However, among 1360 self-reported non-smokers they found 43 with a salivary cotinine above 50 ng/ml. Comparing this with a smokers' mean of around 300 ng/ml it seems reasonable to assume that 20–30 (1.5%–2.2% of their sample) had levels typical of smokers, an estimate which aligns closely with my study (Appendix B) but not with that of Wald et al. (1986).

3.2.2 The Studies

Russell and Feyerabend (1975), using gas chromatographic methods, compared urinary nicotine levels in 4 groups of subjects; 12 non-smokers who spent an average of 78 min in a room so heavily smoke-filled (38 ppm CO) as to be totally unacceptable (group 1), 14 non-smoking members of the Addiction Research Unit staff (group 2), and 13 non-smoking (group 3) and 18 smoking members of the staff of the New Cross Hospital. Plasma nicotine was also measured in the group 1 non-smokers. Compared with the smokers (mean 1236 ng/ml), urinary nicotine in the group 2 and 3 non-smokers was much lower (means 12.4 and 8.9 ng/ml respectively) and the largest value seen, 64.3 ng/ml, in either group, was only 5% as high. Urinary cotinine was only measured after exposure in the group 1 non-smokers, and was markedly highler than in the other groups of non-smokers (mean 80 ng/ml) with 2 of the 12 subjects having levels as high as 208 and 157 ng/ml, 17% and 13% of the smokers' mean. Surprisingly, neither of these subjects showed an increased plasma nicotine comparing levels before and after exposure. The exposure of group 1 subjects is however, very much greater than could be encountered in real life, e.g. Weber (1984) has cited 2.0 ppm CO as an upper tolerable threshold limit.

A problem with this study, compared with the later cotinine studies, is that nicotine has a very short half life and that it is therefore much more difficult to distinguish whether high values among self-reported non-smokers arise as a result of them really being smokers or having a recent exposure to high levels of passive smoke. However the fact that none of the group 2 and 3 non-smokers had urinary nicotine values as high as any of the smokers does not indicate any misreporting of smoking habits in this sample, though it remains possible. The authors did not discuss the possibility of misreporting in this paper.

Russell et al. (1979) allocated 2138 cigarette smokers attending the surgeries of 28 London general practitioners (GPs) to one of 4 groups: non-intervention controls; questionnaire-only controls; those who were advised by their GP to stop smoking; and those that were advised by their GP to stop smoking and given a leaflet to help them and a warning that they would be followed-up. Validation of self-reported outcome was obtained in 23 patients by measuring nicotine concentrations in saliva using gas-chromatographic methods. Fourteen claimed to have stopped smoking, and the salivary nicotine values were consistent with this in all but one, giving a deception rate of 7%. The authors comment on the unreliability of this deception rate due to the unsatisfactory selection of the patients. They do not give their criterion for considering a nicotine value inconsistent with non-smoker status.

Wilcox et al. (1979), in a study in Nottingham, collected random samples of urine for nicotine and cotinine from 104 volunteers (46 non-smokers and 58 smokers) whose smoking history was considered to be reliable. Concentrations were measured by gas-liquid chromatography using confidence detection limits of 2 μg/100 ml and 10 μg/100 ml for nicotine and cotinine respectively. All non-smokers had levels below the detection limits whilst all smokers had levels above the detection limits. They then collected urine samples from 85 myocardial infarction patients who attended their information clinic during the study

period and at that visit recorded the patients' declared current smoking habits. Patients had been strongly advised to stop smoking at each clinic visit. Easily detectable nicotine and cotinine was found in the 36 patients who said they were still smoking. Of the remaining 49 who said they had stopped smoking, no nicotine or cotinine could be detected at all in 36, some, but below the limits, could be detected in 5, while levels above the limits could be detected in 8. This suggests that 8 to 13 ex-smokers were still smoking, a deception rate of about 16–26%.

Paxton (1980) assigned 60 UK smokers to various treatments designed to make them stop smoking and followed them for up to 6 months at regular intervals. Urine samples for nicotine analysis or a check on self-reports of not smoking were taken occasionally at any time after the cessation date. Occasional contact with subjects' relatives was also made for the same purpose. Abstinence rates, shown only graphically in this paper, were about 60% at 2 months and 45% at 6 months. It was noted that in only 2 of the subjects was there a clear discrepancy between self-reports and the results of urinary nicotine analysis, and both admitted the following week to smoking. However, no denominator is shown to allow percentage false claim rates to be calculated. The author notes that their very low rate of "faking" contrasts sharply with the results of Ohlin et al. (1986) and Sillett et al. (1978) and suggests that warning people in advance of occasional biochemical checks may have had the additional benefit of deterring faking. The critical level of urinary nicotine used to detect faking is not given.

Feyerabend et al. (1982) collected saliva and urine samples from 138 staff and outpatients at New Cross Hospital who also completed a questionnaire on smoking habits and exposure to other people's smoke. Mean concentrations of nicotine, as measured by the method of Feyerabend and Russell (1980a), were as shown in the table below. Distributions were only given graphically. According to Wald et al. (1986), none of the 56 self-reported non-smokers had marker levels above 10% of smokers' level. This appears consistent with the graph, although it appears there were a reasonable number of subjects (perhaps about 10%) with marker levels over 5% of smokers' level.

Mean concentrations of urinary and salivary nicotine

Self-reported smoking habits	Exposure to tobacco smoke before sampling	Urinary nicotine (nmol/l)	Salivary nicotine (nmol/l)	Number of subjects
Non-smokers	no	46.2	36.4	26
Non-smokers	yes	133.2	62.3	30
Smokers				
non-inhalers		2455.6	939.0	8
slight inhalers		7786.6	2600.5	15
medium inhalers		8329.2	2800.2	32
deep inhalers		9426.6	5589.4	27

Haley et al. (1983) measured plasma and saliva cotinine by the method of Langone et al. (1973) and thiocyanate by the method of Butts et al. (1974) in 12 smokers and 18 non-smokers in New York. No detectable cotinine was seen in non-smokers, while plasma thiocyanate levels were never greater than about 100 ng/ml. Participants completed a questionnaire on smoking behaviour after providing saliva and blood but no information is given as to whether they were told what the samples were for.

Jamrozik et al. (1984b) carried out a controlled trial of 3 different antismoking interventions on 2110 smokers taken from 6 Oxfordshire general practices. The proportions claiming to have given up smoking after 1 year varied from 11–17% according to treatment. Within at most 3 months of the follow-up questionnaire an attempt was made to interview 122 of those subjects claiming to have gven up. Interviews could not be achieved for 24, while 40 subjects on questionning admitted relapse. Of the remaining 58, 46 provided urine samples (not stated to be for validatory purposes) and 11 had cotinine values (as measured by the method of Langone et al., 1973) above 100 ng/ml considered incompatible with non-smoking. The authors conclude that up to 39.7% (23/58) may have not given up smoking if one takes into account the fact that all the 12 subjects not supplying urine samples may have been true smokers not wanting their false statements to be discovered.

Wald et al. (1984) measured urinary cotinine by radioimmunoassay (Langone et al. 1973) in 221 non-smokers (151 attending BUPA medical centre and

Urinary cotinine levels in self-reported smokers and non-smokers

Urinary cotinine	Non-smokers			Smokers		
	Hours exposure to other people's tobacco smoke (ng/ml)			Cigarettes only	Cigars only	Pipes only
	0	≤7	>7			
<1.0	5	14	1			
1.0–	4	8	5			
2.0–	9	38	11			
4.0–	3	24	26	1		
8.0–	1	18	28	0	1	
16.0–			14	1	2	
32.0–			6	1	4	
64.0			4	0	5	
128.0			0	4	15	
256.0–			2	4	5	2
512.0–				17	8	3
1024.0–				57	12	17
2048.0–				40	7	14
4095.0+				6		6
Total	22	102	97	131	59	42

70 colleagues in Oxford) and used a questionnaire to discover hours of exposure to other people's tobacco smoke in the past 7 days. Cotinine levels were also measured for 232 current smokers at BUPA. There was substantial separation between cotinine levels in non-exposed non-smokers and smokers, but there was some overlap between exposed non-smokers and smokers. As shown above, 2 (0.9%) of self-reported non-smokers had cotinine levels above 256 ng/ml and a further 4 (1.8%) had levels above 64 ng/ml. At the time, the authors did not present a cotinine level which they considered would distinguish misclassified smokers from true non-smokers, though later Wald et al. (1986) cited 2 (0.9%) as the number of non-smokers with $>10\%$ of smokers' level, noting one had 19% and one 24% of the smokers' level.

Subsequently, Wald and Ritchie (1984) followed-up 151 of the non-smoking men whose urinary cotinine and exposure to passive smoking had previously been studied. The men were asked by letter if they were married and, if so, whether their wife smoked. Urinary cotinine was higher in those with smoking wives than with non-smoking wives, as were hours exposure to passive smoke both at home and elsewhere.

Pojer et al. (1984), in an Australian study, measured blood cotinine by gas chromatography (Hengen and Hengen, 1978; Thompson et al. 1982), thiocyanate colorimetrically (Lundquist et al. 1979, 1983) and COHb (spectrophotometrically) (Zwart et al. 1981) in 187 smokers participating in a voluntary smoking-reduction campaign and 181 unselected non-smoking patients who agreed to take part in the development of counselling methods for smokers. Whereas most researchers attempt to use these objectives measures as a check as to whether the statements made on smoking are correct, these authors assumed the smoking statements were correct. It was notable from the distribution presented that none of the self-reported non-smokers had particularly extreme value of any of the 3 markers and one wonders whether some individuals had been excluded from the study without it being stated. The best discriminating values were 250 nmol/l cotinine, 70 μmol/l thiocyanate and 2.0% COHb. Corresponding sensitivities were 95.2%, 75.9% and 87.7% with specificities 98.3%, 96.7% and 95.8%. Using cutoff points to give a specificity of 95% for each test, cotinine was considered the best test. Wald et al. (1986) give an estimate of 3.3% (6/181) for the marker of non-smokers with marker concentration $>10\%$ of smokers concentration, with three subjects 10–14%, one 15–29% and two 30–44% of smokers concentrations. These data were not directly presented in Pojer et al.'s paper.

Jarvis et al. (1984) used several biochemical measures to investigate passive smoke exposure. 215 patients attending cardiology and vascular outpatient clinics in London completed a smoking questionnaire and provided samples of blood, expired air, saliva and urine. Of 121 self-reported non-smokers (smoking no cigarettes, pipes or cigars), 21 (17%) had a plasma cotinine measured gas chromatographically (Feyerabend and Russell, 1980a; 1980b) above 20 ng/ml considered incompatible with non-smoking status. Further details of the results of this study are given in Jarvis et al. (1987). Neither paper indicates whether or not the subjects had been recently advised to give up smoking, but it seems probable a substantial proportion might have been.

In a further study by Jarvis et al. (1985), 10579 British schoolchildren aged 11–16 completed a questionnaire on smoking attitudes and behaviour, having been told that some of them would be selected at random and asked to provide a quantity of saliva, which would be analysed to see if they had been smoking recently. Saliva samples were gathered from 2494 pupils and 1018 analysed for cotinine by gas chromatography (Feyerabend and Russell, 1980a; 1980b). After rejecting 110 samples with insufficient volume, 40 with insufficient concentration, 233 of smokers and 60 where parental smoking data were incomplete, there were 575 subjects who were self-reported non-smokers. 6 (1.0%) of those with cotinine above 11 ng/ml were regarded as smokers, with values 212.2, 81.8, 47.2, 39.3, 14.0 and 11.1 ng/ml respectively.

Haddow, Palomaki and Knight (1986) measured serum cotinine by radioimmunoassay (Knight et al. 1985) in 296 women attending a well person screening examination in Portland, Maine, USA, in 1983. The women were asked, through a self-administered questionnaire, whether they smoked cigarettes and, if so, how many. The distribution of values shown is reproduced below. The highest 7 cotinine values among non-smokers were stated to be 8, 14, 22, 28, 43, 48 and 208 ng/ml respectively. Elsewhere, the conflicting statement was made that there were *5* self-reported non-smokers with values of 10 ng/ml or more (whereas the values would imply 6). Wald et al. (1986) cites this paper as having 3 self-reported non-smokers (1.3%) with values above 10% of a smoker's concentration. The figures of 14%, 16% and 68% imply 300 ng/ml was used for a smoker's level.

Cotinine values according to self-reported smoking category

Serum cotinine (μg/l)	Non-smokers	Smokers
	Number of subjects (%)	Number of subjects (%)
<1.0	93 (40)	1 (2)
1.0–	94 (41)	2 (3)
2.0–	26 (11)	0
4.0–	12 (5)	2 (3)
8.0–	2 (1)	0
16.0	2 (1)	3 (5)
32–	2 (1)	0
64–	0	5 (8)
128–	1 (0.4)	14 (22)
256	0 0	29 (45)
≥512	0 0	8 (13)
All	232 (100)	64 (100)
Summary Statistics	Serum Cotinine (μg/l)	Serum Cotinine (μg/l)
Mean	2.9	304
Median	1.1	305
10th centile	0.4	19
90th centile	3.2	618

Coultas et al. (1987) conducted a population-based household survey of respiratory diseases in 2,029 New Mexico Hispanic children and adults and measured salivary cotinine levels by radioimmunoassay (Langone et al. 1973) in 1,360 self-reported non-smokers and ex-smokers who did not report use of other tobacco products. 63 of these (4.6%) were reported as having cotinine levels greater than 20 ng/ml, 43 of which (3.2%) had levels greater than 50 ng/ml. The authors considered all of the 43 and many of the remaining 20 were deceivers about their smoking status. It can be calculated that at least 12.6% of true current smokers denied smoking at interview, based on the 50 ng/ml cut-off.

Haddow et al. (1987) measured the concentration of serum cotinine by radioimmunoassay (Knight et al. 1985) in 4,211 women between 15 and 21 weeks of pregnancy who provided a blood sample collected as part of a screening program for neural tube defects conducted in Maine, USA. 142 (5%) of 2871 women who said that they did not smoke had cotinine levels above 10 ng/ml. Benowitz et al. (1983) was cited as a reference for the use of this cut-off to distinguish smokers from non-smokers, though it is lower than the figure of 30 ng/ml implicitly used by Wald et al. (1986). No detailed distribution of cotinine values is given.

Lee (Appendix B) interviewed 1775 subjects at home about their current use of tobacco products or nicotine chewing gum. 1537 provided a sample of saliva for cotinine analysis. Of 808 who claimed not to be users of such products, 20 (2.5%) had salivary cotinine values, as measured by gas chromatography (Feyerabend and Russell, 1980b), above 30 ng/ml, suggesting their self-reports were false. On recontact shortly afterwards, 17% (3/18) of "non-users" with cotinine values above 30 ng/ml reported they had smoked manufactured cigarettes as against 1% (6/670) of "non-users" with cotinine below 30 ng/ml.

Russell et al. (1987) studied 4445 cigarette smokers attending 101 UK general practitioners. Subjects were allocated to receive brief intervention with the support of a smokers' clinic, brief intervention without such support, or the general practitioners' usual care. After 1 year 377 reported that they were no longer smoking cigarettes, of which 157 provided a urine sample from which cotinine was measured. 10 of these were pipe or cigar smokers. Of the remaining 147, 57 (39%) exceeded the 50 μg/l cotinine cut off point. Some of these might have used nicotine gum, questions on this issues not being asked.

McNeill et al. (1987) describe a study in which 508 London schoolgirls aged 11–16 completed a smoking questionnaire, had their expired-air CO concentrations measured and produced saliva samples for cotinine analysis. The girls were told before they filled in the questionnaire that the biochemical measures could detect smoking. Of 335 girls who reported being non-smokers, 5 had salivary cotinine exceeding 15 ng/ml. As all were over 20 ng/ml, considered by the authors an upper biological limit to chronic exposure in even the most heavily polluted environments, the 5 were considered deceivers. Three non-smokers had expired-air CO >7 ppm.

3.3 Studies Involving Multiple Reports Concerning the Same Individual - Subject a Lung Cancer Case

3.3.1 Overview

Evidence not involving the use of objective markers is now considered. This section and the one that follows summarise those studies in which information on smoking habits has been collected on more than one occasion or from more than one source on the same idividual. Those studies in which the subjects are lung cancer patients or have later contracted lung cancer are considered first because it is reasonable, as noted earlier, to expect much higher misclassification rates in such subjects than in normal individuals. Some of the studies referred to below consider both lung cancer patients and other subjects. For completeness they are referred to in Sect. 3.3.2 and again in Sect. 3.4.2.

Table 5 summarises the evidence from the studies considered in this section. It should be noted that a number of these studies (Chan, Kabat and Wynder, Garfinkel, Akiba, Pershagen) are part of the evidence relating passive smoking to lung cancer and are described in more detail in Appendix A.

A number of points are apparent from inspection of the material. One is the very wide variation in results. Of those subjects classified as non-smokers originally, three studies (Akiba et al. (1986), Garfinkel (1985) and Berry et al. (1985)) found on further investigation that over 30% of them had smoked. Two of these were based on substantial sample sizes. A fourth small study (Chan et al. (1979)) gave a figure of 20%. The other two studies (Kabat and Wynder (1984) and Pershagen et al. (1987)), on the other hand, gave estimates of less than 10%, both based on moderately large sample sizes. The rate in the latter study, of only 2.4%, seems particularly low and discrepant with the other data. It can be argued that studies where the first source of information was hospital records are likely to overestimate the effects of misclassification compared with studies using a specially designed interview. However the extent of this overestimation may not be large given the fact that patients with lung cancer, especially in the US, are likely to be routinely asked questions on smoking habits in hospital.

The results in Table 5 are presented as percentages of those originally classified as non-smokers subsequently reported to be smokers. For some studies estimates of the percentage of those later classified as non-smokers originally classified as smokers can also be calculated. While the percentages calculated this way are not so different for the Berry study (27.3% vs. 33.3%), they were remarkably different from the Akiba study (3.6% vs. 39.2%). The explanation for this difference, which is more apparent for men (7.1% vs. 51.3%) than for women (0.0% vs. 2.9%), is not at all clear. Certainly it seems unlikely that as many as 96 out of 187 men who said they did not smoke in 1964–68 really had smoked earlier or had taken up smoking later.

Another point that emerges from these studies is the relative lack of information on the extent of smoking where disagreements occur. It is obviously important to know whether it is 20 a day smokers who are denying smoking, or whether it is only occasional smokers, but there is little information on this.

Table 5. Evidence from studies involving multiple reports on smoking habits – Lung cancer cases

Paper	Study/sex	First source of information	Second source of information	% (n/N) Disagreement[a]	Comment
Chan et al. (1979)	Hong Kong case-control study of women	Subject interview	Second interview and interview of relations	20.0% (1/5)	–
Kabat and Wynder (1984)	US case-control study of both sexes	Subject in hospital	Hospital records	8.8% (13/147)	–
Berry et al. (1985)	London prospective study of male asbestos workers	Subject interview or questionnaire when healthy	Next-of-kin or hospital records after death	33.3% (4/12)	Assuming did not start smoking just before death
Garfinkel (1985)	US case-control study of women	Hospital records	Subject in hospital	39.9% (113/283)	–
Akiba et al. (1986)	Japanese prospective study of both sexes	Subject interview when healthy in 1964–68	Subject or next-of-kin in 1982	39.2% (91/232)	Assuming did not start smoking. Rate higher in man than women. Includes cases and controls
Lerchen and Samet (1986)	New Mexico study of males	Subject interview in 1980–82	Wives after death up to 4 years later	0.0% (0/3)	–
Pershagen et al. (1987)	Swedish prospective of women	Subject mailed questionnaire in 1961–63	Subject or next-of-kin in 1984	2.4% (2/92)	–

[a] Base is number of non-smokers according to first source; disagreements are smokers according to second source. Father's habits (M) were supplied by the mother (base) and confirmed by the father (disagreement).

3.3.2 The Studies

In the study by Chan et al. (1979) (see also Appendix A), 5 female patients who had lung cancer and said that they did not smoke were contacted on a second occasion, and their relatives were also questioned. One relative reported that a few hand-wrapped Chinese tobacco cigarettes were smoked for a year at the age of 71. All the others continued to deny smoking, and their relations agreed.

In the study by Kabat and Wynder (1984) of never smoking lung cancer cases and controls (see also Appendix A), hospital records were checked for any indication of ever having smoked. Out of 147 self-reported never smoking cases, mention of a past history of smoking was found in 13 (8.8%), whereas out of 134 self-reported never-smoking controls, mention of a past history of smoking was not found for any.

Berry et al. (1985), in a prospective evaluation of asbestos workers in London, compared smoking data obtained at the start of the study in 1971 by questionnaire or interview, with data obtained by questioning next-of-kin or checking hospital records at the time the workers died from lung cancer between 1971 and 1980 (see table). Of those stated at the time of death to be never smokers, 3 (27%) had stated in 1971 that they were smokers and are clearly discrepancies. Conversely, of the 12 who stated in 1971 that they were never smokers, 4 were stated by their relative to have been smokers. One of these is described as being an ex-smoker for 20 years, and is therefore discrepant, the other 3 one can presume are more likely to be discrepant then to have started smoking just before their death.

Smoking habits obtained at death compared with those obtained earlier in life in a study of London asbestos workers

Smoking habits obtained during life (1971)	Smoking habits obtained at death			
	Never smoked	Formerly smoked	smoked	Smoked at some time[a]
Never smoked	8	2	2	0
Ex-smoker	2	15	3	7
Smoker	1	12	33	30

[a] Could not be discriminated between ex-smoker and smoker at time of death.

In the case control study of Garfinkel (1985) (see also Appendix A), 39.9% (113/283) of women with lung cancer not found to be smokers in their hospital records were reported to be smokers on reinterview. It is interesting to note that in this study Garfinkel presented estimates of relative risk of lung cancer in relation to be husband's smoking habits at home both for "unvalidated" data, i.e. based on hospital records, and for "validated" data, i.e. after excluding women found subsequently to be smokers. These are compared below.

Relative risk of lung cancer among non-smoking women by husband's smoking habits at home

	Cigarettes per day				Cigar and/or pipe	All smoking
	None	<10	10–19	20+		
Unvalidated	1.00	1.31	1.52	2.85	1.41	1.66
Validated	1.00	1.15	1.08	2.11	1.17	1.31

The differences between the validated and unvalidated findings illustrates clearly the dangers of marked bias caused by misclassification of smoking habits. However, the question still arises as to how valid the "validated" data actually are. In this respect, it is notable that, a positive association between husband's smoking habits and the risk of lung cancer was only clearly evident when the smoking habit data were obtained from the daughter or son, who may not have known the full smoking history of their mother, with no association at all being seen when the woman herself or her husband provided the data. It seems very plausible that even the weaker association with husband's smoking habits seen in the "validated" data may have arisen wholly or partly as a bias resulting from misclassification of smoking habits.

In the study by Akiba et al. (1986) of Hiroshima and Nasgasaki atomic bomb survivors followed-up since 1951 (see also Appendix A), smoking status as recorded by the subjects in 1964–68 was related to smoking status as recorded in 1982 by the subject or by a surrogate. As shown in the table below, which relates to cases and controls combined, only 7 of the 98 men and none of the 99 women reported as never having smoked in 1982 previously claimed being smokers. While this finding does not seem indicative of substantial misclassification, it should be noted that there is something odd about the data in that of the 187 men who reported not smoking in 1964–68, as many as 96 (51%) were reported as ever having smoked in 1982. For a population aged over 60 in 1964–68 it is unlikely that more than a handful would have taken up smoking subsequently, while it seems surprising that such a large proportion of them would really be ex-smokers in 1964–68.

Sex	Informant in 1982	1964–68 Current smoker	1982 Smoking status	
			Never	Smoker
Male	Self	No	10	8
		Yes	0	40
	Surrogate	No	81	88
		Yes	7	503
Female	Self	No	39	0
		Yes	0	6
	Surrogate	No	60	3
		Yes	0	29

(N.B. Akiba et al. actually present totals for the 4 sex-informant categories and percentages within. The numbers given are the best approximation.)

Lerchen and Samet (1986) described a study in which 177 male lung cancer cases interviewed in New Mexico in 1980 to 1982 and in which, up to 4 years after their death, interviews were carried out with 80 surviving wives concerning their husbands. Perfect agreement of cigarette smoking status (ever, never) was reported. Concordance for pipe and cigar use (ever, never) was approximately 80%. It is noted that only 66 of the 77 wives married to smokers were able to supply complete details about their husband's smoking, deficiencies mainly relating to age at starting to smoke. Presumably only 3 (= 80–77) of the husbands were non-smokers, so the study provides little information regarding validity of claims about non-smoking.

In the study of Pershagen et al. (1987) (see also Appendix A) smoking habit data were collected from a mailed questionnaire in 1984 for 92 lung cancer cases and 384 controls originally classified as non-smokers from questionnaires over 20 years earlier. 2 of the "non-smoking" cases (2.4%) and 6 of the controls (1.7%) were reported in 1984 to have smoked for at least 2 years. Of these 8, 4 had stopped before 1961/63, 1 had started after that, 2 were smokers of 1–7 cigaretten a day and 1 was a pipe smoker, the last 3 (presumably) being continuing smokers from before the 1961/63 questionnaire. It is not made clear in the paper whether the follow-up questionnaire did or did not mention if these subjects were originally misclassified as never smokers. Nor is it explained who (self, brother/sister, son/daughter, other) provided the further data. Nor is information given on the extent of non-response to these questions.

3.4 Studies Involving Multiple Reports Concerning the Same Individual – Subject not a Lung Cancer Case

3.4.1 Overview

Having considered multiple report evidence from studies where the subjects were lung cancer cases, studies where they are not are now considered. Information from those 14 studies in which estimates of disagreement rates could be made is summarised in Table 6.

In Table 6, the two sources of information on smoking habits are defined. Where possible, two disagreement rates are given for each study, depending on which source is taken as the base for the calculation. Thus, in the Petitti et al. (1986) study, where both a health and a research questionnaire were administered, 9 of the 128 subjects classified as never-smokers by the health questionnaire were classified as ever smokers by the research questionnaire, while 0 of the 119 subjects classified as never-smokers by the research questionnaire were classified as ever smokers by the health questionnaire, giving disagreement rates of 7.0% and 0.0% respectively. Many studies, however, have only provided information from which one disagreement rate can be calculated.

Table 6 also carefully distinguishes whether disagreement concerns reported lifetime habits (never-smoker vs. ever smoker) or reported current habits (non-smoker vs. smoker).

Table 6. Evidence from studies involving multiple reports on smoking habits – Subjects not lung cancer cases

Paper	Study	Sources of information	Sex	Base[a]	Disagreement[a]	%
Todd and Laws (1959)	UK representative samples	1. Interviews in 1948–50, 55, 56 2. Reinterviews for memory enquiry in 1952, 57	M	71 non-smokers (1)	26 smokers (2)	36.6%
Haenszel et al. (1962)	UK smoking and health study	1. Subject interviewed in 1953 2. Relative interviewed after death in 1956	M	153 non-smokers (1)	virtually all correctly identified	
Hammond and Garfinkel (1964)	US prospective study	1. Subject questionnaire in 1959–60 2. Subject questionnaire in 1961–62	M	88479	$\simeq$1850	2.1%
			F	353108 never-smokers of cigarettes (1)	$\simeq$3550 smokers of cigarettes (2)	1.0%
			M	171743	$\simeq$11250	6.0%
			F	382598 non-smokers of cigarettes (1)	$\simeq$5300 smokers of cigarettes (2)	1.4%
Todd (1966)	UK representative samples	1. Interviews in 1948–50 2. Interviews in 1964	M	56 non-smokers (1)	26 smokers (2)	46.4%
Rogot and Reid (1975)	British and Norwegian migrants to US	1. Postal questionnaire to subject in 1962 2. Questionnaire to relative after death in 1963–66	M+F	1290 non+occasional smokers (1)	77 regular smokers (2)	6.0%
			M+F	1289 non+occasional smokers (2)	76 regular smokers (1)	5.9%
Pederson et al. (1977)	Canadian school children	1. Smoking awareness questionnaire 2. Later health questionnaire	M+F	76 non-smokers (1)	4 smokers (2)	5.0%
			M+F	85 non-smokers (2)	13 smokers (1)	15.3%
Petitti et al. (1981)	Californians having health check ups	1. Health questionnaire 2. Research questionnaire at similar time	M+F	128 never-smokers (1)	9 ever smokers (2)	7.0%
			M+F	119 never-smokers (2)	0 ever smokers (1)	0.0%

Hebert and Fry (1982)	Scottish health screening study	1. Initial screening 2. Follow-up screening 2–5 years later	M	≃841	≃51	6.1%
			F	≃2549 never-smokers (1)	≃55 ever smokers (2)	2.1%
			M	≃924	≃133	14.4%
			F	≃2619 never-smokers (2)	≃125 ever smokers (1)	4.8%
Kabat and Wynder (1984)	US lung cancer study – controls with non smoking related diseases	1. Subject in hospital 2. Hospital records	M+F	134 never-smokers (1)	0 ever smokers (2)	0.0%
Herrmann (1985)	US case-control study of colon cancer	1. Subject interviewed 2. Next-of-kin-interviewed or given self-completion questionnaire at about the same time	M+F	? non-smoker (1 or 2)	? smoker (2 or 1)	≃12%
Murray et al. (1985)	Derbyshire schoolchildren	1. Parent (subject) interviewed in 1974 and 1978 2. Child interviewed annually giving data on parent's habits	M	2216	211	9.5%
			F	3146 non-smoker (1)	326 smoker (2)	10.4%
			M	2223	218	9.8%
			F	2905 non-smoker (2)	85 smoker (1)	2.9%
Sandler and Shore (1986)	US study of cancer cases and controls	1. Parents interviewed 2. Cases and controls (subjects) interviewed at same time about parent's habits	F	? never-smoker of cigarettes (1)	? ever smoker of cigarettes (2)	2.7%
			M	? never-smoker of cigarettes (1F)	? ever smoker of cigarettes (2)	17.2%
Lee (1987)	UK representative sample	1. Interview in 1980 2. Reinterview in 1985	M+F	174 never-smoker (1)	22 ever smoker (2)	12.6%
			M+F	166 never-smoker (2)	12 ever smoker (1)	7.2%
Pershagen et al. (1987)	Swedish prospective study	1. Subject mailed questionnaire in 1961–63 2. Subject or next-of-kin in 1984	M+F	384 never-smoker (1)	6 ever smoker (2)	1.7%

[a] Bracketed figures indicate source of information. For the study by Sandler and Shore (1986) the data on the mother's habits (F) were supplied by the mother (base) and confirmed by the subject (disagreement), while the data on the father's habits (M) were supplied by the mother (base) and confirmed by the subject (disagreement).

Table 6 brings out a number of points:

(a) The studies are predominantly of UK or US subjects, with the rest Canadian or Scandinavian. None relate to Japanese or Greek subjects.

(b) Only 2 studies (Todd, 1966; Pershagen et al. 1987) test consistency over a long time period. Most of the studies relate to statements made at time points 5 years or less apart, while a number concern information collected from 2 sources at around the same time point.

(c) Care should be taken to distinguish between disagreement rates based on current smoking status and those based on ever smoking status. It is well known that men and women smokers often give up smoking and then start it again, so that some degree of inconsistency in current smoking status is to be expected when data are collected at 2 different points in time. An ever smoker cannot become a never smoker, so that studies which suggest they have done so indicate inaccuracy in the source data. Also, since people hardly ever take up smoking for the first time after the age of 40, reported switches from never smoking status to ever smoking status among the middle aged or old are also likely to indicate inaccuracy in the source data.

(d) The studies summarised in Table 6 do not include all those considered in the previous section. This is mainly because some studies do not provide information from which a rate can be calculated in the required form. Where a study reports the percentages of smokers reported as non-smokers it is in theory possible to convert this to the Table 6 percentages of non-smokers found to be smokers, provided one knows the overall population distribution of smoking habits. Thus, in a population with E% ever smokers and N% never smokers, an observation that a proportion p of ever smokers deny smoking is equivalent to saying that a proportion pE/(N+pE) of self-reported never smokers are ever smokers. However the data required to carry out the conversion are rarely available so Table 6 does not include results from such studies.

(e) The adjustment factor noted above (which equals E/N approximately for small p) to convert one proportion to another is likely to vary markedly by age, sex, country and time of study. Thus in 1961 in the UK, only 8% of men aged 60+ had never smoked as against 68% of women, yielding adjustment factors (11.5 and 0.47) which differ by a factor of over 20. Care should be taken, therefore, before interpreting sex differences in disagreement rates in Table 6 as indicating differences in the propensity of the sexes to tell the truth – they may only be indicating differences between the sexes in the proportion of ever smokers.

(f) Most of the studies considered in Table 6 concern disagreement about current smoking status. There is considerable variation in disagreement rates, with at one extreme Haenszel et al. (1962) reporting "virtually all correctly identified", and at the other Todd finding 40% disagreement rates. Todd (1966) noted that "the failure of informants in 1964 to remember that they had been non-smokers at the time of the earlier interview in 1948/50 may have been due to them dating later the time at which they had given up smoking, or alternatively their non-smoking at the earlier interview may

have been only a temporary phase and had been forgotten". It should also be noted that his study concerned a period where relatively few men were never smokers. Also that his was a memory enquiry, whereas for many of the other studies the second source of information concerned smoking habits at the second point in time. While there is obvious difficulty in coming to any very meaningful overall average from the combined data from studies of this type, it certainly seems that a number of studies have found that 5% or even 10% of subjects classified as non-smokers by one source or at one time are classified as smokers at another source or time.

(g) The studies relating to ever smoking status are more relevant in that they more directly provide evidence of errors. Here there are 6 studies with rates (averaging multiple results as appropriate) as follows:

Study	Rate
Lee (1987)	10%
Sandler and Shore (1986)	10%
Hebert and Fry (1982)	7%
Pettiti et al. (1981)	3.5%
Pershagen et al. (1987)	1.7%
Kabat and Wynder (1984)	0.0%

In considering these one should note that the Pettiti et al. (1981) study concerns the rather strange situation where the same subject was asked twice at about the same time, which seems hardly likely to produce high inconsistency rates. The Kabat and Wynder (1984) approach of trying to confirm a subject's self-reported smoking status by reference to hospital records is also likely to only pick up a proportion of "deceivers" at best. Of the rest, my study (Appendix B), and those of Sandler and Shore (1986) and Hebert and Fry (1982) all give rates of the order of 7–10%, which are probably consistent with Britten's figure of 4.9% (quoted by Wald et al. 1986) for the proportion of smokers denying smoking. Whether the lower rate of 1.7% from the Pershagen et al. (1987) study is due to Swedes being more honest, a lower rate of ever smokers in Sweden or the study situation is not clear.

(h) Most of the studies give no information as to whether smokers misclassified as non-smokers are typical. Those that do (Rogot and Reid, 1975; Lee, Appendix B; Britten in Wald et al. 1986) all suggest that they are not, being more likely to have been lighter smokers and, if ex-smokers, to have given up a longer time ago than average. However, information is still fairly sparse in this area.

3.4.2 The Studies

Following an initial survey in 1946, Research Services Ltd. have carried out representative surveys of the smoking habits of the British public annually ever

since 1948. Todd and Laws (1959) described the results of "Memory Enquiries" in 1952 and 1957 in which certain informants in these surveys were re-interviewed and asked questions on aspects of their smoking habits about which they had previously provided information. The 1952 memory enquiry involved 982 men and 306 women first interviewed in 1948, 1949 or 1950, while the 1957 memory enquiry involved 662 men first interviewed in 1948–1950, 1955 or 1956. Of the 288 men who took part in the 1952 Memory Enquiry and who stated they were smokers in 1948, 8 (2.8%) claimed when reinterviewed in 1952 that they had been complete non-smokers in 1948. Other similar percentages are shown in the following table:

Percentage of men who failed to remember that they had smoked at all at the time of a previous interview (1952 and 1957 Memory Enquiries)

Time elapsed	% who failed to remember having smoked
6 months	0.5
13 months	0.7
2 years	0.0
3 years	1.5
4 years	2.8 (8/288)
5 years	1.5
7–9 years	3.0 (6/203)

As shown in the next table, the percentage of men who failed to remember in the opposite direction was much higher.

Percentage of men who failed to remember that they had been non-smokers at the time of a previous interview (1957 Memory Enquiry)

Time elapsed	% who failed to remember having not smoked
6 months	5 (2/43)
18 months	22 (10/46)
5 years	37 (15/40)
7–9 years	35 (11/31)

Haenszel et al. (1962) describe the results of a US study in which, in 1956, smoking histories were collected from relatives of 338 men who had died (of all causes) and who, in 1953, had reported on their own smoking history at the start of a smoking and health study. The authors noted that "virtually all non-smokers were correctly identified by the family informant" but no details are given of the level of disagreement.

Hammond and Garfinkel (1964) studied changes in smoking habits between 1959–60 and 1961–62 among 404,000 men and 527,000 women in the American Cancer Society "million person study". 2.1% of men and 1.0% of women who

stated that they had never smoked cigarettes regularly in 1959–60 said that they were smoking cigarettes regularly in 1961–62. The authors note that some of these may have been people who were misclassified ex-smokers in 1959–60. The possibility of misclassified current smoking is not discussed nor are data given on the proportion of 1961–62 never smokers who earlier had stated they had smoked.

Never regular smokers in 1959–60 who reported smoking cigarettes in 1961–62

Sex	Age	Never smoked regularly 1959–60	% Smoking cigarettes in 1961–62
Men	30–39	5183	3.0
	40–49	22661	2.5
	50–59	20868	2.2
	60–69	19528	1.9
	70–89	10239	1.5
	Total	88479	2.1
Women	30–39	24762	1.8
	40–49	95788	1.5
	50–59	116575	0.9
	60–69	77477	0.5
	70–89	38506	0.3
	Total	353108	1.0

The proportion of ex-cigarette smokers who later reported smoking cigarettes is much higher, particularly for short-term ex-smokers and for ex-cigarette smokers still smoking pipes or cigars. Consequently the proportion of non-smokers later reported to be smokers (men 6.6%, women 1.4%) is higher particularly for men than the proportions of never smokers later reported to be smokers (men 2.1%, women 1.0%).

Ex-cigarette smokers in 1959–60 who reported smoking cigarettes in 1961–62

Sex	Subgroup of ex-smokers	Ex-cigarette smoker 1959–60	% Smoking cigarettes in 1961–62
Men	Current pipes and cigars	15864	21.5
	Not current pipes and cigars		
	(a) Stopped cigarettes, <1 year	6782	37.3
	(b) Stopped, 1–2 years	3898	19.1
	(c) Stopped, 2+ years	55029	4.6
	(d) Stopped, time unknown	1691	9.4
	Total	83264	11.3
Women	Total	29490	6.0

A further Memory Enquiry was carried out in which men who had first been interviewed in 1948, 1949 or 1950 was interviewed again in 1964 in order to obtain information about the errors made in recalling past smoking habits over an average period of 15 years. The results were reported by Todd (1966). Interviews were obtained with 395 of the 1085 original informants selected for study and with relatives of a further 193 who had died during the intervening 15 years. As in the earlier study by Todd and Laws, failure to remember non-smoking was far more common than failure to remember smoking.

Time elapsed	Non-smokers at the earlier interview who failed to remember that they had been non-smokers at that time		Smokers at the earlier interview who failed to remember that they had been smokers at that time	
	No.	%	No.	%
6 months	2	5	1	0.5
18 months	10	22	1	0.7
2 years			0	0.0
3 years			4	1.5
4 years			8	2.8
5 years	15	37	3	1.5
7–9 years	11	35	6	3.0
14–16 years	26	46	11	3.2

Rogot and Reid (1975) compared data obtained by postal questionnaire from the subject with data obtained by sending a questionnaire to the next of kin (or other informant) who registered the subject's death. The original subjects were 32 000 British and 18 000 Norwegians who had migrated to the USA by 1962. About 2000 deaths during 1963–66 were followed-up. As shown in the table below, the agreement rate resulting from classifying smokers simply as non/occasional versus regular smokers was 92%. 76 (5.9%) of those claiming to be non-smokers were said by their relative to have been a smoker. Conversely 77 (6.0%) of those whose relative said they were a non-smoker had themselves said they were a smoker.

Smoking obtained by personal questionnaire compared with those obtained by next-of-kin or other informant

Informant questionnaire	Personal questionnaire		
	Non-smoker + occasional	Regular smoker	Total
Non-smoker + occasional smoker	1213	77	1290
Regular smoker	76	587	663
Total	1289	664	1953

On a more detailed classification, there was agreement in 74% of subjects – this varied from 58% among males aged 45–54 to 89% among females aged 65–74. There was a tendency for the relative to report higher consumption than the subject.

Packets of cigarettes smoked per day obtained by personal questionnaire compared with those obtained by next-of-kin or other informant

Informant questionnaire	Personal questionnaire					
	Non/ex	Occ.	<1	1	>1	Total
Non/ex	1133	13	27	7	6	1186
occasional	49	18	31	5	1	104
<1	26	4	92	43	6	171
1	30	6	90	113	39	278
>1	9	1	39	73	92	214
Total	1247	42	279	241	144	1953

The Tucson Epidemiologic Study of Obstructive Lung Disease is a longitudinal study of a population of nearly 4,000 persons in Arizona. In the third year of the study, after using self-administered, standard National Heart and Lung Institute (NHLI) questions in early evaluations, Lebowitz and Burrows (1976) decided to test the comparability of interviewer-adminstered NHLI and British Medical Research Council (BMRC) questinnaires and to compare both to a self-completion questionnaire of their own design (Arizona – ARIZ questionnaire). The subjects were sent the ARIZ-Q for self-completion 2 weeks before a clinic appointment, which they brought with them completed or not completed. If previously completed, or if completed there at that time, it was reviewed for completeness by the nurse interviewers. Subjects then proceeded with other tests after which they were administered either the NHLI-Q (1145 subjects) or the BMRC-Q (1200 subjects). Lebowitz and Burrows compared responses in respect of a range of respiratory symptoms and smoking history responses. As regards "ever smoking", there was a 96.2% agreement between the ARIZ-Q which asked "Have your ever smoked cigarettes regularly" and the NHLI-Q which was based on "Do you now smoke cigarettes regularly, occasionally, or ever?" and "If you do not smoke cigarettes now, did you ever smoke them regularly or occasionally?" There was a 96.6% agreement between the ARIZ-Q and the BMRC-Q which was based on "Do you smoke?" and "Have you ever smoked as much as one cigarette a day (or one ounce of tobacco a month) for as long as a year?" The authors did not discuss the extent to which disagreements were likely to be due to the differences in the questions asked or to one of the answers being incorrect.

In the study by Pedersen et al. (1977) (see Sect. 3.3.2) the children who completed a health questionnaire had earlier answered questions about current smoking habits in a smoking awareness questionnaire. The relationship between the answers is as follows:

Original questionnaire	Later questionnaire		
	Smoker	Non- or ex-smoker	Total
Smoker	11	13	24
Non- or ex-smoker	4	72	76
Total	15	85	100

The authors note that 17% (=13+4/100) of the results were inconsistent although they do not note that theoretically children can legitimately change from current to ex-smoker and vice-versa. They point out that the increased number of self-reported smokers in the original questionnaire (24%) may be because anonymity was ensured only at the original questionnaire.

In a study of the adequacy of survey data collected from substitute respondents, Kolonel et al. (1977) compared information on the smoking, drinking and diet habits of 300 Hawaiian men obtained from two interviews, one of the man himself and the other of his wife or close relative. Care was taken that the members of each pair had no opportunity to communicate with each other between the start and completion of both interviews. There was stated to be agreement over the smoking habit classification never smoked/ever smoked in 96.3% of pairs, equivalent to disagreement in 11 pairs. Although it was also stated that there were 194 pairs in which the husband smoked (according to whom not given), a breakdown which could enable the proportion of self-reported never smokers reported to be ever smokers by the wife to be calculated is not given.

The paper by Luepker et al. (1981) referred to in Sect. 3.1.2 described a study in which Minnesota schoolchildren provided a sample of saliva following a film on how smoking could be detected from such a sample and then provided smoking data. One year earlier, 422 of the children had taken part in an earlier study in which children were randomly assigned to either the same procedure (338 children) or to an altered procedure in which the self-reported smoking measures were taken prior to viewing of the film and collection of the samples (84 children). The proportion reporting regular smoking was twice as high in the former situation (10.7%) as in the latter (4.8%). Although not a statistically significant difference ($p > 0.1$), the results are consistent with knowledge of subsequent biochemical validation affecting answers to smoking questions.

In the study by Petitti et al. (1981) referred to in Sect. 3.1.2 the joint distribution of cigarette smoking habits from the 2 questionnaires was as follows:

Research questionnaire	Health questionnaire				
	Current	Past	Never	No answer	All
Current	60	0	0	2	62
Past	5	55	0	2	62
Never	1	8	119	0	128
All	66	63	119[a]	4	252

[a] The paper gives 123, but this appears to be an error.

Nine of the 128 (7.0%) subjects who reported never smoking on the research questionnaire reported current or past smoking on the other questionnaire, while 5 of the 60 (8.3%) subjects who reported past smoking on the research questionnaire reported current smoking on the other questionnaire. The differences may have arisen in part because the research questionnaire defined regular smoking as "at least 5 cigarettes per week, almost every week for at least one year", whereas the health questionnaire did not define regular tobacco use. The authors note that "subtle differences in the wording of questionnaires results in substantial differences in the way people classify their smoking status.

Pershagen and Axelson (1982) obtained information by questionnaire on occupational exposure and smoking habits from close relatives of 160 deceased Swedish smelter workers and compared the findings with data from employee registers. Data on smoking habits were available from medical files, for only 14 of the subjects, but it was identical to the questionnaire data in each case (1 non-smoker and 13 smokers).

Hebert and Fry (1982) studied 8,518 people in two surveys in West Central Scotland who returned for a follow-up screening examination two to five years after an initial examination. The table below summarises the joint distribution

Smoking habits as reported at initial examination and 2–5 years later in two studies in West Central Scotland

Initial interview	Follow-up never	Interview ex	Current	Impossible answers
Paisley - males				
Never	19.9%	1.2%	0.2%	
Ex	3.0%	27.6%	2.2%	3.7%
Current	0.7%	7.7%	37.4%	
(base = 3046)				
Paisley - females				
Never	50.8%	0.9%	0.3%	
Ex	1.3%	7.6%	1.1%	2.5%
Current	1.2%	4.2%	32.6%	
(base = 3913)				
Renfrew - males				
Never	25.7%	0.8%	0.4%	
Ex	2.2%	28.2%	1.8%	2.9%
Current	0.7%	8.0%	31.3%	
(base = 716)				
Renfrew - females				
Never	60.1%	0.5%	0.4%	
Ex	1.7%	6.4%	1.1%	3.2%
Current	1.5%	4.3%	25.3%	
(base = 843)				

of smoking habits (never, ex, current) from the two surveys. It can be seen that in both surveys and in both sexes about 3% of the population reported they had never smoked at follow-up interview when they had earlier stated that they were current or ex-smokers.

As noted in Sect. 3.3, Kabat and Wynder (1984) found no mention in the hospital records of a past history of smoking amongst any of 134 hospital patients with diseases not related to smoking who reported they had never smoked.

Horwitz and Yu (1985) carried out a case-control study of breast cancer in post-menopausal women at Yale-New Haven Hospital. Interviews were carried out by telephone by 3 interviewers between April 1980 and September 1981. 120 patients were randomly selected and reinterviewed between December 1981 and February 1982. The interviewer was blind to the findings of the first interview and each subject was interviewed by a different interviewer. Data were collected on clinical and pharmaceutical features and on smoking (although no details are given regarding the nature of the question(s) on smoking). There were 4 disagreements (3%) between the interviews about smoking, with 62% positive agreements and 35% negative agreements. All 4 disagreements were found to be due to patient disagreement.

Herrmann (1985) compared medical, smoking, and dietary consumption data obtained from colon cancer cases or controls and, at about the same time, from their respective next-of-kin in a study carried out in Pennsylvania. Questionnaires for cases and controls were administered by interviewers; questionnaires for their next-of-kin were randomly allocated to be self- or interviewer-administered. A total of 191 case/next-of-kin pairs and 192 control/next-of-kin pairs provided information. It was noted that "the percentage of complete agreement on whether the subject smoked exceeds 85% for all types of smoking and comparison groups" and that "the kappa values all exceed 0.68 when the interviewer-administered questionnaire was used for both respondents and are slightly lower when the self-administered questionnaire was used." For a 2×2 table:

Source 1	Source 2		
	Non-smoker	Smoker	Total
Non-smoker	a	b	a+b
Smoker	c	d	c+d
Total	a+c	b+d	N

the percentage agreement is calculated by $100(a+d)/N$ and the kappa statistic by $2(ad-bc)/[(a+c)(c+d)+(a+b)(b+d)]$. Without knowing the actual numbers in the 2×2 tables one cannot calculate the proportion of self-reported non

smokers reported as smokers by the next-of-kin, but one can see from the approximate example below that it would have been quite substantial:

Self	Next-of-kin	
	Non-smoker	Smoker
Non-smoker	55%	7.5%
Smoker	7.5%	30%

% complete agreement 85%; kappa statistic 0.68; proportion of self-reported non-smokers considered smokers 12%.

Murray et al. (1985) studies a cohort of 6000 Derbyshire adolescents aged 11–12 in 1974. They were surveyed annually about smoking behaviour, attitudes and other issues until 1978 and again in 1981. In 1974 and 1978, questionnaires were sent to their parents asking about their own smoking and attitudes to smoking. Results taken and checked from their paper are given below. Of parents who claimed to smoke in 1974, this was agreed by 96% of children for mothers and 92% for fathers. Of parents claiming not to smoke, this was agreed by 90% of children. Of mothers with an anti-smoking attitude, this was agreed by 73% of children, while of mothers who were not against their children smoking, this was agreed by 67% of children. In the discussion, it is suggested that some of the parental smoking reported by children but not by the parents may have been due to smoking only once or twice a year.

Self-reported smoking habits of parents compared with those reported by their children

Table as presented

Child's report	Mother's report		Father's report	
	Smoker	Non-smoker	Smoker	Non-smoker
Boy: Mother smokes	95.8 (1018)	11.1 (1534)		
Father smokes			92.8 (1333)	9.7 (1064)
Girl: Mother smokes	96.0 (1056)	9.7 (1612)		
Father smokes			90.9 (1337)	9.4 (1152)

Deduced from above table

Child's report	Parent's report			
	Mother		Father	
	Yes	No	Yes	No
Yes	1989	326	2452	211
No	85	2820	218	2005

Peach, Shah and Morris (1986) reinterviewed 429 middle-aged men who, 12 years earlier, when participating in a UK Heart Disease Prevention project had completed a self-administered questionnaire about their present and past smoking habits and had claimed to smoke at that time. The main intention of the study was to compare the brand stated 12 years ago to be smoked at the time with the brand remembered 12 years later to be smoked then. Of the 429 men, 43 (10%) claimed not to have been smoking 12 years ago, 216 (50%) could not recall the brand smoked, with only 170 (40%) recalling a brand. In 49% of the latter cases, the brand recalled differed from that previously stated.

In a US study by Sandler and Shore (1986), 518 cancer cases and 518 healthy controls aged 15–59 were asked to provide information about their parents' smoking and drinking habits. Parents (preferably the mother) or siblings of 70% of the study subjects were also interviewed to obtain the same information. Of 982 subjects who lived with their natural mother in childhood, around 97% were able to provide data on whether the mother ever smoked cigarettes, pipes or cigars or used snuff or chewing tobacco. Of 924 who lived with their natural father, the percentage answering these questions varied from 93.5–94.8%.

Of those mothers who reported never having smoked cigarettes, 2.7% were reported as ever having smoked them by the subject. Of those mothers who reported ever having smoked cigarettes, 8.2% were reported as never having smoked.

Of those fathers reported by the mother as never smoked cigarettes, 17.2% were reported as ever having smoked them by the subject. Of those fathers reported by the mother as ever having smoked cigarettes, 12.1% were reported as never having done so by the subject.

There was a 97.4% agreement between subjects and siblings on whether the mother had ever smoked cigarettes and an 87.5% agreement concerning the father.

Wald et al. (1986) reported results supplied by Britten from the Medical Research Council national survey of health and development. In this study, information on smoking was collected on several occasions from 3274 of the subjects from the survey. Of all the subjects who had previously reported they smoked, 4.9% said in their most recent interview that they had never smoked as much as one cigarette a day. Nearly all of these people (93%) had reported smoking 10 or more years earlier but not more recently, and, on average, they had smoked only about a third as many cigarettes per day as those who reported that they were current smokers and had also reported smoking previously.

Lee (Appendix B) interviewed 8800 representative UK men and women aged 16+ in 1980 about their smoking habits and reinterviewed a sample of 540 of them 5 years later. At the follow-up, 166 men and women reported they did not smoke and had never smoked for as long as a year. In 1980, 2 of these subjects had previously claimed to be regular current smokers and 10 ex-smokers, an inconsistency rate of 7.2% (12/166). Conversely, 174 men and women could be classified as never smokers based on answers given in 1980, and, 5 years later, 3 of these reported being current smokers and 19 being ex-smokers,

all stating having started before 1980. This represented an inconsistency rate of 12.6% (22/174). Individuals giving inconsistent information tended to be men, old, smokers of fewer cigarettes and long-term ex-smokers.

As noted in Sect. 3.3, Pershagen et al. (1987) found that among 84 non-lung cancer controls originally classified as non-smokers in the early 1960's, 6 (1.7%) were reported in 1984 to have smoked daily for at least 2 years.

3.5 Other Evidence on Misclassification of Smoking Habits

3.5.1 Overview

Finally evidence on misclassification of smoking habits from a variety of other sources is considered. These sources include, inter alia, studies in which cigarette consumption per adult as estimated from survey data has been compared with known sales figures, studies of children in which the relationship of the interview situation to the reported level of smoking has been investigated, and studies of adults in which general levels of response have been compared using different data collection techniques.

The studies considered in this section are rather a mixture of different techniques studying different aspects of reliability of statements about smoking habits. The studies of children suggest strongly that the information collected depends on the circumstances of the study, including whether or not the children knew their answers would be checked up on. However, the extent of this apparent effect varies – compare the studies of Evans et al. (1977) and Williams and Gillies (1984) – and the situation may well depend on the age of the child. The relevance of studies in 12 year old boys (who may claim they smoke when they do not in order to impress their peers) to lung cancer/passive smoking studies in adults (who are unlikely to do so) is dubious.

Nor is the evidence that surveys tend to underestimate total nuimbers of cigarettes actually sold directly relevant to estimation of the proportion of smokers who deny smoking, since a large proportion of the underestimation seems likely to be due to smokers understating numbers smoked rather than actually denying smoking.

Nevertheless the evidence cited generally adds to the plausibility of the hypothesis that denial of smoking occurs, and that the level of it is likely to be affected by the way the information is obtained.

3.5.2 The Studies

Enterline and Capt (1959) describe a study in which adult males aged 35+ for whom information was desired, but who were not at home at the time the interviewer made her initial visit, were divided randomly into two groups. In

group 1 (312 men) the desired information was provided partly by an eligible household respondent (relative aged 18+) and partly by a questionnaire left at the house to be completed by the male when he returned. In group 2 (307 men), revisits were made until the male was found at home. The questions related to personal characteristics, work history, food habits, cigarette smoking, illness, medical care, health symptoms and characteristics of the parents.

Comparing answers from the person himself as obtained by self-completed questionnaire or by interviewer, the percentages who ever smoked cigarettes were respectively 64.2% and 67.8%, while the percentages who currently smoked cigarettes were 52.0% and 54.4%. while the differences were not significant, the reduced proportions in the first situation were consistent with a general tendency for underreporting for all the questions asked.

Unfortunately, no answers were presented for group 1 comparing smoking habits reported by a relative and those reported by the subject.

Harlin (1972) describes a study of 2350 Seattle students aged 15–20. All completed a standard self-administered questionnaire, students being randomly assigned to answer the questionnaires anonymously ("unsigned") or to identify themselves ("signed"). Among girls, there was little difference in the percentage reporting current smoking in the two groups (signed 25.1%, unsigned 25.8%) or in the percentage reporting never smoking (signed 26.7%, unsigned 27.2%). Among boys, there was a somewhat higher percentage reporting current smoking in the unsigned group (37.9%) than in the signed group (32.9%), though this was not clearly significant ($0.05 < p < 0.1$). The percentages reporting never smoking were similar (signed 15.6%, unsigned 15.7%).

Evans et al. (1977), in a study in Houston, collected data on self-reported smoking habits in two groups of children, one of which had first been shown how saliva could be analysed for nicotine content and had then provided saliva specimens. Only 14.3% (12/84) control children reported being smokers as against 31.4% (27/86) of those providing saliva, a significant difference ($p < 0.05$). No nicotine analyses were actually carried out, the intention merely being to see whether convincing the children (by what the authors refer to as a "bogus pipeline" technique) that their statements could be independently verified affected the answers.

Todd (1978) examined survey data on cigarette consumption per adult from 7 countries and compared the derived estimates of total national cigarette consumption with that based on sales data. A shortfall of 20–30% in the survey data was seen in Australia, Canada, Denmark and USA. Todd noted that in the surveys carried out in USA in 1970 and 1975 the survey figures had to be increased by as much as 52% and 56% respectively, and commented on the fact that on these occasions respondents were asked health questions before being asked their smoking habits. In interpreting such shortfalls, it should be remembered that smokers understating how many they smoke may be a more important cause than smokers claiming to be non-smokers.

Rose and Hamilton (1978) in a randomised controlled trial of the effect on middle-aged men of advice to stop smoking, followed up "normal care" and "intervention" groups after 1 and 3 years. Subjects attending for interview

completed a questionnaire, while those unable to attend returned one by post. Response was higher in the normal care group. Results showed that after 1 year 51% and after 3 years 36% of the intervention group were smoking no cigarettes, although about a third of them were smoking pipes or cigars. Statements were not validated biochemically, but the authors formed a "strong impression" that men who reported complete cessation were nearly always speaking the truth, while those who had reduced often exaggerated the size of the reduction. The results were indirectly validated at 1 year when prevalence of phlegm corresponded to cessation/reduction in smoking and was similar in normal care and intervention groups.

McKennell (1980) studied factors which bias self-reports of smoking behaviour using a balanced sample of over 4000 boys and girls aged 11 to 16 years drawn from 48 British secondary schools. It was found that, for boys, the reported incidence of those smoking one cigarette or more per week tends to increase when the questionnaire is self-administered rather than completed by an interviewer, when the answers are obtained in school rather than in home interviews and, in school, when children were interviewed together in classrooms rather than individually. These effects did not reach statistical significance for girls and were most pronounced for younger boys, among whom there was nearly a five-fold difference between the incidence reported in classroom and home-oral interviews. For younger boys and girls it was found too that the inclusion of a persistently probing question about trying even one cigarette increased the numbers admitting to regular smoking. It was concluded that prevalence estimated from studies of children's smoking are highly contingent, especially for younger boys, on the method by which the data are obtained.

Gillies et al. (1982) carried out a study of 421 children aged 10 or 11 from Sheffield. Pupils were randomly assigned to 3 groups; questionnaire only (A); questionnaire plus saliva specimen without prior knowledge of specimen collection (B); questionnaire plus saliva specimen with advice in advance that immediately after completion of the questionnaire a specimen would be tested for evidence of smoking (C). The smoking question allowed the children to be classified as regular smokers (>6 cigarettes a week or 1–6 cigarettes a week), occasional smokers (<1 cigarette a week), those who had only tried once, and those who had never tried. 100 μg/ml saliva thiocyanate was used as a cut-off point to discriminate smoking, and information was collected on recent consumption of cyanogenic foodstuffs, the 12 reporting having done so being treated separately. 45 of the non-smoking sample of 243 (18.5%) had salivary thiocyanate levels above the critical point. Only 11 children (2.6%) reported regular smoking. Of the remainder, 113 children claimed to have tried, the percentage being significantly ($p < 0.02$) higher in group C (36%) than in groups A + B combined (24%).

Collishaw (1983) studied data collected at regular intervals since 1965 by the Smoking Habits of Canadians Survey on smoking and concluded that they underestimated both the number of cigarette smokers and the total consumption of cigarettes, the most serious underestimation occurring from 1975 to 1981. This agreed with calculations this author has made independently which

showed that, during the period 1965 to 1977, when consumption per adult based on sales had increased steadly, from 3310 to 3605 cigarettes per year, consumption per adult based on survey estimates has decreased, from 2632 (shortfall 20.5%) to 2383 (shortfall 33.9%).

Pickle et al. (1983) studied the ability of surrogate respondents to provide information on a variety of items in case- control interview studies. The studies were carried out in Virginia, Florida and Georgia and involved interviews of some 450 index subjects, 1340 spouses, 210 sibs, 380 offspring and 230 other respondents. The index subjects were either lung (or occasionally larynx) cancer cases or appropriately matched controls. Questions asked included ones on number of years smoked, detailed smoking history and brand smoking history. Non-response rates were lowest when the index subject answered (0.3%, 29% and 3% respectively), higher when the spouse or offspring answered (16%, 44%, 12%), higher still when the sib answered (20%, 53%, 16%) and highest of all when another respondent answered (35%, 59%, 23%). While not providing any direct evidence on accuracy of answers by surrogates, it seems to suggest strongly that studies which force surrogates to provide answers are likely to have a high proportion incorrect, particularly for detailed smoking history.

In the study by Williams and Gillies (1984) referred to in Sect. 3.1.2, some of the Nottingham adolescents knew that an objective test would be performed subsequently and some did not. This knowledge did not significantly affect the reported levels of smoking, 10.1% claiming to be occasional, weekly or daily smokers with prior knowledge of the test, as against 12.9% with no prior knowledge.

In a study of high dietary fat intake and cigarette smoking as risk factors for ischaemic heart disease in Bangladeshi middle-aged male immigrants in East London, Silman et al. (1985) noted "a very high proportion of smokers, approximately twice the national male rate and 50% higher than for a similar Caucasian population adjusted for age and social class". They considered it unlikely that their smoking interview overestimated the number of smokers, suspecting on the contrary that "many of the self-reported Bangladeshi non-smokers were giving false answers as judged by nicotine staining and other signs".

Hansen et al. (1985) re-examined the use of the "bogus pipeline" technique found by Evans et al. (1977), and also by Bauman and Dent (1982), to increase self-report of cigarette smoking. 540 9th grade and 1100 8th grade Californian schoolchildren who had previously completed smoking questionnaires and provided saliva samples (respectively 4 times over the last 2 years, and 2 times over the last year) were randomly assigned to 2 groups. One group completed a questionnaire knowing they would be required to provide a sample of saliva while the other group completed a questionnaire only with no discussion of saliva or samples taken. No significant increase in reported smoking was seen in either cohort of children for any of 7 indicators of smoking status. Indeed the tendency was in the opposite direction. The authors note "given that previous studies had found the effect at the time of first measurement, we suspect that repeated previous testing in this study had resulted in sufficient confidence in the research team to reduce or eliminate subjects' motivation to underreport their behaviour".

In an analysis, for which more details are given in Appendix D, annual data from large smoking habit surveys of the UK has been used to study changes within birth cohorts in the percentage of never smokers over a 5 year period. Comparing the years 1975 and 1980 and the years 1976 and 1980, a statistically significant tendency towards a slight increase was seen. In theory, of course, if smoking habits are correctly recorded, the percentage of never smokers can only reduce or stay still over time.

4 Overview and Unanswered Questions

In Sect. 3, about 100 studies have been reviewed. These cover a wide variety of study situations and it is difficult to identify all important sources of variation in the extent to which smokers are misclassified as non-smokers. Even in the situations which do not seem all that different wide variations in misclassification rates are sometimes found. An example of this is the difference between the Pershagen et al. (1987) study and the other studies of people with lung cancer cases referred to in Sect. 3.1.3. This variability makes the overall picture difficult to interpret reliably.

There are however, some conclusions that can be drawn with a degree of confidence. The first is that the percentage of true smokers found amongst self-reported non-smokers tends to be high in smoking cessation studies. Percentages in excess of 15–20% are commonplace in smoking cessation studies, and figures of up to 40% have been reported. Within smoking cessation studies, percentages tend to be higher in large general population studies where the experimenter has limited contact with the subject than in studies where the procedure to encourage smoking cessation involves considerable contact over a long period of time. They also seem to be higher where the subject is unaware that statements made are going to be validated biochemically. Large percentages are not seen in studies where the subjects have not been very strongly advised to give up. The very existence of this variation implies strongly that denial of smoking is likely to be affected by the situation, and that it is dangerous to extrapolate too readily from one situation to another.

A second clear observation is that the percentage of true smokers found amongst self-reported non-smokers tends to be higher in studies of lung cancer cases than in studies of men and women without lung cancer. This is not surprising in view of the strong association between lung cancer patient and smoking. Thus if 50% of the general population smoke and 2% of smokers deny smoking, the proportion of true smokers among self-reported non-smokers will be 2.0% (1/51). If on the other hand 95% of lung cancer patients smoke and again 2% of smokers deny smoking, the proportion will be as high as 27.5% (1.9/6.9).

A third observation, perhaps less clear (but still reasonably so) is that the misclassification rates I reported in Appendix B for the situation where the respondents are not lung cancer cases and are not under pressure to stop smoking are reasonable. I found that, of self-reported never smokers, 2.5% are actually current smokers and 10% have smoked in the past. The 3 relevant studies using carbon monoxide or thiocyanate as a marker (Jones et al. 1972; Pettiti et al. 1981; Robertson et al. (1987) give a combined estimate of 4.4% for the proportion of non-smokers with high levels of marker, while the 7 most relevant

studies using cotinine or nicotine in Table 4 apart from my study (i. e. Russell and Feyerabend, 1975; Feyerabend et al., 1982; Haley et al., 1984; Wald et al., 1984; Jarvis et al., 1985; Haddow et al., 1986; Coultas et al., 1987) yield a combined estimate of 2.2%. Also, as noted in Sect. 3.4, the estimate of 10% in relation to lifetime studies is similar to that from 3 other studies (Sandler and Shore, 1986; Hebert and Fry, 1982; Britten in Wald et al., 1986) and only materially higher than the 1.7% from the study of Pershagen et al. (1987).

Perhaps more crucial to the misclassification issue is the proportion of misclassified current regular smokers, as this is likely to be a major contributor to the magnitude of any passive smoking/lung cancer bias. This was the major cause of the difference in conclusion between Wald et al. (1986) and Lee (Appendix B) concerning the effects of misclassification of bias. Wald et al. cited 4 studies in which only 1 out of 690 (0.1%) self-reported non-smokers had a nicotine or cotinine level characteristic of a typical smoker. In contrast, Lee found 11 out of 808 (1.4%). While many of the studies reviewed here do not provide information on extent or duration of smoking, merely classifying subjects as smokers or non-smokers (or as ever smokers or never smokers), a number of other pieces of evidence suggest that Wald et al.'s figure may well be substantially too low. One is the recent large salivary cotinine study of Coultas et al. (1987), from which an estimate of 1.5% - 2.0% can be derived. Also the two COHb/thiocyanate studies providing evidence in which the subjects were not advised to give up smoking (Jones et al., 1972; Robertson et al., 1987) gave a combined figure of 4/176 (2.2%), while the study of Rogot and Reid (1975), found that of those men and women reported as being never smokers by a next-of-kin or other informant 13/1186 (1.1%) were reported as smoking 1 or more packets of cigarettes a day by the subjects themselves.

Much more information is needed on this crucial issue, but it seems not unreasonable to believe that, at least in some of the lung cancer and passive smoking studies, the perentage of current regular smokers among self-reported non-smokers is more likely to be around 1 or 2% than around 0.1 or 0.2%.

While the extent to which current regular smokers are misclassified as non-smokers is not fully resolved, there are two further issues on which there is even less information.

Firstly, little is known regarding the extent of misclassification in the countries from which come much of the crucial passive smoking/lung cancer data. None of the evidence relates to Greek subjects, while the small piece of evidence relating to the Japanese (the study by Akiba et al., 1986) is, as noted, in Sect. 3.3.1, full of internal inconsistencies.

Secondly, there is no information on the extent to which misreporting of smoking habits depends on whether of not the subject is married to a smoker. While there is perhaps no prior reason to believe this is a major source of variation, it might conceivably be so.

Although the evidence on misclassification is incomplete, the material reviewed suggests it is a more important source of bias than Wald et al. (1986) would have it. Some other considerations also indicate that the association between passive smoking and lung cancer is unlikely to have arisen predominantly from a cause and effect mechanism.

Firstly, the relative dose of smoke constituents received by passive smokers seems far too low. As I pointed out in Appendix B, compared with average smokers, average passive smokers have less than 1% of the nicotine exposure and less than 0.1% of the exposure to particulate matter. And yet, as shown in Appendix A, the epidemiology taken at face value, suggests that the increase in risk of lung cancer in relation to passive smoking is more than 20% of that in relation to active smoking for a number of the studies.

Secondly (see Appendix A) the only two studies of lung cancer and passive smoking in Table 2 showing a significant association were the studies of Hirayama and Trichopoulos, which were not only published first, but appeared to have been carried out with a considerably less detailed questionnaire/interview than virtually all the other studies.

Thirdly, there are, as noted in Sect. 1, a number of other potential sources of bias, including non-reporting bias, and bias due to subjects with lung cancer, or their spouses or next-of-kin, tending to overstate exposure to passive smoke.

The likely effect of these other sources of potential bias is difficult to estimate. Nonetheless, it seems far more plausible to conclude that the epidemiologically observed association between passive smoking and lung cancer arose from bias due to misclassification of a proportion of smokers as non-smokers than to believe that it arose from any direct effect of passive exposure to low concentrations of environmental tobacco smoke.

Acknowledgements. Invaluable assistance has been provided by Mrs. B. A. Forey and Dr. J. S. Fry to whom I am most grateful. Thanks are also due to Mrs. E. K. Marlow, Mrs. D. P. Morris and Mrs. A. Pearson who patiently typed the numerous drafts it went through.

References

Aaronson NK, Ershoff DH, Danaher BG (1985) Smoking cessation in pregnancy: A self-help approach. Addictive Behaviours 10:103–108

Akiba S, Kato H, Blot WJ (1986) Passive smoking and lung cancer among Japanese women. Cancer Res 46:4804–4807

Alderson MR (1983) An introduction to epidemiology. 2nd edn. Macmillan. London

Alderson MR, Lee PN, Wang R (1985) Risks of lung cancer, chronic bronchitis, ischaemic heart disease and stroke in relation to type of cigarette smoked. J Epidem Commun Health 39:286–293

Bauman KE, Dent CW (1982) Influence of an objective measure of self-reports of behaviour. J Applied Psychol 79:623–628

Belson WA (1986) Validity in survey research. Gower. Aldershot

Belson WA (1981) The design and understanding of survey questions. Gower. Aldershot

Benowitz NL, Jacob P III, Jones R, Rosenberg J (1982) Interindividual variability in the metabolism and cardiovascular effects in man. Pharmacol Exp Ther 221:368–372

Benowitz N, Kuyt F, Jacob P III, Jones RT, Osman A-L (1983) Cotinine disposition and effects. Clin. Pharmacol Ther 12:604–611

Berry G, Newhouse ML, Antonis P (1985) Combined effect of asbestos and smoking on mortality from lung cancer and mesothelioma in factory workers. Brit. J Ind Med 42:12–18

Bliss RE, O'Connell KA (1984) Problems with thiocyanate as an index of smoking status: A critical review with suggestions for improving the usefulness of biochemical measures in smoking cessation research. Health Psychology 3:563–581

Bowler RG (1944) The determination of thiocyanate in blood serum. Biochem J 38:385–388

Buffler PA, Pickle LW, Mason TJ, Contant C (1984) The causes of lung cancer in Texas. In: Mizell M, Correa P (eds) Lung cancer causes and prevention. Verlag Chemie International Inc. New York. pp 83–99

Burling TA, Singleton EG, Bigelow GE, Baile WF, Gottlieb SH (1984) Smoking following myocardial infarction: A critical review of the literature. Health Psychology 3:83–96

Butts WC, Kuehneman M, Widdowson GM (1974) Automated method for determining serum thiocyanate to distinguish smokers from non-smokers. Clin Chem 20:1344–1348

Casapieri P, Scott R, Simpson EA (1970) The determination of cyanide ions in waters and effluents by an auto-analyser procedure. Anal Chim Acta 49:188–192

Castro A, Monji N (1986) Dietary nicotine and its significance in studies on tobacco smoking. Biochem Arch 2:91–97

Chalmers TC, Levin H, Sachs HS, Reitman D, Berrier J, Nagalingam R (1987) Meta-analyses of clinical trials as a scientific discipline. I: Control of bias and comparison with large co-operative trials. Statistics in Medicine 6:315–325

Chan WC, Fung SC (1982) Lung cancer in non-smokers in Hong Kong. In: Cancer campaign, Cancer epidemiology, vol. 6 Grundman E (ed). Gustav Fischer Verlag. Stuttgart, New York, pp. 199–202

Chan WC, Colbourne MJ, Fung SC, Ho HC (1979) Bronchial cancer in Hong Kong 1976–77. Brit J Cancer 39:182–192

Clavel F, Benhamou S, Company-Huertas A, Flamant R (1985) Helping people to stop smoking: Randomised comparison of groups being treated with accupuncture and nicotine gum with control group. Brit Med J 291:1538–1539

Cohen SI, Perkins NM, Ury HK, Goldsmith JR (1971) Carbon monoxide uptake in cigarette smoking. Arch Environ Health 22:55–60

Collishaw NE (1983) Is cigarette consumption declining in Canada? In: Forbes WF, Frecker RC, Nostbakken D (eds). Proceedings of the Fifth World Conference of Smoking and Health, Winnipeg, Canada, 1983. Ottawa, Canadian Concil on Smoking and Health, Ottawa 1:667–677

Correa P, Pickle LW, Fontham E, Lin Y, Haenszel W (1983) Passive smoking and lung cancer. Lancet 2:595–597

Correa P, Pickle LW, Fontham E, Dalager N, Lin Y, Haenszel W, Johnson WD (1984) The causes of lung cancer in Louisiana. In: Mizell M, Correa P (eds). Lung cancer causes and prevention, Verlag Chemie International Inc. New York. pp 73–82

Coultas DB, Howard CA, Peake GT, Skipper BJ, Samet JM (1987) Salivary cotinine levels and involuntary tobacco smoke exposure in children and adults in New Mexico. Amer Rev Resp Dis 136:305–309

Curvall M, Enzell CR (1986) Monitoring absorption by means of determination of nicotine and cotinine. Arch Toxicol Supplement 9:88–102

Dalager NA, Pickle LW, Mason TJ, Correa P, Fontham E, Stemhagen A, Buffler PA, Ziegler RG, Fraumeni JF (1986) Relation of passive smoking to lung cancer. Cancer Res 46:4808–4811

Dawson RF, Solt ML, Christman DR (1960) Nicotine and its botanical sources, 1960. Annals NY Acad Sci 90:7–12

Delarue NC (1973) A study in smoking withdrawal. Canad J Public Health 64:S5–S19

Denson PM, Davidow B, Bass KE, Jones EW (1967) A chemical test for smoking exposure. Arch Environ Health 14:865–874

Doll R (1986) Lung cancer: Observed and expected changes in incidence from active and passive smoking. Paper presented at XIV UICC Conference, Budapest

Enterline PE, Capt KG (1959) A validation of information provided by household respondents in health surveys. Amer J Public Health 49:205–212

Evans RI, Hansen WB, Mittelmark MB (1977) Increasing the validity of self-reports of smoking behaviour in children. J. Applied Psychol 62:521–523

Farquhar JW, Wood PD, Breitrose H, Haskell WL, Meyer AJ, Maccoby N, Alexander JK, Brown BW Jr. McAlister AL, Nash JD, Stern MP (1977) Community education for cardiovascular health. Lancet 1:1192–1195

Feyerabend C, Russell MAH (1980a) Assay of nicotine in biological materials: Sources of contamination and their elimination. J Pharmac Pharmacol 32:178–181

Feyerabend C, Russell MAH (1980b) Rapid gas-liquid chromatographic determination of cotinine in biological fluids. Analyst 105:998–1001

Feyerabend C, Higenbottam T, Russell MAH (1982) Nicotine concentrations in urine and saliva of smokers and non-smokers. Brit Med J 284:1002–1004

Frederiksen LW, Martin JE (1979) Carbon monoxide and smoking behaviour. Addictive Behaviours 4:21–30

Garfinkel L (1981) Time trends in lung cancer mortality among non-smokers and a note on passive smoking. J Nat Cancer Inst 66:1061–1066

Garfinkel L, Auerbach O, Joubert L (1985) Involuntary smoking and lung cancer: A case-control study. J Nat Cancer Inst 75:463–469

Gillies PA, Wilcox B, Coates C, Kristmundsdottir F, Reid DJ (1982) Use of objective measurement in the validation of self-reported smoking in children aged 10 and 11 years: saliva thiocyanate. J Epidem Commun Health 36:205–208

Gillis CR, Hole DJ, Hawthorne V, Boyle P (1984) The effect of environmental tobacco smoke in two urban communities in the West of Scotland. Eur J Respir Dis (Supplement 133) 65:121–126

Glasgow RE, Klesges RC, Godding PR, Vasey MW, O'Neill HK (1984) Evaluation of a worksite-controlled smoking program. J Consult Clin Psychol 52:137–138

Haddow JE, Palomaki GE, Knight GJ (1986) Use of serum cotinine to assess the accuracy of self-reported non-smoking. Brit Med J 293:1306

Haddow JE, Knight GT, Palomaki GE, Kloza EM, Wald NJ (1987) Cigarette consumption and serum cotinine in relation to birthweight. Brit J Obstet Gynaecol 94:678–681

Haenszel W, Loveland DB, Sirken MG (1962) Lung cancer mortality as related to residence and smoking histories. 1. White males. J Nat Cancer Inst 4:947–1001

Haley NJ, Axelrad CM, Tilton KA (1983) Validation of self-reported smoking behaviour: Biochemical analyses of cotinine and thiocyanate. Amer J Public Health 73:1204–1207

Hall SM, Rugg D, Tunstall C, Jones RT (1984) Preventing relapse to cigarette smoking by behavioural skill training. J Consult Clin Psychol 52:372–382

Hammond EC, Garfinkel L (1964) Changes in cigarette smoking. J Nat Cancer Inst 33:49–64

Hansen WB, Malotte CK, Fielding JE (1985) The bogus pipeline revisted: The use of the threat of detection as a means of increasing self-reports of tobacco use. J Applied Psychol 70:789–792

Harlin VK (1972) The influence of obvious anonymity on the response of schoool children to a questionnaire about smoking. Amer J Public Health 62:566–573

Hebert L, Fry JS (1982) A report on a further analysis of the association between smoking behaviour, total mortality and cardiorespiratory disease in West Central Scotland. Unpublished document

Hengen N, Hengen M (1978) Gas-liquid chromatographic determinations of nicotine and cotinine in plasma. Clin Chem 24:50–53

Herrmann N (1985) Retrospective information from questionnasires. 1. Comparability of primary respondents and their next-of-kin. Amer J Epidemiol 121:937–947

Hirayama T (1981) Non-smoking wives of heavy smokers have a higher risk of lung cancer: a study from Japan. Brit Med J 282:183–185

Hirayama T (1984) Cancer mortality in non-smoking women with smoking husbands in a large-scale cohort study in Japan. Preventive Medicine 13:680–690

Hjermann I (1980) Smoking and diet intervention in healthy coronary high risk men. Methods and 5-year follow-up risk factors in a randomized trial. The Oslo study. J Oslo City Hospitals 30:3–17

Horwitz RI, Yu EC (1985) Problems and proposals for interview data in epidemiological research. Int J Epidemiol 14:463–467

Isacsson S-O, Janzon L (1976) Results of quit-smoking research project in a randomly selected population. Scand J Social Med 4:25–29

Jamrozik K, Fowler G, Vessey M, Wald N (1984a) Placebo controlled trial of nicotine chewing gum in general practice. Brit Med J 289:794–797

Jamrozik K, Vessey M, Fowler G, Wald N, Parker G, Van Vunakis H (1984b) Controlled trial of three different antismoking interventions in general practice. Brit Med J 288:1499–1503

Jarvis MJ, Russell MAH, Feyerabend C, Eiser JR, Morgan M, Gammage P, Gray EM (1985) Passive exposure to tobacco smoke: Saliva cotinine concentrations in a representative population sample of non-smoking schoolchildren. Brit Med J 291:927–929

Jarvis MJ, Russell MAH, Saloojee Y (1980) Expired air carbon monoxide: a simple breath test of tobacco smoke intake. Brit Med J 281:484–485

Jarvis MJ, Raw M, Russell MAH, Feyerabend C (1982) Randomised controlled trial of nicotine chewing gum. Brit Med J 285:537–540

Jarvis M, Tunstall-Pedoe H, Feyerabend C, Vesey C, Saloojee Y (1984) Biochemical markers of smoke absorption and self reported exposure to passive smoking. J Epidem Commun Health 38:335–339

Jarvis MJ, Tunstall-Pedoe H, Feyerabend C, Vesey C, Saloojee Y (1987) Comparison of tests used to distinguish smokers from non-smokers. Amer J Public Health 77:1435–1438

Jones RD, Commins BT, Cernik AA (1972) Blood lead and carboxyhaemoglobin levels in London taxi drivers. Lancet 2:302–303

Junge B (1985) Changes in serum thiocyanate concentration on stopping smoking. Brit Med J 291:22

Kabat GC, Wynder EL (1984) Lung cancer in non-smokers. Cancer 53:1214–1221

Kilpatrick SJ (1987) Misclassification of environmental tobacco smoke exposure: its potential influence on studies of environmental tobacco smoke and lung cancer. Toxicol Lett 35:163–168

Kirk CJC, Lund VJ, Woolcock NE, Greenhalgh RM (1980) The effect of advice to stop smoking in arterial disease patients assessed by serum thiocyanate levels. J Cardiovasc Surg 21:568–569

Knight GJ, Wiley P, Holman M, Haddow JE (1985) Minimising the problem of bridge recognition with 125-iodine labeled haptens: Improved assay for cotinine by selective removal of bridge antibodies. Clin Chem 31:118

Kolonel LN, Hirohata T, Nomura AMY (1977) Adequacy of survey data collected from substitute respondents. Amer J Epidemiol 106:476–484

Koo LC, Ho JH-C, Saw D (1984) Is passive smoking an added risk factor for lung cancer in Chinese women? J Exp and Clin Cancer Res 3:277–283

Koo LC, Ho JH-C, Saw D, Ho C-Y (1987) Measurements of passive smoking and estimates of lung cancer risk among non-smoking Chinese females. Int J Cancer 39:162–169

Lando HA (1982) A factorial analysis of preparation, aversion and maintenance in the elimination of smoking. Addictive Behaviours 7:143–154

Lando HA (1981) Effects of preparation, experimenter contact, and a maintained reduction alternative on a broad-spectrum program for eliminating smoking. Addictive Behaviours 6:123–133

Lando HA, McGovern PG (1985) Nicotine fading as a nonaversive alternative in a broad-spectrum treatment for eliminating smoking. Addictive Behaviours 10:153–161

Langone J, Gijka HB, Van Vunakis H (1973) Nicotine and its metabolites: Radioimmunoassay for nicotine and cotinine. Biochem 12:5025–5030

Lebowitz MD, Burrows B (1976) Comparison of questionnaires: The BMRC and NHLI respiratory questionnaires and a new self-completion questionnaire. Amer Rev of Resp Dis 113:627–635

Lee PN (1977) Statistics of smoking in the United Kindom. Tobacco Research Council Research Paper 1 (with annual supplements). Tobacco Research Council, London

Lee PN (1984) Passive Smoking. In: Cumming G, Bonsignore G (eds) Smoking and the lung, Plenum Publishing Corporation. New York. London. pp. 187–216

Lee PN, Chamberlain J, Alderson MR (1986) Relationship of passive smoking to risk of lung cancer and other smoking-associated diseases. Brit J Cancer 54:97–105

Lerchen ML, Samet JM (1986) An assessment of the validity of questionnaire responses proved by a surviving spouse. Amer J Epidemiol 123:481–489

Li VC, Kim YJ, Ewart CK, Terry PB, Cuthie JC, Wood J, Emmett EA, Permutt S (1984) Effects of physician counseling on the smoking behavior of asbestos-exposed workers. Preventive Medicine 13:462–476

Luepker RF, Pechacek TF, Murray DM, Johnson CA, Hund F, Jacobs DR (1981) Saliva thiocyanate: A chemical indicator of cigarettes smoking in adolescents. Amer J Public Health 71:1320–1324

Lundquist P, Martensson J, Sorbo B, Ohman S (1979) Method for determining thiocyanate in serum and urine. Clin Chem 25:678–681

Lundquist P, Martensson J, Sorbo B, Ohman S (1983) Absorption of thiocyanate by anion-exchange resins and analytical applications. Clin Chem 29:403

McKennell AC (1980) Bias in the reported incidence of smoking by children. Int J Epidemiol 9:167–177

McNeill AD (1987) Salivary cotinine as an indicator of cigarette smoking in adolescents. Brit J Addict 82:1355–1360

Malcolm RE, Sillett RW, Turner JAMcM, Ball KP (1980) The use of nicotine chewing gum as an aid to stopping smoking. Psychopharmacology 70:295–296

Mantel N (1987) Lung cancer and passive smoking. Brit Med J 294:440

Murray M, Kiryluk S, Swan AV (1985) Relation between parents' and children's smoking behaviour and attitude. J Epidem Commun Health 39:169–174

Neaton JD, Broste S, Cohen L, Fishman EL, Kjelsberg MO, Schoenberger J (1981) The multiple risk factor intervention trial (MRFIT). VII. A comparison of risk factor changes between the two study groups. Preventive Medicine 10:519–543

Ockene JK, Hymowitz N, Sexton M, Broste SK (1982) Comparison of paterns of smoking behavior change among smokers in the multiple risk factor intervention trial (MRFIT). Preventive Medicine 11:621–638

Ohlin P, Lundh B, Westling H (1976) Carbon monoxide blood levels and reported cessation of smoking. Psychopharmacology 49:263–265

Paxton R (1980) The effects of a deposit contract as a component in a behavioural programme for stopping smoking. Behav Res Ther 18:45–50

Peach H, Shah D, Morris RW (1986) Validity of smokers' information about present and past cigarette brands – implications for studies of the effects of falling tar yields of cigarettes on health. Thorax 41:203–207

Pechacek TF, Luepker RV, Jacobs DR, Fraser GE, Blackburn H (1982) Effects of diet and smoking on serum and saliva thiocyanates. Unpublished manuscript. Laboratory of Physiological Hygiene, University of Minneapolis, Minneapolis

Pederson L, Sidney K, Lefcoe NM (1977) An objective measure of the validity of children's responses to a questionnaire on health and smoking. Canad J Public Health 68:497–498

Pershagen G, Axelson O (1982) A validation of questionnaire information on occupational exposure and smoking. Scand J Work Environ Health 8:24–28

Pershagen T, Hrubec Z, Svensson C (1987) Passive smoking and lung cancer in Swedish women. Amer J Epidemiol 125:17–24

Petitti DB, Friedman GD, Kahn W (1981) Accuracy of information on smoking habits provided on self-administered research questionnaires. Amer J Public Health 71:308–311

Pettigrew AR, Fell GS Simplified colorimetric determination of thiocyanate in biological fluids, and its application to investigation of the toxic amblyopias. Clin Chem 18:996–1000

Pickle LW, Brown LM, Blot WJ (1983) Information available from surrogate respondents in case-control interview studies. Amer J Epidemiol 118:99–108

Pojer R, Whitfield JB, Poulos V, Eckhard IF, Richmond R, Hensley WJ (1984) Carboxyhemoglobin, cotinine and thiocyanate assay compared for distinguishing smokers from non-smokers. Clin Chem 30:1377–1380

Popper KR (1959) the logic of scientific discovery. Hutchinson, England

Powell DR, Arnold CB (1982) Antismoking program for coronary-prone men. An evaluation study. New York State J Med September:1435–1438

Raw M, Jarvis MJ, Feyerabend C, Russell MAH (1980) Comparison of nicotine chewing-gum and psychological treatments for dependent smokers. Brit Med J 281:481–482

Raw M, Russell MAH (1980) Rapid smoking, cue exposure and support in the modification of smoking. Behav Res Ther 18:363–372

Research Committee of the British Thoracic Society (1983) Comparison of four methods of smoking withdrawal in patients with smoking related diseases. Brit Med J 286:595–597

Richmond R, Webster I (1985) Evaluation of General Practitioners' use of a smoking intervention programme. Int J Epidemiol 14:396–401

Ringold A, Goldsmith JR, Helwig HI, Finn R, Schuette F (1962) Estimating recent carbon monoxide exposures. Arch Environ Health 5:308–318

Robertson AS, Burge PS, Cockrill BL (1987) A study of serum thiocyanate concentrations in office workers as a means of validating smoking histories and assessing passive exposure to cigarette smoke. Brit J Ind Med 44:351–354

Rogot E, Reid DD (1975) The validity of data from next-of-kin in studies of mortality among migrants. Int J Epidemiol 4:51–54

Ronan G, Ruane P, Graham IM, Hickey N, Mulcahy R (1981) The reliability of smoking history among survivors of myocardial infarction. Brit J Addic 76:425–428

Rose G, Hamilton PJS (1978) A randomised controlled trial of the effect on middle-aged men of advice to stop smoking. J Epidem Commun Health 32:275–281

Rosenthal R (1979) The "File drawer problem" and tolerance for null results. Psychol Bull 86:638–641

Russell MAH, Feyerabend C (1975) Blood and urinary nicotins in non-smokers. Lancet 1:179–181

Russell MAH, Wilson C, Taylor C, Baker CD (1979) Effect of General Practitioners' advice against smoking. Brit Med J 2:231–235

Russell MAH, Cole PV, Brown E (1973) Absorption by non-smokers of carbon monoxide from room air polluted by tobacco smoke. Lancet 1:576–579

Russell MAH, Merriman R, Stapleton J, Taylor W (1983) Effect of nicotine chewing gum as an adjunct to General Practitioners' advice against smoking. Brit Med J 287:1783–1785

Russell MAH, Stapleton JA, Jackson PH, Hajek P, Belcher M (1987) District programme to reduce smoking: effect of clinic supported brief intervention by general practitioners. Brit Med J 295:1240–1244

Sandler DP, Shore DL (1986) Quality of data on parents' smoking and drinking provided by adult offspring. Amer J Epidemol 124:768–778

Sepkovic DW, Haley HJ, Hoffman D (1986) Elimination from the body of tobacco products by smokers and passive smokers. J Amer Med Ass 256:863

Sillett RW, Wilson MB, Malcolm RE, Ball KP (1978) Deception among smokers. Brit Med J 2:1185–1186

Silman A, Loysen E, De Graaf W, Sramek M (1985) High dietary fat intake and cigarette smoking as risk factors for ischaemic heart disease in Bangladeshi male immigrants in East London. J Epidem Commun Health 39:301–303

Stewart RD (1975) The effect of carbon monoxide on humans. Ann Rev Pharmacol 15:409–423

Thompson JA, Ho MS, Peterson D (1982) Analyses of nicotine and cotinine in tissues by capillary gas chromatography and gas chromatography. J. Chromatogr 231:53–63

Todd GF, Laws JT (1959) The reliability of statements about smoking habits. Tobacco Manufacturers' Standing Committee, Research Paper 2

Todd GF (1966) Reliability of statements about smoking habits. Tobacco Research Council, Research Paper 2A Supplementary Report

Todd GF (1978) Cigarette consumption per adult of each sex in various countries. J Epidem Commun Health 32:289–293

Trichopoulos D, Kalandidi A, Sparros L, MacMahon B (1981) Lung cancer and passive smoking. Int J Cancer 27:1–4

Trichopoulos D, Kalandidi A, Sparros L (1983) Lung cancer and passive smoking: conclusion of Greek study. Lancet 2:677–678

Turner JAMcM, McNicol MW, Sillett RW (1986) Distribution of carboxyhaemoglobin concentrations in smokers and non-smokers. Thorax 41:25–27

U.S. Surgeon General (1985) The health consequences of smoking. Cancer and chronic lung disease in the workplace. US Department of Health and Human Services

Vogt TM, Selvin S, Widdowson G, Hulley SB (1977) Expired air carbon monoxide and serum thiocyanate as objective measures of cigarette exposure. Amer J Public Health 67:545–549

Wald NJ, Boreham J, Bailey A, Ritchie C, Haddow JE, Knight G (1984) Urinary cotinine as marker of breathing other people's tobacco smoke. Lancet 1:230–231

Wald NJ, Howard S (1975) Smoking, carbon monoxide and arterial disease. Ann Occup Hyg 18:1–14

Wald NJ, Ritchie C (1984) Validation of studies on lung cancer in non-smokers married to smokers. Lancet 1:1067

Wald NJ, Nanchahal K, Thompson SG, Cuckle HS (1986) does breathing other people's tobacco smoke cause lung cancer? Brit Med J 293:1217–1222

Weber A (1984) Annoyance and irritation by passive smoking. Preventive Medicine 13:618–625

Wells AJ (1986) Misclassification as a factor in passive smoking risk. Lancet 2:638

Wilcox RG, Hughes J, Roland J (1979) Verification of smoking history in patients after infarction using urinary nicotine and cotinine measurements. Brit Med J 2:1026–1028

Williams R, Gillies P (1984) Do we need objective measures to validate self-reported smoking? Public Health, London 98:294–298

Wu AH, Henderson BE, Pike MC, Yu MC (1985) Smoking and other risk factors for lung cancer in women. J Nat Cancer Inst 74:747–751

Zwart A, Buursma A, Van Kampen EJ, Oesburg B, Van Der Ploeg PHW, Zijlstra WG (1981) A multi-wavelength to spectrophotometric method for the simultaneous determination of five haemoglobin derivatives. J Clin Chem Clin Biochem 19:457–463

Appendix A
Studies of Passive Smoking and Lung Cancer – A Brief Review with Special Reference to the Way the Smoking Habit Information was Obtained

A.1 Introduction

As is discussed in the main body of this monograph, misclassification of smokers as non-smokers in studies of passive smoking and lung cancer can have a serious biassing effect. Apart from studying the direct evidence on misclassification in Sect. 3 it is useful to look briefly at the published studies of passive smoking and lung cancer, paying particular attention to the way the smoking habit information was obtained and to whether there is any indication that this was related to the relative risk estimates obtained. It should be noted at the outset that many of the studies described were not specifically designed to study possible effects of passive smoking. Indeed many of them were started long before passive smoking became an issue.

The material considered below in Sect. A.2 has been summarised in Table 2. It is interesting to note that the only two studies showing a clearly significant increased risk among the non-smokers married to smokers are the studies of Hirayama and of Trichopoulos. A number of features of this observation merit comment.

Firstly, these were the two studies that were published first, and virtually simultaneously. It has been argued (Popper, 1959) that where an hypothesis is first suggested by a study, that study should not be included later in the overall assessment of evidence. This avoids the danger of false positives arising in "fishing expeditions" where an investigator studies a wide range of associations looking for leads. Following this argument, there might be a case for removing these studies from an overall assessment of the evidence. Wald et al. (1986) presented a table of results similar to Table 2 from which a significant overall relative risk of 1.35 with 95% confidence limits 1.19–1.54 was calculated. If this analysis is repeated omitting the results from these 2 initial studies the overall relative risk drops to 1.20 with 95% confidence limits 1.02–1.40, i. e. only of marginal significance.

Secondly, while many of the other studies refer to a detailed interview having been carried out, this does not appear to have been the case for these two studies. The Hirayama study was carried out using a very brief single-page self completion questionnaire, while the Trichopoulos study involved what appears to have been quite a brief interview with a doctor in hospital.

Thirdly, both studies were carried out in countries where smoking by women is relatively rare. Smoking by women in Japan is not socially acceptable and it is plausible that a moderate proportion of smoking women might have denied smoking in Hirayama's study not to offend the interviewer. This may also account for the relative risks seen in Akiba'a Japanese study. While the situation

may be different in Greece, there are no published data available to evaluate the situation there.

A number of other general points seem worth mentioning:

(a) As is normal in published papers describing results of epidemiological studies, full details of the questions asked, the degree of probing that went on, the length of the interview or the reasons given to the respondent for wanting the information are not given.

(b) In 6 of the 15 studies some of the information, often a substantial proportion, was obtained from the next-of-kin.

(c) In 12 of the 15 studies some, if not all, of the respondents were likely to have known of the lung cancer and this may have affected their response.

(d) In 9 of the 15 studies, no attempt appears to have been made to validate the subject's smoking habits. Results from the remaining 6 are discussed in Sect. 3.3.

It is of interest to compare the estimated effects of active and passive smoking in these studies. The table below gives, for those studies where such information was available or could be calculated, the estimated risk, relative to a never smoker married to a never smoker, of a never smoker married to an ever smoker and of an ever smoker. The ratio of excess risks (i.e. relative risks - 1) is also given as an indicator of apparent relative passive/active smoking effect.

Estimated risks of lung cancer relative to a never smoker married to a never smoker

Study	Sex	Never smoker married to ever smoker	Ever smoker	Ratio of excess risks
Hirayama	F	1.63[a]	3.81[a]	0.22
	M	2.25[a]	4.91[a]	0.32
Gillis	F	1.00[a]	1.53[a]	0.00
	M	3.25[a]	5.92[a]	0.46
Trichopoulos	F	2.08	2.9	0.57
Chan and Fung	F	0.75	3.07	−0.12
Correa	F	2.07	18.51	0.06
	M	2.00	18.27	0.06
Buffler	F	0.78	5.37	−0.05
	M	0.52	5.26	−0.11
Koo	F	1.64	3.80	0.23
Wu	F	1.2	4.5	0.06
Akiba	F	1.5	3.36	0.21
	M	1.8	3.55	0.31
Lee	F	1.00	4.75	0.00
	M	1.30	12.91	0.03

[a] Current rather than ever smoker

A number of points are evident from the table. Firstly, there is considerable variation in the estimated relative risk in relation to active smoking. While RR's for males are generally somewhat greater than for females, much of the variation is between study, cf. the two very large RR's from the Correa study.

Secondly, there is also considerable variation in the estimated ratio of excess risks. While 9 of the 16 ratios suggest an effect of passive smoking 6% or less than that of active smoking, 7 suggest an effect 20% or more, an effect which appears totally inconsistent with the estimated relative exposure to smoke constituents of the 2 groups.

Thirdly, while one might expect, on the basis of sampling error alone, some positive correlation between the active and passive smoking estimates, since an abnormally low observed risk in the totally nonexposed group would tend to push both estimates up (and vice versa), there is in fact an observed negative correlation (rank correlation coefficient $= -0.2$). Negative correlation would be expected if there was variable misclassification of active smoking habits as such misclassification tends to have an opposite biassing effect on the observed active and passive smoking effects.

A.2 The Studies

Passive smoking and lung cancer first really became a prominent issue with the almost simultaneous publication in 1981 of results of studies by Hirayama and by Trichopoulos et al.

In the prospective study of Hirayama (1981), more details of which are given in Hirayama (1984), over a quarter of a million Japanese men and women aged over 40 were interviewed at home in 1965. A very simple single page questionnaire was completed which included questions on smoking habits. 200 deaths from lung cancer (mainly adenocarcinoma) occurred during a 16 year follow-up period of 91,540 married women who reported never having smoked. Self-reported smoking habits of the husbands were also available and relative risks of lung cancer in the non-smoking wives were 1.00, 1.36, 1.42, 1.58 and 1.91 when husbands were never smokers, ex-smokers, or daily smokers of 1–14, 15–19 or 20 or more cigarettes a day, respectively. For any current smoking by the husband the relative risk can be calculated as 1.63 (with 95% limits 1.25–2.11), while for non-smoking men the corresponding relative risk for any current smoking by the wife is 2.25 (limits 1.04–4.86), based on 64 deaths.

In the hospital case-control study of Trichopoulos et al. (1981) with updated results given in Trichopoulos et al. (1983), 102 women with lung cancer (other than adenocarcinoma or bronchial alveolar carcinoma) in one hospital, and 251 women with orthopaedic conditions in another hospital, were interviewed by the same doctor. They were asked about their own and their husbands' smoking habits, including age of starting and stopping smoking and number smoked daily. 77 cases and 225 controls reported never having smoked and the risk of lung cancer was 2.11 times higher (95% limits 1.17–3.78) if the husband was a current cigarette smoker than if he had never smoked (of if the woman was single).

Other studies published since Hirayama and Trichopoulos are considered below.

In 1959 and 1960 Garfinkel (1981) enrolled over 1 million men and women in a prospective epidemiological study using volunteer researchers of the American Cancer Society. Subjects were enrolled in family groups, i.e. households, and every person over 30 years of age was requested to fill out a detailed questionnaire which included questions on smoking. Subjects were asked whether they now smoked and if they did not whether they had ever smoked regularly, the word "regularly" being undefined. Further questionnaires were completed on 4 occasions. A subject was classified as a non-smoker if he or she had never smoked only occasionally but had never smoked regularly. Classification was made as of the start of the study, and very few non-smokers reported that they started to smoke subsequently. Risk of lung cancer over the period 1960–1972 was calculated for married women who did not smoke according to whether their husband did not smoke, smoked less than 20 cigarettes per day or smoked 20 or more cigarettes a day. Age standardised relative risk estimates were respectively 1.00, 1.27 and 1.10 which altered to 1.00, 1.37 and 1.04 on standardising for additional factors related to lung cancer. None of these estimates, based on 65, 39 and 49 deaths respectively, were statistically significant.

In a survey of bronchial cancer in Hong Kong, Chan et al. (1979) interviewed 208 male and 189 female patients with lung cancer as well as 204 male and 189 female orthopaedic controls. The interviews, carried out in hospital, included detailed smoking history questions. Subsequently Chan and Fung (1982) reported the results of questions asked of the female non-smokers concerning the smoking habit of their husbands. 40.5% of the cases had smoking husbands as against 47.5% of the controls, yielding a non-significant relative risk estimate of 0.75.

Correa et al. (1983) carried out a case control study involving 1338 lung cancer patients and 1393 comparison subject in Louisiana. Detailed interviews, using professional interviewers, were carried out of subjects (76% of cases and 89% of controls) or their next of kin and included questions on smoking and on the smoking habits of the spouse. Information on spouse smoking was obtained on 8 male and 22 female never-smoking ever married lung cancer cases and on 180 male and 133 female never-smoking ever married controls. Relative risk estimates in relation to whether the spouse had ever smoked were 2.0 for men and 2.07 for women. Neither estimate was statistically significant, though for females the dose-related trend statistic was. More details of this study are given in Correa et al. (1984).

Buffler et al. (1984) carried out at home interviews with lung cancer cases recently reported in Texas hospitals or with their next of kin. Interviews were also carried out with population-based and decedent controls matched on age, race, sex, region and vital status at time of ascertainment. A standardized interview protocol was used and detailed information regarding the primary exposures of interest, including smoking history, was collected. Among men who had never smoked (11 cases and 90 controls) the relative risk in relation to a household member having ever smoked regularly was 0.52. Among women

who had never smoked (411 cases and 196 controls) the relative risk was 0.78. Neither relative risk was statistically significant.

In a study described by Gillis et al. (1984), 16,171 apparently healthy individuals aged betwen 45 and 64, resident in two urban areas in the West of Scotland, took part in a multiphasic cardiorespiratory screening survey. Information on smoking habits was collected using a self-completed questionnaire and, as members of the same household attended the screening unit, it was possible to identify smoking and non-smoking partners of smokers and non-smokers. 6 male and 8 female non-smokers died from lung cancer. In females, risk of lung cancer was the same (RR = 1.00) in those who lived with a smoker as in those who did not. In males, risk was higher in those living with a smoker (RR = 3.25). With such small numbers of deaths, the relative risk estimates were not statistically significant and had very wide confidence intervals.

Kabat and Wynder (1984) extracted all cases of primary lung cancer occurring in subjects who reported never having smoked (as much as one cigarette, pipe or cigar per day for a year) from an ongoing case-control study of tobacco-related cancers conducted in a number of US cities between 1971 and 1980. For each case, the hospital chart was re-examined in order to confirm the diagnosis and the absence of smoking throughout the lifetime and any cases in whom the diagnosis was not primary lung cancer or in whom there was an indication of smoking, even in the remote past, were excluded from the study. Controls with non tobacco-related diseases were matched to each case on age, sex, race, hospital, date of interview and non-smoking status. All subjects were interviewed in hospital with a standardised questionnaire which included questions on tobacco smoking and, later on in the study, questions on passive smoking. Overall, there were 25 male and 53 female never smoking case/control pairs with passive smoking data. Relative risk estimates in relation to smoking at home were 1.26 for men and 0.92 for women; in relation to spouse's current or past smoking, they were 1.00 for men and 0.79 for women. None of these was statistically significant.

Koo et al. (1984, 1987) collected very detailed smoking and passive smoking histories by an in-depth interview from 200 Chinese female lung cancer patients resident in Hong Kong and from 200 healthy controls matched to the cases on age, sex, district and socio-economic status. Analyses based on the 88 cases and 137 controls who had never smoked gave a relative risk of 1.55 in relation to smoking by the husband in the presence of the wife, which was not statistically significant. After adjustment for age and various potential confounding variables the RR became 1.64 with 95% limits 0.87–3.09. There was no relationship to amount smoked, risk in fact being highest in those women whose husbands smoked 1–10 cigarettes a day.

From the records of 4 hospitals, 3 in New Jersey and 1 in Ohio, Garfinkel et al. (1985) identified all lung cancer cases in women recorded during 1971–81. Women with colon-rectum cancer served as controls. Subjects where diagnosis was made clinically or by cytology were excluded, as were those where smoking was mentioned in the hospital record. Slides were reviewed by Auerbach to check the diagnoses and interviews were carried out with the women or with the next-of-kin if she had died to check smoking habits. Of 1,175 women listed

as having lung cancer, 892 (76%) were smokers or had smoked in the past, according to hospital records. Of the remaining 283, 36 proved histologically to have other than lung cancer and 113 were found to be smokers, leaving 134 lifetime non-smokers with histologically proven primary lung cancer, which were compared with 402 histologically proven lifetime non-smokers with colon rectum cancer. Risk of lung cancer was estimated in relation to husband's smoking habits at home, counting cohabitant living in the same household as "husband" for the purposes of analysis. Compared with those whose husband did not smoke, the relative risk was 1.31 (95% limits 0.99–1.73) in those who did smoke. Risk was only slightly and non-significantly elevated in those whose husbands smoked <10 cigarettes a day (RR = 1.15), 10–19 cigarettes a day (RR = 1.08) or only a cigar or pipe (RR = 1.17) but was significantly increased in those whose husbands smoked 20 or more cigarettes a day (RR = 2.11). Risk was much more elevated where the respondent was a daughter or son (RR = 3.19) than where it was the woman herself (RR = 1.00) or her husband (RR = 0.92), consistent with increased misclassification by those less likely to have known the full smoking history.

Wu et al. (1985), in a case-control study of white women in Los Angeles County, interviewed 220 lung cancer patients, 149 with adenocarcinoma and 71 with squamous cell carcinoma, and one individually matched neighbourhood control for each case. Cases and controls were interviewed on the telephone by a detailed structured questionnaire. Only 2 women with squamous cell carcinoma did not smoke and their passive smoke exposure was not reported. In an analysis of the 29 adenocarcinoma cases and 62 controls who did not smoke no relationship was found with passive smoke exposure from the spouse (RR = 1.2, 95% limits 0.5–3.3).

From a cohort of 110,000 Hiroshima and Nagasaki atomic bomb survivors, Akiba et al. (1986) selected all newly diagnosed cases of primary lung cancer during the period 1971 to 1980, together with matched controls without lung cancer. They obtained interviews with cases and controls or from their next of kin for 428 cases and 957 controls, respectively, 81% and 82% of the eligible cases and controls, a structural questionnaire being used to obtain histories of cigarette smoking as well as demographic, medical, occupational and other factors. Only 11% of interviews were with the index case or control, information being obtained from the spouse for 35% of interviews, from a child in 26%, from a daughter-in-law in 14% and from others in a further 14%. Among those who had never smoked cigarettes, the relative risk of lung according to spouse smoking was 1.5 for females and 1.8 for males. Neither increase was statistically significant.

Lee et al. (1986) interviewed 12,693 UK hospital patients with lung cancer, chronic bronchitis, ischaemic heart diesease and stroke using a detailed questionnaire. In 3,832 of the interviews with married patients, questions on passive smoking were included, of which there were 44 lifelong non-smokers with lung cancer and 451 control lifelong non-smokers. Based on these the relative risk of lung cancer associated with spouse smoking was estimated as 0.80. In a follow-up study of 56 currently married lifelong non-smokers with lung cancer (all those interviewed whether or not using the passive smoking questionnaire) and

2 currently married lifelong non-smoking controls for each case, an attempt was made to collect information on spouse smoking habits from the spouse directly. For the 47 lung cancer cases and 96 controls for which information on spouse smoking was obtained (from the patient in hospital and/or from the spouse in the follow-up study), the relative risk of lung cancer was estimated to be 1.11. No attempt was made to check the subject's smoking habits in the follow-up interview but it was interesting to note that there was disagreement between the spouse and the subject in 31% (5/16) of cases and 9% (4/43) of controls on whether the spouse had ever smoked during the marriage. Further details of this study are given in Alderson et al. (1985).

Dalager et al. (1986) combined results from 3 case-control studies of passive smoking and lung cancer, Buffler's Texas study and Correa's Louisiana study, noted above, and a study by Ziegler in New Jersey. The New Jersey study provided data on males only, while the Texas study did not ask questions on spouse smoking, only a more general question relating to whether a household member had ever smoked. Overall the relative risk estimate among never smokers in relation to ever having lived with a household member who smoked was 0.84, with 95% limits 0.52–1.34. As referred to above, the relative risk estimate for the Texas study was less than one while that for the Louisiana study was greater than one. Relative risk estimates for the New Jersey study were not presented separately by Dalager et al. but it can be demonstrated (from the fact overall results for males in relation to spouse smoking had a relative risk less than one) that the New Jersey results also gave a relative risk estimate less than one. While the authors presented some results showing an "overall" positive relationship, these were for spouse smoking in females, automatically excluding the Texas and New Jersey results where there was a negative relationship.

Pershagen et al. (1987) carried out a case-control study based on a cohort of 27,409 "non-smoking" Swedish women identified from mailed questionnaires in 1961 and 1963. The study concerned 92 lung cancer cases and 368 controls (part matched on year of birth and part on year of birth and vital status at time of follow-up) in which further data on smoking habits of the subjects and their spouses were collected from a questionnaire mailed in 1984 to study subjects or their next-of-kin (excluding the husband) if dead. Review of the 92 lung cancer cases showed 9 to be definitely not lung cancer and 6 may well not have been. There was information for 67 of the 77 definite lung cancer cases on marriage to a smoker, with the RR in relation to being married to a smoker calculated as 1.2 (with 95% limits of 0.7–2.1). There was some apparent relationship when the analysis was restricted to the 20 cases with squamous cell or small cell cancer (RR = 3.3, 95% limits 1.1–11.4).

Appendix B
Passive Smoking and Lung Cancer Association: A Result of Bias?*,**

1 Epidemiological studies have reported that non-smokers married to smokers have a lung cancer risk 20–50% higher than that of non-smokers married to non-smokers.
2 In contrast, extrapolation based on relative smoke exposure of passive and active smokers would predict a much smaller effect.
3 This paper examines the possibility that bias due to misclassification of smoking habits, coupled with between spouse smoking habit concordance, could account for this discrepancy.
4 One thousand seven hundred and seventy-five subjects were asked about their smoking habits and use of other nicotine products in a non-health context likely to minimize underreporting of smoking. One thousand five hundred and thirty-seven provided saliva for cotinine analysis. Of 808 who claimed not to be users of such products, 2.5% had cotinine values above 30 ng/ml, suggesting their self reports were false. In another study 540 subjects were interviewed in 1980 and in 1985. Ten per cent claiming on one occasion never to have smoked, made inconsistent statements on the other occasion. A third study showed a strong tendency for smokers to marry smokers.
5 Estimates of bias based on these data indicate that misclassification can explain the unexpectedly high lung cancer risk associated with spouse smoking in epidemiological studies of self-reported never smokers.

Introduction

Since reports from Japan[1] and Greece[2] that never smokers married to smokers have a higher risk of lung cancer than those married to non-smokers, further evidence has accumulated. Although estimates of relative risk (RR) vary from over 2 in two studies[3,4] to about 0.8 in three[5–7] there now seems to be a consensus that the overall data (which relates mainly to female non-smokers) indicate a positive association, with the average RR variously estimated as 1.30,[8] 1.41,[9] 1.2–1.5[10] or 1.35.[11]

Although this association is statistically significant, it is by no means clear that it represents a causal effect of exposure. When viewed against the very low exposure to smoke constituents from passive smoking, the magnitude of this association is surprisingly large[8] and it is necessary to consider the possibility that it might have arisen to a great extent as a result of bias. One possibility of bias,[12] is failure to publish studies which found no association. A second possibility, relevant only to case-control studies, is that knowledge of disease may result in passive smoke exposure being recalled more readily by cases than controls.[13] This paper considers a more generally relevant source of potential bias, that caused by random misclassification of smokers as non-smokers, coupled with a tendency for smokers to marry smokers. Table 1 illustrates this bias, assuming a 5% misclassification of smoking subjects, an RR of 20 in relation to active smoking, no true effect of passive smoking and a between spouse smoking concordance of 3.45. The misclassification has 4 consequences; (i) creation of an apparent passive smoking effect; (ii) under-estimation of the active smoking RR; (iii) slight under-estimation of the concordance; (iv) the creation of a large proportion, 50%, of true smokers among self-reported non-smokers with lung cancer. The size of the passive smoking bias depends critically on the assumed RR for active smoking, the degree of concordance and on the level of misclassification of subject smokers as non-smokers. Other types of random misclassification (spouse smokers as non-smokers, subject or spouse non-smokers as smokers) cause little bias and will for simplicity be ignored.

---

* Any views expressed in this paper are those of the author and not of any other person or company.

** First published in Human Toxicology by The Macmillan Press Ltd. (1987)

Table 1 An example of bias caused by misclassification of the subject's smoking habits

Smoking habits		*Assumed data*		*True*	*Observed data*			*Apparent*
Subject	*Spouse*	N	*RR*	*effects*	N	*D*	*RR*	*effects*
Non-smoker	Non-smoker	65	1	Passive	$65 + 1.75 = 66.75$	100	1.50	Passive
	Smoker	35	1	1.00	$35 + 3.25 = 38.25$	100	2.61	1.75
Smoker	Non-smoker	35	20		$35 - 1.75 = 33.25$	665	20	
	Smoker	65	20		$65 - 3.25 = 61.75$	1235	20	
Non-smoker	Total	100	1	Active	105	200	1.90	Active
Smoker	Total	100	20	20.00	95	1900	20	10.50

Concordance ratio assumed = $65 \times 65/35 \times 35 = 3.45$
Concordance ratio observed = $66.75 \times 61.75/38.25 \times 33.25 = 3.24$

N = relative numbers of subjects.
D = relative numbers of lung cancer deaths.
RR = risk of lung cancer relative to true non-smokers.
Italicized numbers are true smokers.

This report describes results from studies aimed at measuring the accuracy of reported current smoking (Cotinine study), the accuracy of reported lifetime smoking (1980/85 Follow-up study) and concordance (1985 Consumer study) and uses these to estimate bias in passive smoking studies. The results are then compared with estimates derived independently by Wald *et al.*[11]

Methods

Cotinine study
One thousand seven hundred and seventy-five men and women aged 16–74 were interviewed at home in 1985 in 40 different areas of Britain and asked to participate in a 'Lifestyle and Appetite' survey which included questions on smoking (manufactured and handrolled cigarettes, pipe and cigars) by the subject and the spouse and on use of other nicotine products (snuff, chewing tobacco, nicotine gum and tobacco 'teabags') by the subject. After the questionnaire, subjects, with no prior warning, were asked to provide a sample of saliva in a glass collection tube for salivary cotinine analysis. Analyses, by gas liquid chromatography[14] reported to 0.1 ng/ml, were attempted for all self-reported non-users of tobacco or other nicotine containing products, and for 1 in 4 users. A few days later, an attempt was made to recontact respondents during which a backcheck question on manufactured cigarette smoking was asked.

1980/85 Follow-up study
In 1980, 8804 representative UK subjects aged 16+ were interviewed about their smoking, that of other household members, and demographic characteristics. In 1985, in 80 of the original 176 sampling points, an attempt was made to locate and reinterview (using the same main smoking questions) 7 of the subjects aged 25–65 in 1980. After rejecting cases where there was doubt whether the right person had been re-interviewed, data from 540 subjects were available.

1985 Consumer study
In 1985, a further 8857 representative UK subjects aged 16+ were interviewed. Apart from the standard smoking habit and demographic questions, some extra questions on spouse smoking were asked.

Statistical methods
Significance of between-group differences was estimated using non-parametric rank tests. Bias was estimated as shown in the Appendix.

Results

Cotinine study
Quotas for age, social class and (for women) working status were set and were adequately achieved. Two hundred and thirty-eight (13.4%) subjects refused to supply saliva; refusal rates were higher in those aged 65+ particularly in women (28.1%). Age and sex standardized refusal rates were somewhat lower in the higher social classes and in manufactured cigarette smokers. Presence of another person besides the (female) interviewer increased refusal in women and decreased it in men.

Seven hundred and seventy-five subjects reported smoking or use of other nicotine products, either regularly or at all in the last 7 days ('users'). Six hundred and eighty-nine (88.8%) provided saliva with a cotinine analysis made on 176 (25.5%) of these. For the other 1000 ('non-users'), 848 (84.8%) provided saliva with 808 (95.3%) successfully analysed.

The distribution of salivary cotinine for self-reported users and non-users is shown in Figure 1. Median cotinine levels among users were similar in men (319.2 ng/ml, $n = 104$) and women (310.6 ng/ml, $n = 72$). They were much lower in non-users, though here men had significantly ($P < 0.001$) higher levels (0.85 ng/ml, $n = 350$) than women (0.40 ng/ml, $n = 458$). Among self-reported non-users cotinine was higher in those married to a smoker than in those who were not (men 2.9 vs 0.6 ng/ml, women 1.0 vs 0.3 ng/ml, $P < 0.001$); the percentage married to a smoker was much higher in those with measurable cotinine (men 21.4%, women 32.0%) than in those with cotinine recorded as less than 0.1 ng/ml (men 1.2%, women 16.9%). Cotinine also tended to be higher among non-users in sub-groups where above average passive smoke exposure would be expected (e.g. 16–24 age group; 55–74 year olds living with a smoker; lower social classes; working women). No relationship of cotinine to spouse smoking or correlates of passive smoke exposure was seen among users. Among manufactured cigarette only smokers ($n = 108$), cotinine was significantly ($P < 0.01$) but weakly related to number smoked (1–12/d 282 ng/ml; 13–17/d 240 ng/ml; 18–22/d 417 ng/ml; 23+/d 318 ng/ml). Compared with manufactured only smokers, handrolled only smokers had a higher median cotinine (511 ng/ml, $n = 16$, $P < 0.01$) and cigar smokers lower (10 ng/ml, $n = 9$, $P < 0.01$). Smokers of other products only were too few for comparison.

It can be seen from Figure 1 that a cut-off point anywhere between 10 and 100 ng/ml would 'correctly' classify a very large proportion (over 93%) of subjects according to self-reported use or non-use. Between 13 and 20 ng/ml, this percentage would reach almost 96%. The question is to what extent self-reported non-users with cotinine values above this range represent misclassified true users rather than extremes of passive smoke exposure. A number of considerations resulted in the suggested classification shown in Table 2. Firstly, the distribution of cotinine values in self-reported non-users was reasonably continuous up to just over 20 ng/ml. Secondly, statistical techniques based on fitting log-normal distributions showed that self-reported non-users with cotinine above 100 ng/ml fitted the distribution of users very much better than that of non-users. Thirdly, there was a significant ($P = 0.003$) difference in the percentage of self-reported non-users reported as smoking manufactured cigarettes on backcheck between those with cotinine below 30 ng/ml (7/670 = 1.0%) and above 30 ng/ml (3/18 = 16.7%).

Table 2 Suggested classification of 808 self-reported non-users

Classification	*Salivary cotinine (ng/ml)*	n	*Per cent*
Non-users	< 30	788	97.5
Occasional users	30–100	9[a]	1.1
Regular users	> 100	11[b]	1.4

[a] Values 38.9, 40.5, 46.3, 46.6, 56.4, 58.2, 63.3, 80.7 and 87.8 ng/ml

[b] Values 132.2, 201.8, 220.1, 239.7, 268.2, 274.5, 282.2, 307.6, 361.7, 416.3 and 473.5 ng/ml

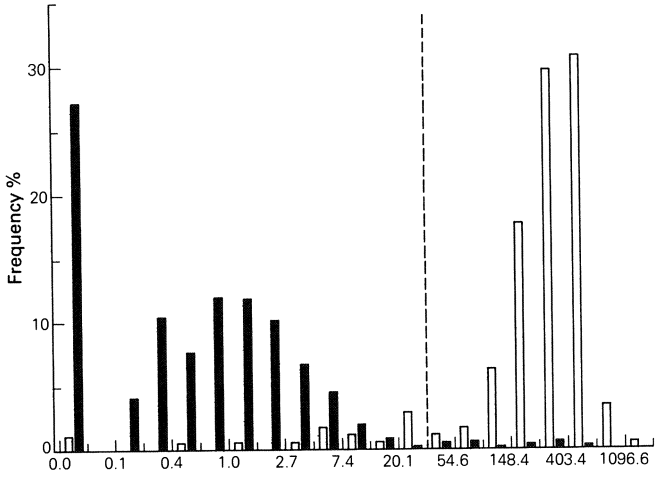

Figure 1 Histogram of salivary cotinine (ng/ml) in self-reported non-users and users plotted on scale of $\log_e$ (cotinine + 0.05). Vertical hatched line indicates 30 ng/ml, above which self-reported non-users were reclassified as users. Self-reported use: □, users (176); ■, non-users (808)

The overall misclassification rate of 2.5% (Table 2) did not vary materially by sex (males 2.9%, females 2.2%).

Among the 10 male and 10 female self-reported non-users with cotinine above 30 ng/ml, only 2 and 3 respectively reported being married to a smoker. Since their statements regarding their own habits were considered implausible, there must also be doubt about their statements regarding their spouse's habits.

1980/85 Follow-up study

Compared with those not followed-up, reinterviewed subjects had similar manufactured cigarette smoking habits but were more likely to live in a large household or have been originally interviewed at home (both sexes), be married and not working full-time (women) and be aged 35 or over and of lower social class (men). These differences were not due to the choice of sampling points for reinterview but, presumably, to the greater difficulty of locating young, mobile, at work people.

For each of the 4 main tobacco products, subjects were on both occasions asked if they smoked them and if not, whether they had ever smoked them for a minimum amount/duration (e.g. as much as one manufactured cigarette a day for as long as a year). From the 1985 answers, 166 subjects were classed as never smokers of any product. However in 1980, 4 of them claimed to be current smokers and 10 ex-smokers. After omitting 2 current smokers who were only occasional smokers, the inconsistency rate could be estimated as 7.2% (12/166).

Conversely, there were 174 men and women who could be classified as never smokers from the 1980 answers. Five years later, 3 reported being current smokers and 19 ex-smokers, all stating having started before 1980. This represents an inconsistency rate of 12.6% (22/174).

Inconsistent individuals were more often men (21/113 = 18.6% for both types of inconsistency combined) than women (13/227 = 5.7%, $P < 0.001$). They were also to some extent older. Where reporting past smoking on one occasion, the time of giving up tended to be longer ago and the number smoked markedly less than consistent ex-smokers.

1985 Consumer study

Defining subjects and spouses as smokers or non-smokers based on current smoking habits, the concordance ratio (see Table 1) was estimated as 3.55 for males and 3.07 for females.

These ratios were similar to those estimated from the 1980/85 Follow-up study (males 2.56, females 2.58), or from the Cotinine study, whether using self-reports (males 3.26, females 3.40), a 30 ng/ml cut-off (males 3.31, females 3.48) or a 100 ng/ml cut-off (males 2.81, females 3.51) to define smokers.

The variation by sex in the 1985 Consumer study was not significant. Nor was there any significant variation by age or social class, though there was an almost significant tendency for concordance to be higher (by 1.35 with 95% limits 0.94 to 1.96) if the spouse was present at interview. Concordance rose with amount smoked. Thus, the chance of having a spouse who was a manufactured cigarette smoker was 22% for subjects who reported no such smoking, and 45%, 52% and 59% respectively for subjects who reported smoking 1–17, 18–22 and 23+ manufactured cigarettes per day.

This study also provided information on ex-smoking of subjects but not of spouses. Using this, together with data on never-ex concordance from control patients with non-smoking associated diseases in a large hospital study,[15] estimates of the joint reported smoking distribution of a typical 10000 married couples in the UK were derived (Table 3).

Estimation of bias

This section estimates the relative risk among self-reported never smokers related to spouse current smoking (in comparison to never smoking) that would arise as a result of misclassification of ever smoking subjects as never smokers. The Appendix describes the method of estimating this bias, taking into account variation in true smoking habits. To carry out the estimation of bias, subjects were classified as never, ex, occasional or regular smokers. The smoking habit

Table 3 Estimated self-reported smoking habit distribution for 10000 UK married couples

	Women			
Men	Never smoked	Ex-smoker	Current smoker	Total
Never smoked	1656	386	531	25.7%
Ex-smoker	1352	802	619	27.7%
Current smoker	1822	624	2208	46.5%
Total	48.3%	18.1%	33.6%	100.0%

Concordance ratios: never smoked/ex-smoker 2.54
never smoked/current smoker 3.78

distributions required were taken from Table 3, with the further assumption (derived from the cotinine study) that 6.9% of current smokers were occasional smokers. Misclassification rates for regular and occasional smokers were taken from Table 2. It was also assumed that a further 10% of self-reported never smokers were ex-smokers. This was based on the inconsistency rates in the follow-up study, assuming that most were due to misclassification of true smokers as non-smokers rather than the reverse, and taking account of the fact that some ex-smokers would deny smoking on both occasions. Based on epidemiological data, RRs assumed for lung cancer were 10 for regular smoking, 2.5 for occasional smoking (based on linear extrapolation using cotinine levels) and 2.0 for ex-smoking, the relatively low value reflecting that many of the ex-smokers smoked little and a long time ago.

Results are given in Table 4. For both sexes, about seven-tenths of the bias came from misclassified regular smokers, about a quarter from misclassified ex-smokers, with only a small part coming from misclassified occasional smokers. Under the given assumptions it was also calculated that 27% of lung cancer deaths in self-reported never smokers actually occurred in current or ex-smokers.

Table 4 Estimated bias in relative risk of lung cancer among never smokers comparing spouse current smoker vs spouse never smoker

Misclassification taken into account	*Bias*	
	Males	*Females*
Current regular only	21.7%	15.2%
Current regular or occasional	25.1%	17.6%
Current and ex-smoker	31.4%	24.0%

Discussion

The increase in median cotinine in relation to spouse smoking is 0.72% for men and 0.23% for women of that in relation to active smoking. Linear extrapolation based on an assumed tenfold relative risk for 20 a day smokers would then predict a relative risk in relation to being married to a smoker of 1.07 for men and 1.02 for women. Using mean rather than median cotinine (but omitting self-reported non-users with cotinine > 30 ng/ml) the relative risk estimate would increase to 1.04 for women but not alter that for men.

These estimates are about an order of magnitude lower than the relative risks observed epidemiologically in relation to spouse smoking. While some of the shortfall might be explained in terms of longer durations of exposure for passive rather than active exposure and perhaps, by differences in composition of sidestream and mainstream smoke, other arguments suggest the true effect of passive smoking might be substantially less than suggested by the above linear extrapolation. One is that the true dose–response relationship may have a quadratic component.[16] More important, estimates of relative exposure of passive and active smokers based on retained particulate matter (arguably a more appropriate indicator of risk than cotinine which is not a carcinogen) are substantially lower than those based on cotinine. It has been estimated on this basis for the US that passive smokers have 0.02% of the exposure of active smokers for men and 0.01% for women.[17] Using linear extrapolation, these figures would provide relative risk estimates of 1.002 and 1.001, two orders of magnitude lower than those observed in epidemiological studies. Robins[18] also calculated that non-smokers take in the equivalent of an extremely small number of cigarettes per day in terms of respirable particulates. He further points out that higher cigarette equivalent numbers which can be calculated for the nitrosamine NDMA are likely to be very misleading since NDMA is in the vapour phase and is water soluble and, with shallow inhalation, will be dissolved in the mucous membranes before it can reach the lungs. He notes too that estimates based on cotinine may also give a misleadingly high indication of relative lung exposure of passive and active smoker since nicotine, which is also water soluble, is present mainly in the vapour phase in environmental tobacco smoke, whereas it is mainly in the particulate phase in mainstream smoke.

While these dosimetric arguments predict a very small increase in risk of lung cancer in non-smokers in relation to spouse smoking, the estimate of bias due to random misclassification of smokers as non-smokers is much larger, and of similar order to the average increase in risk observed epidemiologically. Before accepting that most of the epidemiological association is due to bias one must consider the various assumptions involved in the derivation of the bias estimate.

Looking at the estimated proportion of self-reported non-users who are in fact current true users, four points should be borne in mind.

(i) Nicotine can be found in non-tobacco dietary sources. However, concentrations are very low[19] (I estimate one must eat about 25 kg eggplant or 60 kg green tomato per day to reach a cotinine of 30 ng/ml!) so this can be ignored.

(ii) Duplicate determinations carried out in a pilot study showed reproducibility of the assay to be adequate (± 8%) and such analytical variation would not have affected the misclassification estimates at all.

(iii) It has been reported[20] that the half-life of cotinine in saliva is much longer than the day or so found for plasma or urine. If this is so, and other work has not confirmed it,[21] it is possible that some subjects with salivary cotinine > 30 ng/ml correctly stated not

having smoked in the last 7 days. They would, however, still be correctly reclassified as users.

(iv) 30 ng/ml may not be an optimal cut-off point. Since most of the estimated bias comes from subjects with cotinine over 100 ng/ml, who (having a median cotinine of almost 300 ng/ml) are surely regular smokers, this choice is not critical. Furthermore, while some subjects may have had cotinine above 30 ng/ml resulting from extreme passive smoke exposure, there may also be some counterbalancing subjects below 30 ng/ml who denied occasional use.

The last two points seem more important. One is sampling variation, our estimate of 1.4% regular users among self-reported non-users having 95% confidence limits of 0.6–2.2%. The other is the study situation. A number of other non-nationally representative studies have reported the proportion of self-reported non-smokers 'found out' to be higher; between 5% and 40%.[22–26] The fact that our study was carried out in a non-health context may explain our lower rates. Other factors affecting misclassification will include whether the subjects knew they were going to be checked up on, whether they had been previously advised to quit, the marker and the cut-off point used, whether questions on all major nicotine sources were included, and accuracy of data processing.

The estimated proportion of self-reported never smokers who have smoked in the past is clearly more open to doubt since the follow-up study only measured inconsistency between answers at two points in time. The estimated inconsistency of 10% in this study is somewhat higher than the figures of 6–8% seen in two other studies reporting smoking data on the same individual at different time points.[27,28] Under the misclassification hypothesis, such inconsistency rates should be even higher among self-reported never smoking lung cancer patients. Two studies[29,30] which have looked at this issue found this to be so, with a second source of information claiming past smoking in 27 and 40% of such cases respectively. Akiba *et al.*,[31] on the other hand, reported data which they interpreted as indicative of low misclassification rates in Japan. Among 98 and 99 women reported as never having smoked in 1982, only 7 men and no women were reported to be current smokers when investigated previously in 1964–1968. Three points should be made here. Firstly, although Akiba's[31] paper concerned lung cancer, those data came from a table based on results for cases and controls combined. Secondly, since smoking by women is not socially very accepted in Japan, some women may have kept their smoking secret with their next-of-kin not knowing about it. Thirdly, of the 187 men who reported not smoking in 1964–1968, as many as 96 (51%) were reported as smoking in 1982. This would seem far too high a proportion to be actually taking up smoking in this population (mean age over 60 in 1964–1968) and indicative of substantial misclassification of smoking habits.

A number of features of the bias estimation should be clearly understood. One is the assumption that subject misclassification rate is independent of spouse smoking. If, for example, people denied smoking only if their spouse did not smoke then a reverse bias would occur. While misclassification rates could be calculated in relation to reported spouse smoking status in this study, it was obviously unsound to rely on the accuracy of reported spouse smoking by subjects who had already given incorrect answers about their own smoking. It would need a study where both subject and spouse habits were validated by cotinine to test this hypothesis properly—for the moment there is no reason to believe this theoretical possibility will have any material effect in practice.

The bias estimation did not take into account quantity smoked (other than to distinguish regular and occasional smokers) because cotinine does not clearly distinguish heavy and light smokers. Were the proportion of regular smokers denying smoking in fact independent of amount smoked, the bias estimations ignoring quantity would be underestimates, but only to a minor extent. Variation in bias by level of spouse smoking will, however, be quite substantial due to the increasing concordance with increasing amount smoked.

Misclassification rates have been assumed invariant of sex in the analysis. This is valid enough for current habits, the major source of bias, so any error resulting from failure of this assumption will not be large. However, the higher inconsistency rates in men in the follow-up study suggest that the bias estimates may be somewhat understated for men and overstated for women.

More crucial to the accuracy of the estimates are the lung cancer RR values assumed, particularly for regular smokers. Wells[9] has pointed out that for women the estimate used of 10 is higher than that seen in some of the old prospective studies, feeling a figure of 5 to be more appropriate. In view of the marked increase in average duration of smoking among older women over the last 20 years in many countries and in view of the very large concommitant rise in lung cancer rates, inexplicable in terms of changes in the percentage of smokers, the relative risk of women smokers seems likely to have changed substantially. In any case, the lower the risk assumed in relation to active smoking the more difficult it becomes to explain the association seen with passive smoking purely on dosimetric grounds.

A recent paper by Wald *et al.*[11] reached a different conclusion from mine. First, based on the overall epidemiological evidence, they calculated an average figure of 1.35 for the relative risk of lung cancer of non-smokers married to smokers compared to non-smokers married to non-smokers. Next, based on

four studies in which cotinine levels had been related to statements made about smoking habits they concluded the effects of misclassification of the type I have discussed were relatively minor, adjusting their figure of 1.35 down only slightly, to 1.30, to take account of this bias. Finally, they noted that even non-smokers married to non-smokers are not completely non-exposed and estimated that, compared to a completely non-exposed non-smoker, non-smokers married to a smoker would have a 53% excess risk of lung cancer and non-smokers in general would have a 38% excess risk.

The estimate of the effect of misclassification of active smoking habits by Wald *et al.*[11] is less than mine for three reasons. (i) They used an assumed relative risk of 8 rather than 10 for the effect of active smoking observed in women. (ii) Their mathematical calculations of bias were incorrect, due to confusion between true relative risks in relation to active smoking and those observed (which are affected by misclassification). Both of these reasons have relatively little effect. (iii) In the four smaller studies which they have cited only one self-reported non-smoker out of 705 had a nicotine or cotinine level even 50% as high as that seen in an average smoker. This contrasts markedly with my study in which 10 out of 808 self-reported non-smokers had a cotinine level of over 150 ng/ml. This reason does have a substantial effect. Although my misclassification estimates are higher than those of Wald *et al.*[11] they are lower, as noted above, than those provided by a number of other published studies.

Wald *et al.*[11] state that the 'magnitude of the excess risk' (of lung cancer) 'appears to be reasonable in the light of the extent of exposure.' Even based on their own data this does not appear to be the case. According to their figures, non-smokers married to a smoker have 1% of the cotinine level of smokers. Extrapolating linearly from the 38% increase they claim for this group would suggest that active smokers should have a risk 39 times that of non-smokers, markedly discrepant from the relative risk of 8 they actually assumed. The discrepancy would be even greater (130 vs 8) if one further took into account the fact that in *women* (Wald *et al.* only studied men) non-smokers married to a smoker only have 0.3% of the cotinine level of smokers. I suggest that Wald *et al.* have seriously underestimated the effect of misclassification and that a true 53% increase in risk for a non-smoker married to a smoker is implausible.

Taking into account the available information, it seems more reasonable to conclude that exposure to smoke constituents of non-smokers is too low to explain the moderate increase in risk of lung cancer seen in epidemiological studies in self-reported never smokers married to smokers. This increase in risk is much more plausibly explained by misclassification of smokers as non-smokers than by a direct effect of passive smoking.

The studies were funded by the Tobacco Advisory Council to whom I am most grateful. Interviewing was carried out by Research Surveys of Great Britain and by Research Services. Cotinine analysis was carried out by Hazleton Laboratories Europe. Mrs B. A. Forey and Dr J. S. Fry provided invaluable assistance.

References

1. Hirayama T. Non-smoking wives of heavy smokers have a higher risk of lung cancer: a study from Japan. *British Medical Journal* 1981; **282**: 183–5.
2. Trichopoulos D, Kalandidi A, Sparros L & MacMahon B. Lung cancer and passive smoking. *International Journal of Cancer* 1981; **27**: 1–4.
3. Correa P, Pickle LW, Fontham E, Lin Y & Haenszel W. Passive smoking and lung cancer. *Lancet* 1983; **ii**: 595–7.
4. Trichopoulos D, Kalandidi A & Sparros L. Lung cancer and passive smoking. Conclusion of Greek study. *Lancet* 1983; **ii**: 677–8.
5. Buffler PA, Pickle LW, Mason TJ & Contant C. The causes of lung cancer in Texas. In Lung Cancer Causes and Prevention, eds M Mizell & P. Correa, pp. 83–99. New York: Verlag Chemie International Inc., 1984.
6. Kabat GC & Wynder CL. Lung cancer in non-smokers. *Cancer* 1984; **53**: 1214–21.
7. Chan WC & Fung SC. Lung cancer in non-smokers in Hong Kong. In: Cancer campaign, Cancer epidemiology, vol. 6 ed. E. Grundmann, pp. 199–202. Stuttgart, New York: Gustav Fischer Verlag, 1982.
8. Lee PN. Passive smoking. In Smoking and the Lung, eds G Cumming & G. Bonsignore, pp. 187–216. New York, London: Plenum Publishing Corporation, 1984.
9. Wells AJ. Misclassification as a factor in passive smoking risk. *Lancet* 1986; **ii**: 638.
10. Doll R. Lung cancer: observed and expected changes in incidence from active and passive smoking. Paper presented at XIV UICC conference at Budapest, 1986.
11. Wald NJ, Nanchahal K, Thompson SG & Cuckle HS. Does breathing other people's tobacco smoke cause lung cancer? *British Medical Journal* 1986; **293**: 1217–22.
12. Mantel N. Lung cancer and passive smoking. *British Medical Journal* 1987; **294**: 440.
13. Kilpatrick SJ. Misclassification of environmental tobacco smoke exposure: its potential influence on studies of environmental tobacco smoke and lung cancer. *Toxicology Letters* 1987; **35**: 163–8.
14. Feyerabend C & Russell MAH. Rapid gas-liquid chromatographic determination of cotinine in biological fluids. *Analyst* 1980; **105**: 998–1001.
15. Alderson MR, Lee PN & Wang R. Risks of lung cancer, chronic bronchitis, ischaemic heart disease, and stroke in relation to type of cigarette smoked. *Journal of Epidemiology and Community Health* 1985; **39**: 286–93.
16. Doll R & Peto R. Cigarette smoking and bronchial

carcinoma: dose and time relationships among regular smokers and lifelong non-smokers. *Journal of Epidemiology and Community Health* 1978; **32**: 303–13.

[17] Arundel A, Irwin T & Sterling T. Non-smoker lung cancer risks from tobacco smoke exposure: an evaluation of Repace and Lowrey's phenomenological model. *Journal of Environmental Science and Health Part C* 1986; **4**: 93–118.

[18] Robins J. Risk Assessments—Exposure to Environmental Tobacco Smoke and Lung Cancer. Appendix D to *Environmental Tobacco Smoke. Measuring Exposures and Assessing Health Effects*. Committee on Passive Smoking. Board on Environmental Studies and Toxicology, pp. 294–336. Washington, DC. National Research Council. National Academy Press, 1986.

[19] Castro A & Monji N. Dietary nicotine and its significance in studies on tobacco smoking. *Biochemical Archives* 1986; **2**: 91–7.

[20] Sepkovic DW & Haley NJ. Biochemical applications of cotinine quantitation in smoking related research. *American Journal of Public Health* 1985; **75**: 663–5.

[21] Curvall M, Kazemi-Vala E & Enzell CR. Nicotine and cotinine in body fluids after exposure to environmental tobacco smoke (ETS). Paper presented at 40th Tobacco Chemists' Research conference 1986.

[22] Williams R & Gillies P. Do we need objective measures to validate self-reported smoking? *Public Health London* 1986; **98**: 294–8.

[23] Jarvis M, Tunstall-Pedoe H, Feyerabend C, Vesey C & Salloojee Y. Biochemical markers of smoke absorption and self reported exposure to passive smoking. *Journal of Epidemiology and Community Health* 1984; **34**: 335–9.

[24] Richmond R & Webster I. Evaluation of general practitioners' use of a smoking intervention programme. *International Journal of Epidemiology* 1985; **14**: 396–401.

[25] Silman A, Loysen E, de Graaf W & Sramek M. High dietary fat intake and cigarette smoking as risk factors for ischaemic heart disease in Bangladeshi male immigrants in East London. *Journal of Epidemiology and Community Health* 1985; **39**: 301–3.

[26] Neaton JD, Broste S, Cohen L, Fishman EL, Kjelsberg MO & Schoenberg J. The multiple risk factor intervention trial (MRFIT) VII. A comparison of risk factor changes between the two study groups. *Preventive Medicine* 1981; **10**: 519–43.

[27] Rogot E & Reid DD. The validity of data from next-of-kin in studies of mortality among migrants. *International Journal of Epidemiology* 1975; **4**: 51–4.

[28] Peach H, Shah D & Morris RW. Validity of smokers' information about present and past cigarette trends—implications for studies of the effects of falling tar yields of cigarettes in health. *Thorax* 1986; **41**: 203–7.

[29] Berry G, Newhouse ML & Antonis P. Combined effect of asbestos and smoking on mortality from lung cancer and mesothelioma in factory workers. *British Journal of Industrial Medicine* 1985; **45**: 12–8.

[30] Garfinkel L, Auerbach O & Joubert L. Involuntary smoking and lung cancer: A case-control study. *Journal of the National Cancer Institute* 1985; **75**: 463–9.

[31] Akiba S, Kato H & Blot WJ. Passive smoking and lung cancer among Japanese women. *Cancer Research* 1986; **46**: 4804–7.

(Received 8 April 1987; accepted 22 April 1987)

Appendix

Let us assume *observed* (indicated by a star) data as follows:

Subject self-reported smoking habits	Relative numbers of subjects: Spouse never smoked	Spouse current smoker	Relative lung cancer risk
Never smoked	U_0^*	V_0^*	1
Smoked at level j	U_j^*	V_j^*	S_j^*

Let p_j^* be the probability that a self-reported never smoker actually is a smoker at level j, i.e. the misclassification rate.

To estimate the bias (in the absence of a true effect of passive smoking) proceed as follows:

Calculate correction factor $F = (1 - \sum_j p_j^*)/(1 - \sum_j s_j^* p_j^*)$

Calculate *true* (no star) relative risks $S_j = S_j^* F$

Calculate risk in self-reported never smokers

(i) Married to never smokers

$$R_1 = 1 + \frac{(U_0^* + V_0^*)}{U_0^*} \sum_j \frac{(S_j - 1)U_j^* p_j^*}{(U_j^* + V_j^*)}$$

(ii) Married to current smokers

$$R_2 = 1 + \frac{(U_0^* + V_0^*)}{V_0} \sum_j \frac{(S_j - 1)V_j^* p_j^*}{(U_j^* + V_j^*)}$$

Calculate bias = R_2/R_1

Appendix C
Major and Minor Sources of Misclassification Bias in Passive Smoking Studies - Mathematical Details

C.1 Situation 1: Misclassification in a 2×2 Table; Misclassification Rates Unrelated to Spouse Smoking Habits

C.1.1 Terminology and Assumptions

In a study of N married individuals, suppose that the true division by smoking habits of the subjects and their spouses is as follows:

Subject	Spouse	
	Non-smoker	Smoker
Non-smoker	N_1	N_2
Smoker	N_3	N_4

Suppose further that in the absence of spouse smoking, subject smoking multiplies risk of lung cancer by a factor S (for smoking) and that in the absence of subject smoking passive smoking (from the spouse) multiplies risk of lung cancer by a factor P (for passive). If a multiplicative model of risk is assumed the relative risks in the 4 cells of the table will be respectively 1, P, S and SP. If an additive model is assumed the relative risks will be 1, P, S and $P+S-1$.

Suppose that a proportion p_1 of non-smokers are misclassified as smokers and that a proportion p_2 of smokers are misclassified as non-smokers, these misclassification rates being assumed to be independent of spouse smoking habits.

Further define N_1^*, N_2^*, N_3^*, N_4^* as the corresponding observed proportions of the subjects by smoking habits and p_1^*, p_2^* as respectively the proportion of observed non-smokers who are really smokers and the proportion of observed smokers who are really non-smokers.

C.1.2 Estimating True Distribution of Smoking Habits

The following equations can be written down:

$$N_1^* = (1-p_1)^2 N_1 + p_2(1-p_1) N_2 + p_2(1-p_1) N_3 + p_2^2 N_4 \tag{1}$$

$$N_2^* = p_1(1-p_1) N_1 + (1-p_1)(1-p_2) N_2 + p_1 p_2 N_3 + p_2(1-p_2) N_4 \tag{2}$$

$$N_3^* = p_1(1-p_1) N_1 + p_1 p_2 N_2 + (1-p_1)(1-p_2) N_3 + p_2(1-p_2) N_4 \tag{3}$$

$$N_4^* = p_1^2 N_1 + p_1(1-p_2) N_2 + p_1(1-p_2) N_3 + (1-p_2)^2 N_4 \tag{4}$$

$$p_1^* = [p_2(1-p_1) N_3 + p_2^2 N_4 + p_1 p_2 N_3 + p_2(1-p_2) N_4]/(N_1^* + N_2^*) \tag{5}$$

$$p_2^* = [p_1(1-p_1) N_1 + p_1 p_2 N_2 + p_1^2 N_1 + p_1(1-p_2) N_2]/(N_3^* + N_4^*) \tag{6}$$

(5) and (6) simplify respectively to:

$$p_1^* = p_2(N_3 + N_4)/(N_1^* + N_2^*) \tag{7}$$

$$p_2^* = p_1(N_1 + N_2)/(N_3^* + N_4^*) \tag{8}$$

Adding (1) and (2) gives:

$$\begin{aligned} N_1^* + N_2^* &= (1-p_1)(N_1 + N_2) + p_2(N_3 + N_4) \\ &= (N_1 + N_2) - p_1(N_1 + N_2) + p_2(N_3 + N_4) \end{aligned} \tag{9}$$

Substituting from (7) and (8) gives:

$$N_1^* + N_2^* = \frac{p_2^*(N_3^* + N_4^*)}{p_1} - p_2^*(N_3^* + N_4^*) + p_1^*(N_1^* + N_2^*) \tag{10}$$

Rewriting (10) gives

$$p_1 = \frac{p_2^*(N_3^* + N_4^*)}{(1-p_1^*)(N_1^* + N_2^*) + p_2^*(N_3^* + N_4^*)} \tag{11}$$

Similarly:

$$p_2 = \frac{p_1^*(N_1^* + N_2^*)}{p_1^*(N_1^* + N_2^*) + (1-p_2^*)(N_3^* + N_4^*)} \tag{12}$$

Formulae (11) and (12) allow calculation of the true misclassification rates p_1 and p_2 in terms of the observed smoking habit distribution and the observed misclassification rates.

Note that Eq. (1) to (4) can be rewritten in matrix form:

$$\begin{vmatrix} N_1^* & N_2^* \\ N_3^* & N_4^* \end{vmatrix} = \begin{vmatrix} 1-p_1 & p_2 \\ p_1 & 1-p_2 \end{vmatrix} \begin{vmatrix} N_1 & N_2 \\ N_3 & N_4 \end{vmatrix} \begin{vmatrix} 1-p_1 & p_1 \\ p_2 & 1-p_2 \end{vmatrix}$$

or $\underline{N}^* = \underline{P}\,\underline{N}\,\underline{P}^T$

where $\underline{N}^*$ and $\underline{N}$ are the observed and true matrices of smoking habits, $\underline{P}$ is the misclassification matrix and $\underline{P}^T$ is its transpose.

This gives the immediate solution:

$$\underline{N} = \underline{P}^{-1}\,\underline{N}^*\,(\underline{P}^T)^{-1} \tag{13}$$

where $\underline{P}^{-1}$ is the inverse of the misclassification matrix.

Thus, solving (11)–(13) allows complete reconstruction of the true data from the observed data and also allows comparison of the true concordance rate:

$$C = N_1 N_4 / N_2 N_3 \tag{14}$$

with the observed concordance rate:

$$C^* = N_1^* N_4^* / N_2^* N_3^* \tag{15}$$

C.1.3 Relationship of Observed Active and Passive Smoking Effects to their True Values

The normal way of estimating the risk of lung cancer in relation to passive smoking is to compare the risk in groups N_1^* and N_2^*, while the normal way of estimating the risk of lung cancer in relation to active smoking is to compare the risk in groups $N_3^* + N_4^*$ combined and in groups N_1^* and N_2^* combined. Define these as P* and S* respectively and compare these with their true values P and S.

The relevant equations for the multiplicative model can be written down as follows:

$$P^* = \frac{N_1^*[p_1(1-p_1)N_1 + (1-p_1)(1-p_2)PN_2 + p_1 p_2 SN_3 + p_2(1-p_2)PSN_4]}{N_2^*[(1-p_1)^2 N_1 + p_2(1-p_1)PN_2 + p_2(1-p_1)SN_3 + p_2^2 PSN_4]} \tag{16}$$

$$S^* = \frac{(N_1^* + N_2^*)[p_1 N_1 + p_1 PN_2 + (1-p_2)SN_3 + (1-p_2)PSN_4]}{(N_3^* + N_4^*)[(1-p_1)N_1 + (1-p_1)PN_2 + p_2 SN_3 + p_2 PSN_4]} \tag{17}$$

For the additive model the term PSN_4 is replaced by $(P+S-1)N_4$ in both equations.

C.1.4 A Simple Example

As an example of the magnitude of biasses in P and S and the relationship between true and observed misclassification rates, consider the simple situation:

$P = 1$	No true passive smoking effect (note that in this case the additive and multiplicative models are identical)
$S = 20$	Large true active smoking effect
$p_2 = 0.05$	5% of smokers deny smoking
$p_1 = 0$	All non-smokers report they are non-smokers
$\underline{N} = \begin{vmatrix} 60 & 40 \\ 40 & 60 \end{vmatrix}$	50% of the population smoke in each sex and there is a concordance of $2.25 = C$

From (1) to (4):

$$N_1^* = 60 + 2 + 2 + 0.15 = 64.15$$
$$N_2^* = 0 + 38 + 0 + 2.85 = 40.85$$
$$N_3^* = 0 + 0 + 38 + 2.85 = 40.85$$
$$N_4^* = 0 + 0 + 0 + 54.15 = 54.15$$

The observed concordance $C^* = 2.08$
From (7) and (8):

$$p_1^* = 0.047619$$
$$p_2^* = 0$$

From (16) and (17):

$$P^* = \frac{64.15\,[\,0 + 38 + 0 + 57]}{40.85\,[60 + 2 + 40 + 3]} = 1.42$$

$$S^* = \frac{105\,[\,0 + 0 + 760 + 1140]}{95\,[60 + 40 + 40 + 60]} = 10.50$$

In this simplified situation, it can be seen that a relatively small proportion of smokers denying smoking has resulted in the observed active smoking effect being almost a half of what it should have been and has resulted in a spurious passive smoking effect, with observed non-smokers married to observed smokers having a 42% higher risk of lung cancer than observed non-smokers married to observed non-smokers.

C.1.5 Further Examples Illustrating the Effect of Misclassification

Table C1 illustrates how the observed and true values of N, p_1, p_2, C, P and S relate to each other under various different situations.

Analysis 1 is the simple example given above, and is the central analysis around which the other analyses vary. Analyses 2 to 5 look at the effect of

Table C1. Relationship of observed (O) smoking habit distributions (N), misclassification rates (P), smoking concordance (C) and relative risks in relation to active (S) and passive (P) smoking to their true values (T)

Analysis	True or observed	Smoking habit distribution				Misclassification rates		Concordance	Relative risks	
		N_1	N_2	N_3	N_4	p_1	p_2	C	Active S	Passive P
1	T	60	40	40	60	0	0.05	2.25	20	1
	O	64.15	40.85	40.85	54.15	0.048	0	2.08	10.50	1.42
2	T	60	40	40	60	0	0.01	2.25	20	1
	O	60.81	40.19	40.19	58.81	0.010	0	2.21	16.83	1.14
3	T	60	40	40	60	0	0.02	2.25	20	1
	O	61.62	40.38	40.38	57.62	0.020	0	2.18	14.57	1.24
4	T	60	40	40	60	0	0.10	2.25	20	1
	O	68.60	41.40	41.40	48.60	0.091	0	1.95	7.33	1.53
5	T	60	40	40	60	0	0.20	2.25	20	1
	O	78.40	41.60	41.60	38.40	0.167	0	1.74	4.80	1.53
6	T	60	40	40	60	0	0.05	2.25	10	1
	O	64.15	40.85	40.85	54.15	0.048	0	2.08	7.00	1.25
7	T	60	40	40	60	0	0.05	2.25	50	1
	O	64.15	40.85	40.85	54.15	0.048	0	2.08	15.00	1.67
8	T	60	40	40	60	0	0.05	2.25	20	1.50
	O	64.15	40.85	40.85	54.15	0.048	0	2.08	10.92	2.08
9	T	60	40	40	60	0	0.05	2.25	20	2
	O	64.15	40.85	40.85	54.15	0.048	0	2.08	11.20	2.71
10	T	60	40	40	60	0.01	0.05	2.25	20	1
	O	62.92	41.08	41.08	54.92	0.048	0.010	2.05	10.35	1.42
11	T	60	40	40	60	0.02	0.05	2.25	20	1
	O	61.69	41.31	41.31	55.69	0.049	0.021	2.01	10.20	1.41
12	T	60	40	40	60	0.05	0.05	2.25	20	1
	O	58.10	41.90	41.90	58.10	0.050	0.050	1.92	9.77	1.40
13	T	60	40	40	60	0.10	0.05	2.25	20	1
	O	52.35	42.65	42.65	62.35	0.053	0.095	1.79	9.10	1.38
14	T	55	45	45	55	0	0.05	1.49	20	1
	O	59.64	45.36	45.36	49.64	0.048	0	1.44	10.5	1.19
15	T	65	35	35	65	0	0.05	3.45	20	1
	O	68.66	36.34	36.34	58.66	0.048	0	3.05	10.5	1.71
16	T	70	30	30	70	0	0.05	5.44	20	1
	O	73.18	31.83	31.83	63.18	0.048	0	4.56	10.5	2.08
17	T	120	80	40	60	0	0.05	2.25	20	1
	O	126.15	78.85	40.85	54.15	0.024	0	2.12	13.67	1.27
18	T	120	40	80	60	0	0.05	2.25	20	1
	O	126.15	40.85	78.85	54.15	0.042	0	2.12	11.13	1.43
19	T	240	80	80	60	0	0.05	2.25	20	1
	O	248.15	78.85	78.85	54.15	0.021	0	2.16	14.22	1.28
20	T	60	40	80	120	0	0.05	2.25	20	1
	O	66.3	43.7	81.7	108.3	0.091	0	2.01	7.33	1.56
21	T	60	80	40	120	0	0.05	2.25	20	1
	O	66.3	81.7	43.7	108.3	0.054	0	2.01	9.87	1.40
22	T	60	80	80	240	0	0.05	2.25	20	1
	O	68.6	87.4	87.4	216.6	0.103	0	1.95	6.78	1.53

varying p_2, the proportion of smokers misclassified as non-smokers. Analyses 6 and 7 look at the effect of varying the true active smoking effect, whilst 8 and 9 look at the effect of varying the true passive smoking effect under the multiplicative model. Analyses 10 to 13 look at the effect of varying p_1, the proportion of non-smokers misclassified as smokers. Analyses 14 to 16 look at the effect of varying the concordance rates while keeping the overall proportions of smokers constant. Analyses 17 to 22 keep the concordance rate constant, but study in turn the effect of increasing the proportion of non-smoking subjects (17), the proportion of non-smoking spouses (18), both the proportion of non-smoking subjects and spouses (19), the proportion of smoking subjects (20), the proportion of smoking spouses (21) and the proportion of smoking subjects and spouses (22).

From these analyses a number of general conclusions emerge:

Bias in Active Smoking Risk

a) The observed relative risk in relation to active smoking, S*, is always less than the true relative risk, S. S*, as a proportion of S, decreases markedly with increasing misclassification of smokers as non-smokers.

Analysis	p_2	S*/S
2	0.01	0.84
3	0.02	0.73
1	0.05	0.52
4	0.10	0.37
5	0.20	0.24

b) It is much less affected by the reverse misclassification.

Analysis	p_1	S*/S
1	0	0.52
10	0.01	0.52
11	0.02	0.51
12	0.05	0.49
13	0.10	0.45

c) It is not affected at all by variation in concordance, given the same marginal distribution of smoking habits.

Analysis	C	S*/S
14	1.49	0.52
1	2.25	0.52
15	3.45	0.52
16	5.44	0.52

d) For a given level of concordance it is much more affected by an increase in the overall percentage of subjects who smoke than by an increase in the overall percentage of spouses who smoke, which has very little effect.

Analysis	% Subjects smoking	% Spouses smoking	S*/S
22	70	70	0.34
20	67	53	0.37
21	53	67	0.49
1	50	50	0.52
18	47	33	0.56
17	33	47	0.68
19	30	30	0.71

e) The larger the assumed relative risk in relation to smoking, S, the greater is the proportional reduction in S* caused by misclassification.

Analysis	S	S*/S
6	10	0.70
1	20	0.52
7	50	0.30

f) Given S, however, the assumed relative risk in relation to passive smoking has little effect.

Analysis	P	S*/S
1	1	0.52
8	1.5	0.55
9	2.0	0.56

Bias in Passive Smoking Risk

g) The observed relative risk in relation to passive smoking, P*, is always more than the true relative risk, P. As for active smoking, the relative bias (P* – P)/P increases markedly with increasing misclassification of smokers as nonsmokers over the likely range of p_2.

Analysis	p_2	(P* – P)/P
2	0.01	0.14
3	0.02	0.24
1	0.05	0.42
4	0.10	0.53
5	0.20	0.53

h) Again, as for active smoking, it is little affected by the reverse misclassification.

Analysis	p_1	$(P^* - P)/P$
1	0	0.42
10	0.01	0.42
11	0.02	0.41
12	0.05	0.40
13	0.10	0.38

j) Unlike active smoking it is increased markedly by increasing concordance.

Analysis	C	$(P^* - P)/P$
14	1.49	0.19
1	2.25	0.42
15	3.45	0.71
16	5.44	1.08

k) As for active smoking the relative bias is much more affected by an increase in the overall percentage of subjects who smoke and little affected by an increase in the overall percentage of spouses who smoke.

Analysis	% Subjects smoking	% Spouses smoking	$(P^* - P)/P$
22	70	70	0.53
20	67	53	0.56
21	53	67	0.40
1	50	50	0.42
18	47	33	0.43
17	33	47	0.27
19	30	30	0.28

l) Again, as for active smoking, the larger the observed relative risk in relation to smoking, S, the greater relative effect misclassification has:

Analysis	S	$(P^* - P)/P$
6	10	0.25
1	20	0.42
7	50	0.67

m) Here also, given S, variation in P has little effect on the relative bias (though of course varying P affects P*). As shown below, this conclusion differs for the additive model.

Analysis	p	(P* – P)/P
1	1	0.42
8	1.5	0.39
9	2.0	0.36

Bias in Concordance

n) Observed concordance, C*, is always somewhat less than the true concordance, C, in the range of concordances studied. Generally it increases with increasing misclassification of either sort. Even for relatively large misclassification, the difference is not great and, given the general level of accuracy of estimates of C* due to the sampling variation, it seems reasonable to take C* as a fair approximation to C.

Stability of Conclusions

Conclusions a–e, g–l and n, as derived from Table C1, were generally based on analyses in which no true passive smoking effect was assumed. Further work showed that inclusion of a small true passive smoking effect, whether assuming a multiplicative or an additive model, did not affect those general conclusions (except that conclusion C became approximate rather than exact).

Assuming an additive rather than a multiplicative model also did not affect conclusion F, that the bias S*/S was materially unaffected by variation in P. As shown below, however, conclusion M, concerning the effect of variation in P on the relative bias (P* – P)/P is affected by the choice of model.

Additive Model

P	P*	(P* – P)/P
1	1.421	0.42
1.1	1.479	0.34
1.2	1.537	0.28
1.3	1.594	0.23
1.4	1.652	0.18
1.5	1.709	0.14
1.6	1.766	0.10
1.7	1.822	0.07
1.8	1.879	0.04
1.9	1.935	0.02
2.0	1.991	−0.00

Here the bias decreases with increasing P. However, for values of P in the range suggested by estimates of relative exposure of passive and active smokers (<1.1) the bias does not vary materially with variation in P.

C.1.6 Exact Results in a Simpler Situation

From Sect. C.1.5 it has been demonstrated that:

(a) moderate misclassification of non-smokers as smokers has little effect on bias in estimation of the active and passive smoking effects,

(b) the relative bias on the true passive smoking effect caused by misclassification of smokers as non-smokers is little affected by a true small passive smoking effect.

This suggests that useful results could be gained by considering the simpler situation in which it is assumed that:

(a) no non-smokers are misclassified as smokers and

(b) there is no true passive smoking effect.

Here it can be shown that the true active smoking effect, S, can be estimated from the observed active smoking effect, S*, and the observed proportion of non-smokers who are smokers, p_1^*, by the formula

$$S = (S^* - S^* p_1^*)/(1 - S^* p_1^*) \tag{18}$$

The risks of lung cancer (relative to true non-smoker rates) in non-smokers married to smokers, R_2, and in non-smokers married to non-smokers, R_1 can be estimated by the formulae

$$R_2 = 1 + (S-1)\, p_1^* N_4^* (N_1^* + N_2^*)/N_2^* (N_3^* + N_4^*) \tag{19}$$

and

$$R_1 = 1 + (S-1)\, p_1^* N_3^* (N_1^* + N_2^*)/N_1^* (N_3^* + N_4^*) \tag{20}$$

It can be seen that the ratio of excess risks, $(R_2 - 1)/(R_1 - 1)$ is equal to the observed concordance ratio. R_2/R_1 is of course the observed effect of passive smoking in non-smokers P*.

C.1.7 Approximate Results in a Simpler Situation

In the mathematics considered in Sects. C.1.1–C.1.5 account has been taken of both misclassification of the subject's smoking habits and the spouse's smoking habits. One can simplify C.1.6 further by only taking account of misclassification of subject's smoking habits.

It is easy to see that this will have no effect on the formula relating p_1^* to p_2, which based on (12) becomes

$$p_2 = \frac{p_1^*(N_1^* + N_2^*)}{p_1^*(N_1^* + N_2^*) + (N_3^* + N_4^*)} \tag{21}$$

for the situation of misclassification in only 1 direction. Nor will it have any effect on formula (18) which relates the observed active smoking effect to the true active smoking effect, since the observed total number of smokers, $N_3^* + N_4^*$, and non-smokers, $N_1^* + N_2^*$, are unaffected.

It can also be shown that formulae (19) and (20) for the passive smoking effect will still hold, though, given N_1, N_2, N_3, N_4 and p_2, the actual values of N_1^*, N_2^*, N_3^* and N_4^* will change somewhat.

Thus, for the example of Sect. C.1.4, where

$N_1^* = 64.15$, $N_2^* = 40.85$, $N_3^* = 40.85$, $N_4^* = 54.15$ and $p_1^* = 0.047619$

was computed resulting in

$R_1 = 1.637$ and $R_2 = 2.326$

with $P^* = 1.42$

here, under the alternative assumption of misclassification of subjects only, the values

$N_1^* = 62$, $N_2^* = 43$, $N_3^* = 38$, $N_4^* = 57$ and $p_1^* = 0.047619$

are computed resulting in

$R_1 = 1.613$ and $R_2 = 2.326$

with $P^* = 1.44$.

It can be seen that P^* is very similar under the alternative assumptions, since the absolute values of the N_i^* vary little. Using true values for N in the above calculations results in

$R_1 = 1.667$ and $R_2 = 2.500$

with $P^* = 1.50$

C.2 Situation 2: Misclassification in a 2×2 Table; Misclassification Rates Related to Spouse Smoking Habits

In theory, a smoker might more readily deny his habit on interview if he is married to a non-smoker, especially if the fact that he smokes is not known to

his spouse. To consider this possibility, p_2 is redefined as the probability of a smoker being misclassified as a non-smoker if his spouse is a smoker and p_3 is introduced as the probability of a smoker being misclassified as a non-smoker if his spouse is not a smoker. For simplicity, and as it made little difference in the previous section, p_1, the probability of the reverse misclassification, is taken to be zero.

The following equations can now be written down:

$$N_1^* = N_1 + p_3 N_2 + p_3 N_3 + p_2^2 N_4 \tag{22}$$

$$N_2^* = (1-p_3) N_2 \qquad + p_2(1-p_2) N_4 \tag{23}$$

If a risk of S among smokers and 1 among non-smokers is assumed, i.e. there is no true passive smoking effect, the mean risk of the group observed as N_1^* will be given by

$$1 + \frac{(S-1)(p_3 N_3 + p_2^2 N_4)}{N_1 + p_3 N_2 + p_3 N_3 + p_2^2 N_4} \tag{24}$$

while the mean risk of the group observed as N_2^* will be given by:

$$1 + \frac{(S-1)(p_2(1-p_2) N_4)}{(1-p_3) N_2 + p_2(1-p_2) N_4} \tag{25}$$

It is clear that if p_3 is large and p_2 is zero, then the risk will be higher in the N_1^* group, i.e. there will be an apparent negative effect of passive smoking.

On the contrary, if p_3 is zero, or if p_2 and p_3 are equal, there will be an apparent positive effect of passive smoking (assuming $C > 1$).

In general, it seems that as p_2/p_3 increases, the apparent relative risk in relation to passive smoking increases. This is illustrated in Table C2.

Table C2. Observed risk of lung cancer in non-smokers by spouse smoking habit assuming a proportion p_2 of smokers married to smokers are misclassified as non-smokers and a proportion p_3 of smokers married to non-smokers are misclassified as non-smokers (Given $N = 60$, $N_1 = 40$, $N_2 = 40$, $N_3 = 60$, $R_4 = 20$, $P = 1$ - see text)

p_2	p_3	Risk of lung cancer in non-smokers		
		Spouse a non-smoker	Spouse a smoker	Relative risk
0.05	0.00	1.047	2.264	2.162
0.05	0.01	1.171	2.276	1.944
0.05	0.03	1.410	2.300	1.631
0.05	0.05	1.637	2.326	1.421
0.05	0.07	1.852	2.352	1.270
0.05	0.10	2.157	2.394	1.110
0.05	0.1125[a]	2.278	2.412	1.059
0.05	0.15	2.620	2.469	0.942

[a] $p_3 = p_2$ multiplied by the concordance ratio. Note that here the relative risk is approximately one.

There will be no bias if the expressions in (24) and (25) are equal. This can be shown to occur if:

$$p_3(1-p_3)N_2N_3 - p_2(1-p_2)N_1N_4 = (p_2p_3 - p_2^2)N_2N_4 \quad (26)$$

For small p, it can be seen (by ignoring terms in p^2) that an approximate condition for equality is given by:

$$p_3/p_2 = N_1N_4/N_2N_3 = C \quad (27)$$

In other words, misclassification of smokers as non-smokers will cause positive bias unless the misclassification rate in smokers married to non-smokers is higher than the misclassification rate in smokers married to smokers by a factor equal to (about) the concordance ratio. It seem unlikely that negative bias will occur in practice, given the fairly large concordance ratios usually observed (see e.g. Appendix B).

C.3 Situation 3: Misclassification in an n × 2 Table; Misclassification Unrelated to Spouse Smoking Habits

Sections C.1 and C.2 habe bee concerned with the simple smoker/non-smoker classification. Clearly risk of lung cancer is strongly related to a number of aspects of the smoking habits, in particular number smoked per day and number of years smoked, and the estimates produced so far on the effect of misclassification may be in error if subjects misclassified are not representative in terms of smoking habit. Thus, if it is only occasional smokers or long-term ex-smokers who get misclassified as never-smokers, little biassing effect on risk in relation to passive smoking will be expected as those individuals do not have markedly increased risk.

To look at this the simple assumptions shown to yield excellent approximations in the 2 × 2 situation have been used:

(a) misclassfification only in the direction smoker to non-smoker
(b) no true passive smoking effect
(c) misclassification only for subjects not spouses.

Attention is also restricted to the situation where misclassification rates are unrelated to spouse smoking habits.

Consider a k level smoking classification, with true numbers of subjects as follows:

Subject	Spouse	
	Non-smoker	Smoker
Non-smoker	U_0	V_0
Smoker - level 1	U_1	V_1
⋮		
level k	U_k	V_k

If p_1 represents the probability of a smoker at level i being misclassified as a non-smoker observed U_i^*, V_i^* can be written down in terms of the U_i, V_i as follows

$$U_0^* = U_0 + \sum_{i=1}^{k} p_i U_i \tag{28}$$

$$V_0^* = V_0 + \sum_{i=1}^{k} p_i V_i \tag{29}$$

$$U_i^* = (1-p_i) U_i \tag{30}$$

$$V_i^* = (1-p_i) V_i \tag{31}$$

If p_i^* represents the probability that a nonsmoker actually is a smoker at level i, then it can be seen that p_i and p_i^* are related by

$$p_i^* = \frac{p_i(U_i + V_i)}{(U_0^* + V_0^*)} \tag{32}$$

$$\text{or} \quad p_i^* = \frac{p_i(U_i^* + V_i^*)}{(1-p_i)(U_0^* + V_0^*)} \tag{33}$$

$$\text{or} \quad p_i = \frac{p_i^*(U_0^* + V_0^*)}{p_i^*(U_0^* + V_0^*) + (U_i^* + V_i^*)} \tag{34}$$

If the observed relative risks in relation to smoking at level i are S_i^*, the true relative risks, S_i, can be estimated from them by

$$S_i = S_i^* F \tag{35}$$

where the correction factor F is given by

$$F = \frac{1 - \sum_{i=1}^{k} p_i^*}{1 - \sum_{i=1}^{k} S_i^* p_i^*} \tag{36}$$

The observed risk in nonsmokers married to nonsmokers (relative to true nonsmokers) can then be calculated by

$$R_1 = 1 + \frac{U_0^* + V_0^*}{U_0^*} \sum_{i=1}^{k} [(S_i - 1) U_i^* p_i^* / (U_i^* + V_i^*)] \tag{37}$$

while the observed risk in nonsmokers married to smokers can be calculated by

$$R_2 = 1 + \frac{U_0^* + V_0^*}{V_0^*} \sum_{i=1}^{k} [(S_i - 1) V_i^* p_i^* / (U_i^* + V_i^*)] \tag{38}$$

For a given level of smoking the contribution to the excess risk $R_2 - R_1$ (which is closely correlated with R_2/R_1 where R_1 and R_2 are only slightly greater than 1) can be seen to be

$$(S_i - 1)\, p_i^* \frac{(U_0^* + V_0^*)}{(U_i^* + V_i^*)} [V_i^*/V_0^* - U_i^*/U_0^*] \tag{39}$$

This can be broken down into a product of 5 terms:

(a) the true excess risk due to smoking at level i: $(S_i - 1)$
(b) the observed misclassification rate: p_i^*
(c) the observed relative frequency of nonsmokers and smokers at that level for the whole data: $(U_0^* + V_0^*)/(U_i^* + V_i^*)$
(d) the observed relative frequency of smokers at that level and nonsmokers for subjects married to nonsmokers: U_i^*/U_0^*
(e) the excess concordance ratio between smokers at level i and nonsmokers: $C_i^* - 1 = V_i^* U_0^*/U_i^* V_0^* - 1$

To illustrate this by an example:

True data

Subject	Spouse		Risk	p
	Non-smoker	Smoker		
Non-smoker	60	40	1	
Light smoker	10	12	2	0.05
Medium smoker	20	30	5	0.03
Heavy smoker	10	18	20	0.02

Observed distribution of population

Subject	Spouse		Total
	Non-smoker	Smoker	
Non-smoker	61.30	41.86	103.16
Light smoker	9.50	11.40	20.90
Medium smoker	19.40	29.10	48.50
Heavy smoker	9.80	17.64	27.44

Observed distribution of deaths

Subject	Spouse		Total
	Non-smoker	Smoker	
Non-smoker	68	52.9	120.90
Light smoker	19	22.8	41.80
Medium smoker	97	145.5	242.50
Heavy smoker	196	352.8	548.80

This gives observed relative risks as follows:

1, 1.7065, 4.2663 and 17.0653

Among the 103.16 non-smokers, there are 1.1 light smokers, 1.5 medium smokers and 0.56 heavy smokers, which are percentages of 1.066, 1.045 and 0.543 respectively.

To calculate the bias the following steps should then be taken:

(a) Calculate $F = 0.9694/0.8271 = 1.1720$

(b) Correct the relative risks to give 1, 2, 5 and 20.

(c) Calculate $R_1 = 1 + \frac{103.16}{61.30}[1 \times 0.00485 + 4 \times 0.00582 + 19 \times 0.00194] = 1.109$

(d) Calculate $R_2 = 1 + \frac{103.16}{41.86}[1 \times 0.00582 + 4 \times 0.00872 + 19 \times 0.00349] = 1.264$

(e) Calculate the apparent passive smoking effect = 1.140.

$s_i - 1$	p_i^*	$\frac{U_0^* + V_0^*}{U_i^* + V_i^*}$	$\frac{U_i^*}{U_0^*}$	$C_i^* - 1$	Product
1	0.0107	4.936	0.155	0.757	0.006
4	0.0105	2.127	0.316	1.197	0.034
19	0.0054	3.759	0.160	1.636	0.101
					0.140

The 3rd and 4th columns have relatively least effects, and for rough estimation concordance ratio, excess risk and misclassification rate can be multiplied to estimate relative importance.

Appendix D
Trends in the Percentages of UK Men and Women who Have Never Smoked

If an individual claims to be a current or ex-smoker at one time point, a later claim to be a never smoker is indicative that one (or both) of the statements is in error. If statements made on smoking habits are valid, the proportion of never smokers among a defined cohort of individuals should therefore decrease with age.

Tables D1 and D2, based on annual data on the percentage of United Kingdom men and women who have never smoked broken down by 5-year age groups (taken from Lee (1977) with supplements), provides evidence of an increase in the proportion of *never* smokers. In these tables, data for men and women in a given 5-year group in one year are compared with data for the same birth cohort 5 years later. For example, the first line of Table D1 compares percentages for men and women born around 1953, who were 20–24 in 1975 and 25–29 in 1980.

While the results at the different time points are based on different samples of men and women, the interviewing technique did not change, and the rise in the proportion of never smokers, by about 2%, cannot be explained by sampling error and is fairly consistent for the sexes and the two comparisons

Table D1. Trends in percentages of men and women who have never smoked (1975–80 comparison)

Age in 1975	Percentage reported never smokers			
	Men		Women	
	1975	1980	1975	1980
20–24	29.2	34.2	40.8	43.2
25–29	26.9	25.2	35.6	42.6
30–34	23.3	22.8	39.3	39.8
35–39	22.7	23.1	42.4	41.5
40–44	18.2	22.4	37.7	43.8
45–49	16.1	15.3	35.4	32.1
50–54	8.0	15.6	38.4	36.6
55–59	13.1	13.5	33.9	40.0
60–64	11.1	15.9	42.9	44.7
Sample size	5482	5211	5544	5362
Never smokers	1060	1123	2132	2174
%	19.3	21.6	38.5	40.5
χ^2	7.93		4.89	
p	<0.01		<0.05	

Table D2. Trends in percentages of men and women who have never smoked (1976–81 comparison)

Age in 1975	Percentage reported never smokers			
	Men		Women	
	1975	1980	1975	1980
20–24	35.8	33.0	40.1	41.8
25–29	29.4	35.8	41.7	42.6
30–34	23.0	24.1	40.9	43.8
35–39	21.5	25.5	40.6	39.6
40–44	20.9	26.7	43.1	41.1
45–49	17.3	19.5	36.9	40.5
50–54	10.6	10.3	32.9	35.7
55–59	14.1	18.0	33.9	40.9
60–64	11.6	17.5	45.9	49.0
Sample size	5610	5104	5677	5302
Never smokers	1188	1229	2247	2215
%	21.2	24.1	39.6	41.8
χ^2	12.72		4.38	
p	<0.001		<0.05	

(1975–80 and 1976–81). Differential survival of never and ever smokers cannot be an explanation as mortality is effectively negligible in the younger age groups and the increase is as evident in younger as in older age groups. Nor are changes in the population due to emigration or immigration likely to have any material effect.

The most plausible explanation seems to be that an increasing proportion of ever smokers are reporting that they have never smoked, perhaps because of the increasing discouragement of smoking in the media.