# How many people does smoking actually kill?

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## Introduction. The problem.

President Richard M. Nixon signed the National Cancer Act in 1971, and initiated the "war on cancer". The National Cancer Institute felt so strongly about our ability to find ways to destroy cancer cells and increase the body's resistance to the disease that it set as its goal, in 1984, to cut cancer deaths in half by the year 2000 (1). After 15 years, and the expenditure of 25 billion dollars, the U.S. cancer death rates went up by 7 per cent between 1975 and 1990 (2). (This number has been adjusted to compensate for the changing size and composition of the population with respect to age, so the increase cannot be blamed on people'dying less often from other diseases.) In five-year survival there has been an improvement of only four percent. Interested parties are of course only too ready to offer excuses, but it may be time to take a hard look at some of the causal theories underlying our thinking in this field, in particular the alleged role of smoking in causing cancer, and the neglect of psychosocial factors in this connection.

Epidemiologists have published estimates of the number of people killed annually by cigarette smoking that suggest a more deadly role for smoking than for diet/activity patterns, alcohol, microbiological agents, toxic agents, fire arms, sexual behaviour, motor vehicles, or illicit use of drugs. As the latest review in J.A.M.A. suggests, "tobacco accounts for approximately

400,000 deaths each year among Americans".(3) The authors admit that their estimate might be as low as 257,000 or as high as 468,000 for tobacco-attributable deaths in 1990. A sizeable discrepancy. Using a specially developed software package(4), the Center for Disease Control and Prevention (CDC) estimated that 418,000 deaths were caused by tobacco in 1990, including approximately 30% of all cancer deaths and 21% of cardiovascular disease deaths(5,6). Similarly, in the United Kingdom, the Health Education Council, jointly with the British Medical Association, published "The Big Kill"(7), according to which smoking annually kills 77,774 people in England and Wales. These are startling figures, even given the wide fiduciary limits mentioned above. But are they reliable?

Epidemiology has often been criticized severely for its lack of scientific discipline and disregard for customary safeguards; it is inevitably observational rather than experimental, and hence subject to the usual problems inherent in scientific argument relying on purely circumstantial evidence, rather than direct empirical testimony(8,9). Hence any such pronouncements regarding numbers killed by smoking are subject to many valid criticisms that may very well impugn the methodology used, the statistical techniques involved, and the results claimed(10). These estimates certainly contradict results of large-scale studies such as the Australian Bureau of Statistics National Health Survey (11), which showed that smokers were the healthiest

group, followed by non-smokers, and a long way behind ex-smokers.

Methodological and statistical criticisms will be dealt with in later sections. Here I want to comment on the ambiguities and equivocations involved in such a statement as "Smoking Kills X people". This would normally be interpreted in an analogous manner to a statement like: "Shooting kills x people." But there are many important differences between these two statements. (1) The effects of shooting are both a necessary and a sufficient cause of this type of death; smoking is neither a necessary nor a sufficient cause of death as far as smoking-related diseases are concerned. (2) There are no problems in recognizing a <u>direct causal relation</u> in connection with the shooting, while smoking is only <u>statistically</u> related to mortality from smoking-related diseases. (3) Effects of shooting are immediate and obvious; effects of smoking are delayed for an unspecified period often suggested to be 30 years or more, and far from obvious; they require epidemiological evidence which inevitably is <u>circumstantial</u> only. (4) Shooting is a <u>single</u> cause of death; smoking is one of a large number of risk factors, interacting in a complex fashion and difficult or impossible to disentangle without the use of untestable assumptions. Altogether the term . "Smoking kills" has emotional overtones that make it suitable for Public Relations work, but not for scientific discourse, unless all the problems associated with its use are solved rather than disregarded.

The history of how estimates of this kind developed must make for caution in accepting them as meaningful. One of the earliest such estimates appeared in a book by Senator M.B. Neuberger(12) who quoted Dr. D. Horn as saying it would be his "best guess" to blame smoking for "300,000 to 500,000...deaths per year" (p.15). The Surgeon General's report itself(13) rejected the theory of "excess deaths": "The total number of excess deaths cannot be accurately estimated". The Assistant Surgeon General, who was vice chairman of the Advisory Committee, gave the reason at a news conference when the report was relayed: "The Committee considered the possibility of trying to make such calculations but it involves making so many assumptions that the Committee felt that it should not attempt this..."(14). In spite of this wise decision, many (and very different) figures were subsequently quoted, nearly always without explanation of how they were derived.

The first attempt to justify these estimates I can trace was made by Dr. M. Lewin at a Congress Hearing(15). He said it was done "taking into account the age distribution of the male population, the number of smokers and non-smokers, and the number of various causes in 1962. Over 200,000 deaths, about one in every four, are due to excess mortality among cigarette smokers. Of the estimated 658,000 deaths among male cigarette smokers, over 33 per cent were excess deaths." Lewin also gave a tabulation of his estimate, but did not explain the basis for the numbers on which his

calculations depended. As far as it is possible to follow his reasoning, the phrase "excess deaths due to smoking", is defined by age-controlled differences in mortality between smokers and non-smokers for diseases labelled smoking-related. Other equally mysterious formulae appeared, impossible to understand or justify, and the Surgeon General at the time, Dr. Luther Terry, disregarding the sage advice of his Committee, extended these meaningless figure to women and declared that: "A reasonable estimate of excess deaths among women, added to the total of 240,000 for men, would bring the overall total to 300,000. I consider this total to be a reasonable estimate."(16)

The Doll-Peto Model.

The first intelligible, and very influential method of calculating "deaths due to smoking" was developed and published by Doll and Peto.(17) They first calculated age-specific death rates from lung cancer (using this as an example) observed among a large group of non-smokers in 1959-72, and argue that this "would have applied to the whole country in 1978 if no-one had ever smoked" (p.1222). They went on to work out how many U.S. lung cancer deaths would thereby have been predicted (about 12,000). They go on to argue that, since there were actually some 95,000 lung cancer deaths in the United States in 1978, we can "ascribe the excess (~80,000-85,000 lung cancer deaths) to tobacco." They admit that "this method does suffer from some sources of

uncertainty, but none seriously affect the final estimate." (p.1222). Extending this method to three other types of cancer they argue that "the results suggest that there would have been only about 40,000. deaths attributable to these four types of cancer in 1978 if no American had ever smoked, instead of the 155,000 or so that actually occurred. The difference (~115,000) represents, in our view, a fairly reliable estimate of the number of U.S. deaths from these four types of cancer that were caused by smoking in 1978."(p.1222). And on a later page they assert that "we can estimate reasonably accurately the present percentage of cancers due to smoking" (p.1224).

This very simplistic formulation is not based on any firmly-grounded model of the smoking-cancer relation but essentially assumes (without proof) a causal relation, although only a statistical relation is demonstrated, and also assumes that the excess mortality of smokers is due to smoking in proportion to the following argument.

If p is the proportion of smokers and R is the relative risk associated with smoking, then for every (1-p) deaths in non-smokers there are Rp in smokers, (R-1)p of which are due to smoking, i.e. the attributable proportion is $p(R-1)/(1+p(R-1))$, a calculation which is correct providing smoking is not associated with exposure to another risk factor (which it is, as we shall see), and providing that smoking and this other risk factor act multiplicatively on risks. The nature of the underlying model can be derived from the methodology suggested.

Essentially, it assumes that (1) all risk factors are independent of each other, and (2) risk factors interact multiplicatively to produce cancer.

### Independence of risk factors

Let us take just a few well-established risk factors for cancer: Smoking, genetic predisposition, drinking, poor diet, exposure to air pollution, stress. Imagine a person who is genetically predisposed to cancer, is stressed, smokes, drinks, has a poor diet, and is exposed to air pollution. If such a person were to die of lung cancer, his death would, on the Doll & Peto premise, be attributed to smoking to an extent following from the formula given above, i.e. a proportion (R-1)/R of the death of a smoker would be ascribed to exposure from a risk factor (smoking) with a relative risk of R for the disease in question. But if we started with stress, rather than smoking, his death would be attributed to stress, equally to the extent of R. When there are several risk factors, how can we make any one responsible for mortality?

Doll and Peto recognize that proceeding in this fashion, deaths due to smoking and deaths due to other factors, when added, may well exceed total deaths observed. Doll and Peto would justify their procedure as follows. Consider a single case where we have two risk factors, smoking and stress, and death only occurs in persons who are smokers and under stress. Under these circumstances, all the deaths would be due to smoking -

in the sense that they would not have occurred had the people involved not smoked. But equally, all the deaths would be due to stress - in the sense that they would not have occurred had the people involved not been under-stress. Thus cause X accounts for 100% of all deaths, and cause Y accounts for 100% of all deaths, and we have accounted for 200% of all deaths! This is Alice in Wonderland arithmetic, and is certainly not what most people would understand when told that all deaths are due to smoking!

An acceptable approach might be possible if these factors were independent, so that variances were additive; this would enable us to sort out the relative contribution of all the factors involved (as far as they were known) provided we had reliable measures of them all. But of course Doll & Peto did not have available reliable measures of any of these variables, and in addition it is well known that they are correlated. People who smoke also tend to drink, to have a poor diet, to live in highly polluted town areas, and to be stressed; all of these variables are much more highly represented in people of low socio-economic status, who are also known to have much higher mortality than people of high socio-economic status(18,19,20). Doll and Peto do not present us with any method that would enable us to give a proper allocation of total variance to these correlated factors.

The interdependence of risk factors is shown very clearly in an important study by Thornton, Lee & Fry

(21). They investigated the extent to which current, ex- and passive smoking are associated with other risk factors, and the potential for confounding arising from these associations, using a representative sample of 9003 British adults. Of the 33 risk factors studied, 27. showed a significantly higher prevalence in heavy smokers than in never-smokers. For many risk factors, prevalence increased with amonnt smoked, decreased with time of smoking cessation, and was increased in passive smokers. The conclusion of this study was very clear: "The results of this study...have demonstrated unequivocally that smokers tend to have unhealthier lifestyles than non-smokers in very many respects." (p.1161).

The result of such overlapping of other risk factors with smoking will inevitably be confounding, i.e. the attribution of mortality risk to variable X which are really due to variable Y which is correlated with X. Thornton, Lee & Fry(21) develop and apply the argument when there are more than one factor acting to produce confounding. They also note that for a large bias to occur one needs a potential confounding variable to have a strong influence on risk of the disease, to be relatively uncommon in those unexposed to the factor of interest and to be much more common in those exposed to the factor of interest. Psychosocial factors have been shown to have many of these properties (10,22).

Given reliable measurements, not only of all the risk factors involved, but also of the correlations between them, we might arrive at some acceptable

statistical estimate. A multiple regression analysis might be performed, but that would only tell us the relative weights useful in predicting cancer, but not anything about the causal relations between the risk factors, and between the risk factors and cancer. I shall discuss this problem in detail later. Here let me just point out that the imaginary model underlying the Doll and Peto calculations incorporates assumptions that are demonstrably incorrect, and invalidate any conclusions based upon them. Oddly enough, Doll & Peto acknowledge the interconnection and synergistic interactions between smoking and drinking on the production of cancers, but do not seem to realize that it fatally affects their statistics. They also mention socio-economic status, but do not discuss how this might affect their estimates of cancer mortality due to smoking (17). No statistical procedure that does not take into account confounding can give acceptable results worthy of scientific consideration.

## Recent models.

The simple act of merely looking at the differences in mortality between smokers and non-smokers, and attributing an attributable portion to smoking, is unacceptable, for reasons given. Other authorities have tried to estimate the "attributable portion" in some fashion. As the Royal College of Physicians admits, "It is not possible to give a precise estimate of the proportion of these excessive deaths among smokers which

are caused by smoking. There can be little doubt that at least half the estimated 31,000 excess deaths among male smokers, aged 35-64, in the United Kingdom, were due to smoking."(23) As Burch(8) comments: "This passage shows a recognition by the Royal College that not all of the association between smoking and mortality is necessarily causal. However, no procedure is described whereby an objective estimate of the magnitude of the causal contribution might be derived and the choice "at least half" would seem to be arbitrary" (p.956). Why one-half rather than one-quarter? The Royal College makes additional arbitrary attribution estimates(23). "It should not be unreasonable to attribute to cigarette-smoking 90% of the deaths from lung cancer, 75% from chronic bronchitis and 25% of those from coronary heart disease." For women, the report acknowledges the greater difficulty of precise attribution but continues undaunted to say, "It can reasonably be assumed that at least 40% of the deaths from lung cancer, 60% of those from bronchitis, and 20% of those from coronary heart disease in women aged 35-64 may well be due to cigarette-smoking." The sophisticated reader will be aware that expressions like "would not be unreasonable," "may well be due to," and "it can reasonably be assumed that," have no scientific standing or meaning; they refer simply to guesses that can easily be doubled or halved. Thus, The Big Kill(7) raises the percentage of deaths from cigarette smoking for lung cancer in women from 40% (Royal Society) to 80%, without batting an eyelid. Such

estimates are meaningless, even if the figures for the statistical association between smoking and disease could be accepted.

The subjectivity of attempts to allocate a proportion of all deaths to smoking is apparent in some figures cited in the JAMA report(3). For cancer deaths, tobacco's contribution ranges from 11% to 30%; for cardiovascular deaths from 17% to 31%. Thus errors of 100% to 300% are built into the assumptions underlying the process of estimation. Even if we assume that a certain proportion of excess mortality is actually due to smoking (however we derive our estimate), such an assumption is scientifically unacceptable unless we specify a testable model of this assumption. What precisely does it mean to say that 40% (Royal Society) or 80% (The Big Kill) of deaths from lung cancer in women are due to cigarette smoking? Several models might serve to mediate such interaction(10).

The first model asserts that out of 10 deaths from lung cancer in women, 4 (or 8) are directly and solely due to smoking. This simple-minded model can hardly can be intended to be taken seriously, but the arguments advanced by the U.S. Surgeon General and the Royal College of Physicians often seem to assume its correctness. The notion that risk factors other than smoking play absolutely no part in these deaths conflicts with all we know about smoking and its many connections with other risk factors (drinking, stress, life-style, etc.) and is quite untenable.

A second model asserts that there are many risk factors for lung cancer (or CHD, or whatever disease is linked with smoking) and that, in every sufferer from lung cancer, 40% (or 80%) of these risk factors are constituted by cigarette smoking. This scenario also is unrealistic; it is simply not reasonable to assume that the proportion of all risk factors contributing to disease is identical for all sufferers, and there is solid evidence to contradict it(10). This model, too, often seems to be assumed by writers on the subject.

A third model asserts that risk factors are unevenly spread among sufferers, so that the percentages mentioned apply only on average but not in any particular case. Thus, for a smoker who has been in touch with asbestos, the percentage of risk that is due to smoking might be only 10%, while someone else not associated with any other risk factor, the percentage might be 100%. This model seems more realistic, but of course, it suffers from the fact that there is no known method of calculating the importance of risk factors for individuals. The model also makes the unlikely assumption that risk factors act in a simple additive or multiplicative fashion; as demonstrated in the following discussion, the evidence strongly opposes such a view.

Finally, the fourth model seems to be more in accord with the facts than any of the preceding models(10). It asserts that smoking linked diseases are caused by multiple risk factors combining synergistically, that is, the interaction is multiplicative rather than additive.

The evidence for the model will be discussed in a later section. It suggests strongly that smoking by itself has little effect on cancer or CHD; in samples free from other risk factors, smoking hardly correlates at all with these diseases. It is only in combination with other risk factors (in particular psychosocial ones) that smoking shows statistical associations with these diseases(10). Whether these statistical associations can be interpreted in a causal manner is still an unsolved question (24, 25).

### Major problems in mortality estimation

Clearly, smoking is not the only risk factor for smoking-related diseases, even for lung cancer. Thornton & Lee (26) have reviewed evidence in 143 risk factors reported to be correlated with lung cancer, concluding that for almost 50% of these there is reasonable evidence of such a relationship. If these risk-factors could be estimated for each person, if they were independent, and if they acted multiplicatively, we might be able to attribute a reasonable proportion of the excess mortality of smokers to smoking. But no such figures exist, and the evidence concerning lack of independence is overwhelming. It does seem, however, that interaction between risk factors is clearly synergistic or multiplicative. Thus smoking by itself, or stress by itself, show little surplus mortality, but jointly they exert a much greater influence than that due to the addition of their single effects. As an example,

consider a study of 2,374 healthy probands followed up for a period of 10 years(27)(Table 1). These are the mortality percentages for lung cancer mortality. It is clear that the interaction is synergistic; the addition shows stress effects (2.54%) plus smoking effects (0.45%) = 2.99%, while the true observed effect of combining stress and smoking is 15.56% - 0.35% = 15.21%.

**Table 1 here.**

I have reviewed the evidence about synergistic interaction elsewhere; it is clear that physical factors interact synergistically, and that physical and psychological factors interact synergistically also (28). But this makes estimates of proportions of mortality due to smoking meaningless unless we have accurate figures on all the risk factors involved, as well as sound knowledge of their interaction in society. No such knowledge exists.

It is usually assumed that observed correlation figures are based on environmental causes. Thus the correlation between depression and smoking might be due to the fact that depressives smoke in order to relieve tension. An alternative hypothesis was originally presented by Sir Ronald Fisher(29), namely, that genetic factors might link smoking with other risk factors and cancer. I have tried to make this rather vague hypothesis more testable by suggesting a genetic link between smoking and personality(25), and recently a study by Kendler and his colleagues(30) found, in a study of female twins, that, (controlling for personal smoking

history of MD/manic-depressive illness), family history of MD predicted smoking. "The best-fitting bivariate twin model suggested that the relationship between lifetime smoking and lifetime MD resulted solely (my italics) from genes that predispose to both conditions. These results suggest that the association between smoking and MD in women is not a causal one but arises largely from familial factors, which are probably genetic, that predispose to both smoking and MD" (p.36).

Depression, of course, has been linked to cancer, and the connection receives a causal explanation in terms of the association between depression and cortisol level, which in turn has an immuno-suppressive effect(10,31). It will be clear that any simplistic estimate of cancer mortality due to smoking that leaves out connections of this kind cannot be assumed to reveal scientifically relevant information.

**Heterogeneity of effects.**

Links between risk factors may be caused environmentally, or genetically, or jointly, but we usually assume homogeneity of effects. Yet there is good evidence to doubt the existence of such homogeneity. A recent prospective study of drinking behaviour found that more important for the prediction of future morbidity and mortality than amount of drinking was the reason for drinking (32). Drinking to drown one's sorrows had a very deleterious effect on health; drinking for pleasure and celebration did not affect health, except in excess.

There are different reasons for smoking, too, as shown in the Eysenck and the Tomkins models(33). Psychological factors interact with physical ones in a complex manner, and their neglect cannot be reconciled with a properly scientific approach.

What is suggested here is that just as in drinking, the motivation and mental status of the drinkers may have powerful effects on the health consequences of the alcohol consumption involved, so in smoking also the motivation and mental status of the smoker may be important. In the Eysenck model the two major causal factors are the decision to increase cortical arousal, and the need to reduce tension. Smoking to achieve the latter aim may have harmful consequences, smoking to achieve the former aim may not. There is no direct evidence on this point, but the personality types ivolved make such a possibility quite likely; after all, smoking and drinking tend to be quite highly correlated (20,30).

The association between personality and smoking that has given rise to the Eysenck model(24) has also resulted in the isolation of typical and atypical smokers, who may be considered likely to react differentially to smoking as far as health is concerned. If, as I have shown, smokers tend to be extraverted and non-smokers introverted, then introverted smokers and extraverted non-smokers are atypical(34). Such atypical people have been found to be very significantly more neurotic than extraverted smokers and introverted non-smokers. It is psychologically impermissible to look simply at smoking-

nonsmoking as meaningful risk factors; type of smoking, reason for smoking, personality-smoking concordance may all be as important as, or even more important than the simple act of smoking.

Even the effects of such stimulant or depressive substances as caffeine and diazepam can affect mortality in opposite ways depending on types of personality(35). In a prospective study, it was predicted and found that in cancer-prone probands (as determined by interviewer-controlled psychological testing), coffee consumption was related to low incidence of cancer and high incidence of coronary heart disease, while diazepam showed the opposite trend. In coronary heart disease probands, coffee drinking was also linked with low incidence of cancer and high incidence of coronary heart disease, with diazepam again showing the opposite trend. In a personality type not prone to either disease, neither coffee consumption nor drinking was linked with death from cancer or coronary heart disease(26). The predictions were based on a general theory linking central nervous system effects and disease.

**Effect size for smoking and stress**

It may be objected that the effect of smoking is so much stronger than effects from other risk factors, that these may safely be disregarded. For cancer and coronary heart disease, the risk ratios are roughly 2.3 and 1.8. We may compare this with the results of C. Thomas' pioneering study of the influence of personality on

cancer(36,37). She and her co-workers evaluated 1,300 medical students and followed them up over a 40-year period to determine cause of death. For cancer, she found that persons described as "loners", emotionally detached people lacking closeness to their parents, were 16 times as likely to develop cancer as were people who gave vent to their emotions. Others have found similar results, suggesting that psychosocial factors are several times more potent than smoking as risk factors for cancer and CHD than smoking(10). There is now a large body of data supporting the view that personality/stress have strong causal and predictive links with these two disease groups(10,38-44). The position of benign neglect, adopted by Doll & Peto(17), is unacceptable. They write "Two categories of environmental factors that we have ignored, are that of psychological stress and that of some form of breakdown of immunological control. It is possible, of course, that psychological factors could have some effect, e.g. by modulating hormonal secretions, but we know of no good evidence that they do, nor that they affect the incidence of cancer in any other way, except insofar as they lead people to smoke, drink, over-react, or enjoy some other harmful habit.' (p.1255-56). The evidence against this view was already strong in 1984, when these words were written, indicating the arbitrary nature of the exclusion. Since then, the evidence has accumulated steadily to indicate that these neglected factors are significantly more powerful than

those considered by Doll & Peto, and interact synergistically with them. (10,44)

A strong case can be made for lung cancer, where the risk can hardly be explained in toto through confounding, even when psychosocial variables exert a very strong influence on mortality. I have no wish to argue against the possibility of a causal connection here, but there are two patent reasons for caution. (1) The data relating to synergistic action between smoking and stress suggest that smoking by itself does not have the strong effect suggested; it is only when combined with some other factor (stress; genetic) that these large effects are observed (25). (2) Data on racial groups, other than the Caucasian group usually cited, give a very different picture of the smoker/non-smoker ratios, namely a very much smaller figure. Liu (45) summarized eight studies of smoking and lung cancer in China, and found that quantitatively the relative risks, in relation to ever having smoked is markedly less than usually reported in Western countries, being only 2.17 for the sexes combined. Many other studies document this large difference between mongoloid and caucasoid groups (e.g. 46-49), although whether it is due to racial causes, or to differential customs (wood burning, use of wok stoves), is not really known.

**Unreliability of basic data.**

The criticisms of the received view that I have made so far would apply even if the data on which the received

view is based were reliable and valid. However, the evidence against such an optimistic view is very strong (10). If the original data, usually death certificates containing details of diagnosis, are faulty, and in particular if they are biased, erroneous conclusions may be drawn even though methodology and statistical analysis appear impeccable. As it happens, there has been a good deal of criticism of the use of statistics derived from cause of death diagnoses and death certificates; they have been generally considered to be inaccurate and unreliable. Britton(50), for instance, found that the reported frequency of disagreements between clinical and autopsy diagnoses ranges from 6% to 65%! If we regard autopsies as completely reliable criteria (an assumption which, as will be discussed, is not entirely true), then clearly, the amount of inaccuracy in diagnoses is unacceptable for serious statistical work.

Some quotations may give a rough idea of the consensus in this area. Bauer and Robbins(51) state that "our study indicates that accurate clinical diagnoses of cancer are as much a problem today as they were a half-century ago" (p.1474). Abramson, Sacks, and Cobana(52) state that "the death certificate data had marked limitations as an indication of the presence of myocardial infarction, cerebrovascular disease, pulmonary embolisms or infarctions...They gave a fairly accurate indication of the presence of malignant neoplasms but not of the specific sites or categories of neoplasms" (p.430). And Britton(50) concluded that "autopsies

earlier did and still do reveal a considerable number of errors in clinical diagnoses...There is no convincing sign that the rate of errors had dimished over the years" (p.208). So much for the accuracy of the data on which the "orthodox" view is based.

As an example of the most carefully planned and conducted work in this field, let us consider the study by Cameron and McGoogan (53). They reported a prospective study of 1,152 hospital autopsies, comparing these with death certification in each case. They were merely concerned with the major disease leading to death, as indicated by the physician completing the death certificate. They found that the main clinical diagnosis was confirmed in 703 out of 1,152 cases, or in 61%, leaving an error of 39%. This figure is not far removed from that observed by Britton(50) in Sweden, where he found, in a careful, clinically controlled assessment, that main clinical diagnoses were confirmed in 57% of cases, leaving an error of 43%. Heasman and Lipworth (55), and Waldron and Vickerstaff(54) reported confirmed diagnoses in only 45% and 48%, respectively, leaving error rates of 55% and 52.5%. It is small surprise that Cameron and McGoogan(53) concluded that, "In our experience, statistics from death certificates are so inaccurate that they are not suitable for use in research or planning" (p.281). If this be true, then, clearly, all the statistical work using death certificates and supporting the received view is based on extremely uncertain foundations.

One other item of interest emerged from the Cameron and McGoogan study(53): a marked increase in the proportion of diagnostic discrepancies with increasing age of the subjects. For subjects less than 45 years of age, diagnoses were correct in 78%, but thereafter, they fell off in a step-like manner with each succeeding decade until, for subjects over 75 years, fewer than half were confirmed. This has particular relevance to the incidence of cancer and heart disease, because these, of course, occur mainly in older men and women.

It is of interest to look specifically at data for neoplasms and for CHD diagnoses, because errors in these are of special relevance to the topic of this article. Cancer of the bronchus/lung was correctly diagnosed in 88 cases and wrongly diagnosed in 61 cases, thus, the error rate is about the same as for all diseases. Bauer and Robbins(51) looked at autopsies on 2,734 cancer patients and found that 26% had clinically undiagnosed cancer; in a further 14%, the condition was incompletely diagosed, that is, cancer was suspected, but its primary site was not known or was wrongly indentified. Cameron and McGoogan(53) conclude their comments on neoplasms by stating, "Carcinoma of the bronchus was the most common neoplasm in our series and provided the largest group of misdiagnoses" (p.294).

Turning now to cardiorespiratory conditions, for acute myocardial infarct, agreement occurs in 198 cases, and disagreement in 109 cases - again, an unacceptable level of error of diagnoses. Cerebrovascular disease

scored an agreement in 129 cases and disagreement in 118 cases, with an error rate of almost 50%. "The most common problem of differential diagnosis appeared to be in distinguishing it from cardiovascular disease" Cameron and McGoogan stated (p.293). Hartveit(56), Heasman and Lipworth(55), and Kagan, Katsuki, Sternley, and Venecek (57) also found a large amount of overdiagnosis of cerebrovascular disease, and Waldron & Vickerstaff (55) give a good survey of the whole matter.

## Detection Bias

When diagnoses are as unreliable as they have been found to be in the case of lung cancer and CHD, one must be particularly concerned about the phenomenon of "detection bias," that is, the tendency of the physician to diagnose "smoking related diseases" in smokers rather than in non-smokers. Feinstein and Wells(58) have published data to show that such detection bias is a reality and might easily lead to false conclusions in the absence of careful necropsy examinations of the causes of death. Detection bias undoubtedly contributes part of the high mortality ratios for lung cancer often reported and should be carefully excluded in any study purporting to have scientific validity.

Feinstein and Wells(58) looked at data concerning 654 patients who were diagnosed after necropsy as having died of lung cancer. In this series, they studied the relationship between the rate of non-diagnoses during life and the amount of antecedent cigarette smoking. In

patients whose history of cigarette smoking was unknown, this non-diagnosis rate was 37%. The rate of non-diagnosis then portrays a distinctive downward gradient, falling from 38% undetected among non-cigarette smokers, to 20% among the light smokers, 14% in the moderate, and 10% and 11%, respectively, in the heavy and extreme smokers. "The data therefore suggested that the more patients smoked, the more likely they were to have the lung cancer detected during life," stated Feinstein and Wells (p.185).

Feinstein and Wells(58) also investigated how this pre-mortem detection gradient was related to the intensity of diagnostic examinations received during life by patients in their entire series, which included 677 cases that were diagnosed during life but received no neocropsy. The authors used for this purpose the Papanicolaou cytologic examination (or pap smear) of the sputum. Because this test had not been obtained by all of their patients, its solicitation might have been affected by diverse factors, including the patient's smoking history. They therefore examined the pap smear research rate, and the results are in agreement with this hypothesis. The test was requested more frequently in smokers than in nonsmokers. Statistical tests showed that the trend was very highly significant. Detection bias was consequently found to be distinctly related to the amount of cigarette smoking.

Space does not permit discussion of the other analyses by Feinstein and Wells, which tend to support

the following general conclusions: "Cigarette smoking may contribute more to the diagnosis of lung cancer than it does to producing the disease itself...It seems important to recall that in epidemiology surveys of causes of disease, the investigators get data about the occurrence of diagnoses not the occurrence of diseases, and that the rates of diagnosis may be affected by bias in the way that doctors order and deploy the available diagnostic technology." (p.184).(See also 59).

Taken together with the general unreliability of diagnoses of lung cancer, these findings make it doubly improbable that the observed diagnostic data that furnishd the foundations for epidemiological studies can be taken seriously by scientific investigators. More research is urgently required on the actual unreliability of diagnoses, as well as on "detection bias"; if reliable data on these two points were available, then statistical corrections might be made to the published data on the relationship between smoking and lung cancer based on death certificates. Without such data, conclusions clearly are based on unfirm foundations.

**Errors in smoker identification**

Even statements concerning a person's smoking habits, on which most of the evidence depends, are far from reliable. Lee (60) who has carried out a survey of the published literature on smoking habit misclassification, has pointed out that even a small proportion of smokers claiming to be non-smokers can

cause a marked upward bias in estimates of the relative risk associated with marriage to a smoker. Because (as has been confirmed) smokers tend preferentially to marry smokers, subjects reporting being non-smokers married to smokers are more likely actually to be smokers than non-smokers married to non-smokers. Lee (who also noted that the reverse misclassification, of non-smokers as smokers, has only a minor biasing effect) concluded that bias due to misclassification of smokers as non-smokers could explain most, if not all, of the alleged effect of passive smoking on lung cancer (an allegation which is based in large part on evidence of a risk increase in relation to marriage to a smoker). Thus, not only does the uncertain state of death certificates diagnosis cause errors in estimating risk, so too does inaccurate ascertainment of smoking status.

One study looked at the accuracy of such statements, better ways of getting accurate statements, and directionality of errors(10). In the first study, probands estimated the number of cigarettes smoked, and close relatives (usually the spouse) made an analogous estimate. Finally, probands were instructed to keep a 7-day journal, noting down each cigarette smoked and the occasion. It was found, for 136 participants, that the self-estimate was 12 cigarettes per day. Relatives estimated 18; the journal disclosed 19. The proband's own estimate was a 50% underestimate.

In this study, a personality inventory was given after the estimate was made. The hypothesis was advanced

that if the inventory was administered first, it would make the proband more likely to give truthful answers, due to a certain relationship of trust having been formed. In the matched group of 136 smokers, the three estimates agreed very well; own estimate 17, relative's estimate 16, journal record 18. This may be one way of improving accuracy of smoking estimates.

This degree of inaccuracy is particularly troublesome if it is directional, that is, if cancer-prone probands were to overestimate and not-prone probands were to underestimate the number of cigarettes smoked. In a group of 128 cancer-prone probands, ascertained on the basis of a personality inventory, the self-estimation averaged 17, relative's estimation averaged 16, and the journal averaged 15. The other personality types investigated showed underestimations of between 2 and 18 cigarettes per day, instead of the overestimation of 2 cigarettes of the cancer-prone probands(10). This tendency, if general, would greatly exaggerate the statistical correlation between cancer and smoking. Clearly, careful experimenters would look at sources of error of this kind and try to eliminate them; this has not happened in the studies examined.

I have devoted a considerable amount of space to a discussion of the reliability of the data and possible biases in the data, because all conclusions in science depend absolutely on the quality of the data. When the data are as poor as those used by epidemiologists to establish a relationship between smoking and cancer, and

smoking and CHD, then a detailed demonstration of the unreliability and invalidity of the data is imperative. It is noteworthy that those who maintain the "orthodox" view seldom argue the case; they accept faulty data without any query and without answering the critics who draw attention to these fundamental faults.

**The causal argument .**

The arguments presented so far relate to methodological and statistical errors and over-simplification underlying the postulate that hundreds of thousands of people are killed by cigarette smoking each year. Even more fundamental is an assumption which underlies the whole argument, namely that the connection with both cancer and CHD is causal, not merely statistical. This argument has been clearly stated on the Surgeon General's report in 1982: "The causal significance of an association is a matter of judgment which goes beyond any statement of statistical probability. To judge or evaluate the causal significance of the association between an attribute or agent and the disease, or the effect upon health, a number of criteria must be utilized, no one of which is an all-sufficient basis for judgment. These criteria include (a) the consistency of the association; (b) the strength of the association; (c) the specificity of the association; (d) the temporal relationship of the association, and (e) the coherence of the association."(61).

Note the subjectivity implicit in this statement. If the causal significance of the association is a matter of judgment, it departs from typical scientific statements of lawful association that rely on direct proof. Judgment based on the points mentioned above has frequently been biased by the oft-noted neglect of contrary evidence by the authors involved in writing the Surgeon-General's or the Royal College of Physicians' reports; these leave out criticisms that have been levelled at the studies summarized, the methodology adopted or the statistical treatment given. Alternative hypotheses are not considered(59,60), and non-sequitur conclusions reached on the basis of insufficient evidence. In addition, there is no clearly stated theory or model that is being tested. Such models as exist, e.g. Doll's model, have been severely criticized and shown not to be compatible with the data(62,63). Nor are the many anomalies that occur given appropriate weight, or discussed in sufficient detail to estimate their relevance to the (non-existent) model.(64-68).

As an example, consider the dose-response relationship that must be assumed to be basic to any such model. The causal hypothesis, in its pure form, would predict the same response from the same "dose" in different populations. The observed relationship between national mortality from lung cancer and national cigarette consumption is not very strong. An example of discordance is the age-standardized mortality from lung cancer in Finnish men in 1960 to 1961, which was about

double that in U.S. white men, whereas cigarette consumption in 1950 in Finland was about half that in the United States(24).

As Sterling(67) has pointed out, "the highest known lung cancer rates occur in England, Austria, Belgium, and Finland. The United States, Canada, Australia, and New Zealand report a much smaller rate of lung cancer deaths. The lowest lung cancer rates are in such countries as Norway and Italy. Yet, per capita, smoking rates are, by far, the greatest in Canada, the United States, and New Zealand, and considerably lower in England, and lowest in Finland and Austria." (p. 947). There are many other anomalies of this kind, but as Burch(63) has pointed out: "The pure causal hypothesis might, by this test alone, appear to be untenable." (p.826). Other criticisms against the "causal" hypothesis serve to make it less acceptable than one might gather from official pronouncements(10).

Mortality from tobacco in developed countries.

In a much quoted study, Peto and his colleagues(69,70) have extended their efforts to estimate the mortality rate due to smoking to a variety of developed countries. They estimated that in the countries included in their list, about 21 million in the decade 1990-1999 would suffer death from smoking, with more than half these deaths due to smoking occurring at age 35-69. This extrapolation is even more far-fetched than those criticized in the preceding sections, but it

is also subject to additional criticisms. The first objection relates to the meaning of "deaths due to smoking", already considered in a previous section and found to be difficult to interpret. As we have seen, "deaths due to smoking" are calculated by comparing the number of deaths that actually occur with the number of deaths that would have occurred in that year had no-one in that population ever smoked. If we accept that if the whole population had never smoked, then, given the implied assumption that smoking increases death rates, the number of survivors at the start of the year would have been much larger. But no account is taken in the Peto calculation of the extra deaths resulting from the extra population thus produced. Given Peto's assumption, there will be fewer deaths in the next year, but the population at risk will then be greater so that in subsequent years, the advantage will reduce and eventually reverse, producing ultimately more deaths in later years than there would have been under existing smoking rules. A much better, and more correct estimate might have been arrived at by using additional years of survival as a measure, although even that would be subject to many criticisms.

Peto's procedure attempts to counter some earlier criticisms of the methods discussed in previous sections, and to obviate the problem of missing data in many of the countries in question. He compares the age/sex specific mortality rate for a country with that observed for life long non-smokers in the last 4 years of the huge American

Cancer Society Cancer Prevention Study 2 (CPS2), the difference being attributed wholly to smoking. The next steps are rather more complex. First, one views the population in question as a mixture of CPS2 current smokers and lifelong never-smokers and uses data on lung cancer mortality to estimate the mixture. Second, one uses this proportion in conjunction with the relative risk for the disease in question, to calculate the proportional increase in the disease in question due to smoking. Third, in an attempt to try to take into account the possibility that some of the excess death rate associated with smoking is due to factors other than smoking, half of the excess rate is (arbitrarily) discounted. Finally, the attributable proportion is multiplied by the observed number of deaths from the disease for the country, age, sex and year in question to give the estimated number of deaths due to smoking. This procedure is then extended to other cancers, COPD, other respiratory disease, vascular disease, and other medical diseases.

There arise a number of criticisms. (1) The lung cancer rates of non-smokers in the various countries studied cannot reasonably be based on CPS2 statistics, even though these rates are not dissimilar to the old CPS1 or the British doctors' study. These dealt with above average social class people, far less occupationally exposed than the British or American average; and clearly there is simply no comparison with

Eastern European working class subjects in exposure to occupational hazards.

Even in the USA, CPS1 (ACS) has been severely criticized on methodological and selection grounds, and its data are quite unrepresentative. As Sterling(67) has pointed out, when we compare the distribution of causes of death for most deaths in the ACS population with the distribution of deaths for the same causes that would be expected from a segment of the US population that was constituted similarly, by age, sex, and race to the ACS population, "we find that the ACS males die from lung cancer proportionately twice as frequently as do US males, and the ACS females die proportionately three times as frequently from the disease as do US females. Twice as many females also die from breast cancer."(p.943). As Sterling says, "it is difficult to explain such startlingly peculiar results"(p.943), but whatever the explanation, clearly such very unrepresentative data cannot be used to form a basis for extrapolation to other countries.

We may mention one further cause of doubt. (4) Peto estimated 1995 death rates by proportional extrapolation of 1975 and 1985 rates. This is a very poor method of extrapolation, especially in the presence of "cohort effects", i.e. an effect on rates related to year of birth. For lung cancer in men in the U.K, risk at a given age is about a maximum for men born around the turn of the century, and falls continuously for men born earlier or later. Extrapolation methods that do not take

this characteristic into account may cause substantial error.

Adding all these unsubstantiated assumptions to the many methodological and statistdical criticisms already discussed, we must conclude that Peto's figures may bear very little relation to reality. Extrapolation is always dangerous; when based on assumptions either doubful or almost certainly mistaken, it is unlikely to lead to scientifically meaningful conclusions. I have already mentioned the problem of diagnosis, and the many problems associated with the unreliability associated with it in the USA and the UK; these problems are likely to be multiplied many times when we look at countries like Romania, Bulgaria or Yugoslavia. Can it be seriously maintained that conditions in these countries over the past decades were sufficiently similar to those in the USA or in the UK to make statistical comparisons, and extrapolations meaningful?

Intervention effects.

The most impressive, and possibly the only direct proof of the causal effect of smoking, would be by way of intervention. Such intervention by way of prophylactic psychological therapy has been successfully used to demonstrate the causal role of psychosocial factors in cancer and coronary heart disease (10,71). In the case of smoking, we can determine the role of causality by studying the effects of quitting. The causal theory implies that those who quit smoking should have a lower

mortality than those who continue smoking. Even this prediction, however, is subject to many qualifications. There is an assumption that when we compare quitters and continuing smokers, the state of health of the quitters is no better than that of the continuing smokers; if it were better, the ultimate lower mortality of quitters might be due to their better health status at the time of quitting. But it has been shown that in actual fact quitters have better health at the point of quitting than carry-on smokers(72). Further, as we clearly cannot assign smokers on a random basis to either the quitting or the carry-on category, motivation and other factors may determine their final fate rather than quitting or not quitting. There is evidence to show that stress may lead to smoking, and that stress is independently linked with cancer and CHD(8, 41). If people quit smoking because they are no longer stressed, it may be the removal of stress that is responsible for their greater longevity. Thus, even if the results of empirical studies happened to show that quitting was related to lower mortality, the outcome could not be attributed unequivocally to quitting.

In actual fact it is not true, as often asserted, that quitting necessarily lowers the incidence of cancer and CHD. The most frequently cited study, namely that of British doctors, many of whom gave up smoking, and whose mortality was lower than that of a group probably not containing many quitters, seemed to show a positive effect of quitting(73,74), but there are so many

methodological and statistical faults in this study that it has been subject to serious criticisms which render it nugatory (74-77). It certainly cannot claim to provide conclusive evidence. Other direct studies with proper experimental and control groups have failed to show any effects of quitting on health(78,79). Whole multiple factor intervention studies have had very disappointing results, with intervention groups not showing the expected superiority over control groups(80.81). One notable study looked at the health status of a large random sample of Australian men and women, with the result that smokers emerge as the healthiest group, followed by never-smokers. Quitters were far and away the least healthy(11). These results did not take into account the fact that most smokers were of low socio-economic status, and poor education; this group has always been found to have much the poorest health record. When allowance is made for this factor, the slight superiority of smokers over non-smokers becomes quite strong. Overall, it is certainly premature to suggest that quitting has been <u>proved</u> to improve health, thus knocking away the apparently strongest support for the causal hypothesis.

In multiple risk factor intervention studies(79), the overall failure of the experiment and control groups to show differential mortality must arouse one's suspicion of the alleged health-giving properties of any <u>specific</u> change; gains on one front may be compensated (indeed <u>must</u> be compensated) by losses on another. This

is clearly illustrated in the Finnish Multifactorial Primary Prevention study (81), where efforts were made (successfully) to reduce risk factors in an at-risk group for cardiovascular disease, including dietary instruction, medical intervention, advice to quit smoking, etc. The overall results were disappointing: "despite the highly significant reduction in the risk factor level, the five-year intervention did not reduce coronary mortality or morbidity...In fact, the number of total coronary events tended to be higher in the intervention group than in the control group (19 vs. 9 cases, P = .057)" (p.2099.) Thus while stroke incidence was significantly reduced, coronary incidence was higher in the intervention group than in the control group. In fact, twice as many probands died in the intervention group as in the control group. It is not correct to look at isolated corners of a large-scale study for positive results if overall figures fail to show significant effects of intervention. Oliver(82) has summarized the evidence from several intervention trials aiming to reduce cholesterol level, and found that "the same adverse trend appears constantly in almost all the trials, regardless of the means used to lower cholesterol." (p.814). Serious cholesterol reduction may lessen the risk of heart disease and increase that of cancer, suicide rates, etc.

Unless such countervailing effects are taken into account, large-scale primary prevention studies should be looked at critically, and with regard to overall effects.

Highlighting single effects, usually involving very small numbers, without regard to overall mortality rates is methodologically faulty. As McCormick and Skrabanek(83) have pointed out, "coronary heart disease is not preventable by population intervention" (p.839); I am not certain that this does not apply equally to cancer.

In stark contrast to the relative sparsity of evidence that quitting smoking will reduce mortality from cancer and coronary heart disease is the finding that psychological treatment of cancer-prone and coronary heart disease-prone healthy people is very effective in preventing mortality incidence of both these types of disease (10). This is not the place to review studies supporting this statement, but I have reviewed representative studies elsewhere, as well as studies showing that psychological therapy is equally successful in prolonging life of incurable cancer sufferers to a very meaningful extent (10). In assessing the strength of the causal argument for smoking and psychosocial factors respectively, these facts shuld be kept firmly in mind.

**Passive smoking.**

What applies to estimates of the evil effects of smoking applies <u>a fortiori</u> to the alleged effects of <u>passive smoking</u> (ETS - environmental tobacco smoke). The most recent estimate of the number of deaths due to smoking is 3,000 annually in the U.S. among non-smokers (84). It is also stated to be <u>causally</u> associated with an increased risk of lower respiratory tract infections

such as bronchitis and pneumonia, 150,000 to 300,000 cases annually in infants and young children up to 18 months of age being attributable to ETS. It is also said to be responsible for new cases of asthma in children, and for additive episodes of increased severity of symptoms in children with asthma, 200,000 to 1,000,000 asthmatic children having their condition worsened by exposure to ETS. Note the wide gap here between minimal and maximal estimates, amounting to a 500% difference; such wide discrepancies indicate the uncertain nature of the methods of estimation employed. It is also obvious that if it is difficult to nail down the effects of smoking, the inevitably much more modest effects of ETS, if any, will be much more difficult to establish.

In looking at the literature, it is not reassuring to note that two frequently cited studies that started the avalanche of research devoted to this topic, and appeared to establish a solid case in its favour, drew conclusions based on elementary statistical errors. The work of Hirayama(85) and of Trichopolous and his colleages (86,87) has been severely criticized on statistical grounds(88-91), and clearly is at best careless, and certainly fails to establish anything. More recent studies, too, make many errors that invalidate the conclusions reached; I shall be particularly concerned with the recent EPA report (United States Environmental Protection Agency(93).) Before giving a brief discussion of these errors, it may be useful to mention the National Health Survey of the

Australian Bureau of Statistics, which looked at the health status of Australian adults and children(11). The survey showed "only slight differences between children living in households with or without smokers in the likelihood of children experiencing recent and/or long-term conditions. In households with smokers there was a slightly higher prevalence of disorders of refraction and accommodation, influenza, emphysema and asthma among children." (p.10). This slight difference is calculated for overall data: it does not take into account the fact that smoking households are usually lower socio-economic status households, and disease is much more frequent among lower socio-economic groups. Any correction for SES will more than eliminate the alleged influence of smoking.

What are the main criticisms of the EPA report? The prime one refers to lack of statistical significance. Thirty epidemiological studies were reported, but while most found positive associations, only six were significant, and nine went in the wrong direction - living with a smoker was associated with reduced risk of lung cancer. The risk ratio was only 1.19 overall, and this tiny difference from 1.00 might, even if statistically significant, be due to differences in socio-economic status, stress, or to failure to tell the truth about smoking, as Lee(94) has shown. To make the data more persuasive, the authors changed the accepted standard of statistical significance from .05 to .10; this is clearly not acceptable. Neither is the failure

to use something like the Bonferroni correction to evaluate individual tests of significance when more than one test is involved. The evidence proclaimed as "conclusive" is nothing of the kind. It suggests at most a tiny effect of ETS, and fails completely to establish a causal basis for this hypothetical effect. Previous studies suggested a similar conclusion, making any decision difficult (95). Certainly it is scientifically meaningless to assert that 3,000 deaths from lung cancer among non-smokers in the U.S. are due to ETS.; the true figure might be none, or anything in between.

A detailed statistical examination of the EPA report by Lee (96), concludes that "no lung cancer deaths have actually been demonstrated to result from ETS exposure". A similar conclusion has been arrived at by Feinstein (97) who concludes that "neither science nor public policy is well served if the integrity of science is sacrificed to meet the goals of public policy." A thorough examination of the whole problem of ETS has been published by Lee(95), who concludes that "there is no convincing epidemiological evidence that exposure to ETS results in an increased risk of death from cancer, heart disease or any other disease in non-smokers." (P.XIX).

## Conclusions.

To be able to give a scientifically meaningful estimate of the number of people killed by smoking in a given population, it is necessary to have a proper <u>model</u> of the relationships involved, and a proper <u>definition</u> of

what is meant by "killing", seeing that the usual conditions involved in postulating a causal relationship do not obtain. No such model exists, and no such definition is available. It is possible, however, to deduce some necessary features such a model must have in order to justify the kind of calculations used to establish the published estimates of smoking-produced mortality.

To begin with, the data (frequently death certificates) on which most studies are based have to be reliable and lacking in detection bias. Neither of these necessary preconditions is fulfilled. Next, there has to be good, universally acceptable evidence that the relation between smoking and disease is a causal one, not merely statistical. Such evidence does not exist at present. Furthermore, the major risk factors must be known, as well as their intercorrelations. While many such factors are known, the correlations for the most part are not. Nor are the relative contributions of genetic and environmental factors, and although synergistic interaction has been demonstrated in many cases, for most interactions no firm data are available. In the absence of knowledge on all these points, no proper estimation procedure is available.

Calculations routinely leave out of account psychosocial factors like personality and stress, although several studies have indicated that these factors are significantly more closely linked with cancer and coronary heart disease than smoking, and interact

synergistically with smoking(10) No estimates of smoking-linked mortality are acceptable that do not take into account these facts. Causal links between psychosocial factors and smoking are both genetic and environmental, but our knowledge of such causal links is rudimentary. Absence of such knowledge makes any estimates mere guesswork.

Estimates are generally based on impermissible extrapolations from a fundamentally flawed basis. Extrapolations are only permissible if there exists a quantitative model for the phenomena in question, firmly based on experimental evidence. In the absence of such a model, objective modes of estimation are not available, and subjective methods take their place. Above all, the hypothesis of a causal link between smoking and disease has to find much stronger support than it has found at present before it is possible to postulate any deaths as being due to smoking.

What would constitute a proper model from which to calculate mortality due to smoking? A minimum requirement on the statistical side would be a structural equation model, including all the major risk factors, and taking due account of synergistic interaction effects. Such a model combines the techniques of path analysis and multivariate regression to construct a causal model of the relationships among variables. Structural equation modelling can help to introduce a hypothesis-testing approach to correlational data. The almost universal reliance in epidemiology on univariate analysis cannot

begin to satisfy the most elementary demands of a proper statistical analysis, and estimates of mortality based on such analyses are scientifically inadmissible. Multivariate analyses of the structural equation modeling type are mandatory, although of course no statistical procedure can compensate for the many methodological faults in data collection usually found in epidemiological studies of smoking effect.

This is not to deny that smoking is a risk factor for cancer and CHD. Unfortunately research has been largely devoted to establishing this fact over and over, to the neglect of a search for causal links, and to the virtual exclusion of work on psychosocial factors, in spite of their demonstrated importance from both the scientific and the social points of view; this is difficult to understand. Quite generally there is an almost absolute refusal to take into account alternative hypotheses to the "smoking causes death" one in explaining existing data. The recent increases of lung cancer mortality in women is usually explained in terms of increased smoking by women. The equally appealing hypothesis that these women smoke, and also develop lung cancer because they are working and thus more stressed than women in earlier times would be equally applicable, but has never been considered. Science demands the empirical investigation of all hypotheses for a given phenomenon which have theoretical and experimental backing, as the stress hypothesis undoubtedly has. Yet such possibilities are cold-shouldered, instead of

forming, as they should, the main point of attack of detailed epidemiological studies. The complete neglect of psychological factors is the major weakness of existing studies, and makes their findings unacceptable.

Popular accounts often give the impression that the war on cancer, officially declared by President Richard Nixon, on December 23rd, 1971, is being won, and that the expenditure of 25 billion dollars has actually paid off. Reality, as pointed out earlier, is very different (1,2,98). The death rate from cancer actually increased by 7 per cent between 1975 and 1990. Perhaps the exclusive concern with medical causes should give way to a consideration of psychosocial factors as well as, and in addition to, those hitherto considered in isolation. Similarly, therapy might with advantage add psychological and behavioural measures to the purely physical and chemical ones used at present. Yet practically no research funds are available for work along these lines.

Given the importance of prevention of cancer and CHD, the stress on quitting smoking seems misplaced, in view of the weak and doubtful evidence that quitting results in better health. On the other hand, psychological treatment of psychosocial factors has given strong evidence of effectiveness both in prevention of cancer and coronary heart disease, as well as in prolonging life after diagnosis (10,99) yet orthodox opinion has singularly failed to support work in this field. Unjustified belief in the over-riding importance of smoking as the universal killer has practically closed

the doors on any alternative theories and practices. This is bad science, and difficult to condone. Our main concern should be disease prevention, not the maintenance of unproven shibboleths.

The inclusion of psychological factors into medical practice may present problems, but nature cares little for the arbitrary dividing lines between disciplines. The ancient Cartesian separation of body and mind has not stood up to scientific investigation; we are dealing with a mind-body entity, just as physicists deal with a space-time continuum. As Sir William Osler once said: "It is many times much more important to know what person has the disease, than what disease the person has."(99). As Miller and Swartz(100) have pointed out, psychology and epidemiology have formed an uncomfortable alliance, and until much greater use is made by epidemiologists of the large psychological contributions, both factual and methodological, it is unlikely that epidemiology will achieve its aim of scientific respectability. If I am right in suggesting that psychosocial factors are at least as influential risk factors as smoking and other physical factors, then it is no longer permissible to neglect personality, stress, and similar psychological concepts. The answer to the question: "How many people does smoking actually kill?" is at the moment no more susceptible of a scientific answer than the question: "Who killed Cock Robin?" Indeed, as Evans(101) has asked, is health promotion science or ideology? Sir Ronald Fisher many years ago said: "The question seems

to be a serious one; when is serious investigation going to begin?" He might ask the same question today.

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# C A P T I O N S

Table 1. Synergistic effects on lung cancer mortality of smoking and stress (28)

Table 1.

| | No Smoking. | Smoking. | Smoking effects: |
|---|---|---|---|
| No Stress. | 0.35% | 0.80% | 0.45% |
| Stress. | 2.89% | 15.56% | |

Stress Effects: 2.54%