American Journal of Epidemiology
Vol. 133, No. 5

Were We Really Wrong?

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Editor's note: *For a discussion of this paper, see pages 428, 434, and 435.*

In recent correspondence, Vandenbroucke (1, 2) has stated that Fisher, Berkson, and I "were wrong" in our view that the evidence implying a causal role for smoking in the genesis of cancer and coronary heart disease was insufficient to derive such a conclusion. Greenland (3) in his reply agrees with us that a causal role for smoking had not been proved beyond reasonable doubt. He feels that likelihood (or even suspicion) is sufficient when intervention is weighed in its consequences against nonintervention. He follows Pascal's famous statistical argument for believing in God; i.e., the consequences of not believing in God, should he exist, are so horrendous that even a very small probability that he might exist would swing the balance. Thus, he seems to argue that we were right in substance but wrong in disregarding the social consequences of our doubt; as he says, it is his impression that all three of us "would have opposed action against smoking on the grounds that the causal association had not been 'proven.'"

Terms like "proof" and "cause" always give rise to argument, because they do not refer to absolutes but are capable of degrees. Proof of causation in the absolute sense is impossible, as Hume recognized hundreds of years ago. We did not demand such absolute proof, but merely a reasonable level of support for the views of Doll, Peto, and their colleagues. What we have found are serious *methodological* weaknesses in the design of the studies quoted in support of these theories, *statistical* errors, and unsubstantiated *extrapolations* from dubious data to unconfirmed conclusions. There are too many anomalies in this account, and too little theory, to make the resulting mess acceptable as "proof" of causality. All we asked for was proof in the sense usually accepted in science, but we were fobbed off with half-truths and disregard of anomalies and contrary facts.

Vandenbroucke is, of course, in error in saying that we were "wrong" in saying what we did, namely, that *at the time of writing* the evidence was clearly insufficient to establish smoking as a (major) cause of cancer and coronary heart disease. He argues that we *now* have much better evidence to support such a view, but we never engaged in prophesy as to what future evidence might disclose; our statements were correct at the time; no scientist can do more than evaluate the existing evidence. Vandenbroucke himself lists cogent criticisms of many of the original studies.

But were we wrong in the sense that the hypotheses criticized by us turned out to be right after all? I take leave to doubt this. Cornfield et al. (4) wrote in what Vandenbroucke calls "the now classic paper on smoking and lung cancer" that, in order to be able to act as a confounder, a third variable should be an even stronger determinant of the disease at issue than the actual determinant being studied, i.e., smoking. Both our critics seem to imagine that no such determinant exists, but they are factually

Received for publication November 28, 1990, and in final form December 11, 1990.

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mistaken. Personality has been found very significantly more predictive in normal, healthy people of cancer and coronary heart disease than smoking. Studies by Eysenck (5–8) and Grossarth-Maticek et al. (9–11) are based on lengthy follow-ups of large samples, replicated twice, and demonstrate this point quite convincingly. Hence, the very criterion suggested by Vandenbroucke demonstrates that we were not wrong, even in this extended sense.

Greenland asks whether we have "a complete epidemiologic perspective on (our) own arguments and the arguments of those who were right." Scientifically speaking, I submit that we are now approaching this point; I tried to give such a perspective in my latest book (12). This discussion of all the most important contributions to the debate suggests that 1) smoking is indeed a (statistical) risk factor; 2) other risk factors are more closely associated with cancer and coronary heart disease, such as genetic predisposition and above all personality and stress; 3) risk factors act synergistically; and 4) intervention can be shown to be most effective in the prevention of cancer and coronary heart disease when addressed to the personality and stress side, rather than to the smoking side.

Thus, our perspective takes into account Greenland's argument. Even when viewed from the point of view of the consequences of social action, society would benefit much more healthwise by trying to modify psychosocial factors than habits such as smoking and drinking. Eysenck (13), Eysenck and Grossarth-Maticek (14, 15), Grossarth-Maticek (16), Grossarth-Maticek et al. (17), and Grossarth-Maticek and Eysenck (18) have furnished ample evidence for this proposition. In other words, if we are concerned with scientific truths and correct estimation of the evidence for causal attributions to cigarette smoking, then we were right. If we look at the social consequences of blaming smoking and not looking for additional or alternative risk factors of greater importance and modifiability, then I suggest we were right, too. The debate, and the research, must take a broader view than the eternal repetition of cigarette condemnation. We have come a long way from the days when this single-mindedness could be considered a reasonable and rational course; both scientifically and in terms of social responsibility we must use multivariate analyses, not rest content with univariate analysis. Epidemiology is a complex discipline; we must honor this complexity in our theories and our research designs.

There are additional reasons for doubting the correctness of Greenland's argument. In his balance sheet, he contrasts the possibility of saving lives by taking action against smoking with the economic cost to the tobacco industry and the loss of tax revenue. However, there are many more factors on the negative side than are considered by Greenland. In the first place, smoking confers substantial benefits on those who smoke: it raises cortical arousal and reduces boredom; it reduces tension from stress; and it increases alertness, to name but three benefits (19). To many people, these are vital, and being deprived of them is a serious loss. In the second place, the constantly repeated warnings against smoking cause stress in many people and may lead to illness and death (20); this causal chain should be taken seriously. In the third place, asking governments to intervene in the private affairs of individuals runs counter to the democratic desire for freedom and may lead to very undesirable consequences; we may recall the evils of prohibition!

Above all, scientific values have been downgraded by the blatantly one-sided advocacy of the antismoking lobby, often descending to simple propaganda. Official publications, such as the those of the Surgeon General or the Royal College of Physicians, have never given a fair picture of the controversy but have printed only facts and figures, interpretations, and comments favorable to the antismoking side, while omitting mention of disagreeable, contrary, and confounding facts and arguments. Seltzer (21) has compared the actual results of the Framingham study with what the Surgeon

General says about these results, showing up the many discrepancies; I have given other examples (12). This is a serious business. Science should be objective above all and eschew the evils of *suppressio veri* and *suggestio falsi*. Science is not in the business of propaganda; once it descends to these levels, it will lose public recognition and esteem. We may cry "wolf!" once too often and be disregarded when we have a real warning to give. This argument, too, should be weighed in the balance against public intervention; the premature crystallization of spurious orthodoxies is not in the public interest. As Claude Bernard said, "In ignorance, abstain!"

The companion commentary by Stolley entitled, "When Genius Errs: R. A. Fisher and the Lung Cancer Controversy," and Vandenbroucke's reply, "How Much Retropsychology?" raise other matters. There is no doubt that Fisher was eccentric, cantankerous, opinionated, and often vehemently subjective; so was J. B. S. Haldane. I was fortunate enough to have known, as a student, Fisher and, later on more intimately, Haldane. I also took lessons in statistics from Egan Pearson, who showed none of these infuriating characteristics, which are perhaps the privilege of genius (22). I agree with Vandenbroucke, however, that our argument must be *ad rem, non hominem*; whatever Fisher's motivation, we must deal with his arguments. When I wrote my autobiography (23), to which Vandenbroucke refers, I had to come to terms with the sad fact that, although I was a psychologist, I could not honestly say what motivated me to do the things I did, such as oppose the almost unanimous belief that cigarette smoking caused cancer and coronary heart disease, as well as many other diseases, or that giving up smoking would be a miraculous prescription for longevity. Motivation is still one of the least developed parts of psychology, and Stolley's primitive attempts in that direction cannot command agreement. Having known Fisher, I think that if he felt that, having been engaged as a consultant, he would be expected to abandon his integrity, he would have reacted very strongly against the tobacco firms, indeed, and would have leaned over backwards to preserve intellectual integrity and independence of thought.

I do not wish to invert the argument, but I am sure many readers have encountered, as I have, strong and unreasoned opposition to research and arguments critical of the orthodox position. This goes so far as to reject papers of high quality in favor of printing papers of lower quality, and subject to damaging criticism, as long as these support the status quo; to keep back from professional advancement scholars who do not toe the line; to refuse grants for studies that would investigate alternative and possibly more important risk factors than smoking; and even to malign and spread false stories about scientists whose results did not find favor with orthodoxy but could not be faulted on grounds of methodology or statistical treatment. I have given examples of these in my autobiography (23). Such treatment may provide motivation to some to support orthodoxy but, even were such motivation present, we would still have to deal with the arguments and the facts presented, not to discuss the orthodox view as being based on prejudice.

What, then, are Fisher's arguments? As stated by Stolley, these are as follows:

1) While smoking may cause lung cancer, it may be that lung cancer, in its early stages, may cause smoking. In some way, some suggest, our demonstration that personality is correlated with lung cancer (24, 25) may really be the demonstration of cancer causing changes in personality. Both are unlikely but may play a part; however, prospective studies in both cases fail to support the criticism.

2) There may be a genetic predisposition to smoke. There undoubtedly is, as Eaves and I have demonstrated (26). What is inherited is not initiation of the habit but its continuance; the possible link (through personality) with genetic factors in the causation of cancer has not been established nor has it been disproved.

3) Secular trends do not support the view

that smoking causes lung cancer. Some do, but many others do not (27, 28). Reports from the Surgeon General and the Royal College of Physicians usually only quote the facts which support their case; it is enlightening to look at the studies which support Fisher.

4) Inhaling is not likely to increase the probability of lung cancer in smokers. In principle, Fisher was right, although he exaggerated the difference in favor of inhaling as a causal factor in lung cancer, and at best the difference has been found to be small.

However, most important, to my mind, in Fisher's contribution has been an argument not listed by Stolley, which I will phrase as follows and which is fundamental to all epidemiology. 5) Risk factors interact in complex ways, and univariate analysis is quite inappropriate to the elucidation of causality (12). This argument in favor of multivariate analysis is undoubtedly true; it may be illustrated by reference to cancer of the cervix. *a*) Nuns do not smoke and have little incidence of the disease; prostitutes do smoke and suffer a high incidence. Women who are neither nuns nor prostitutes show a positive correlation. Does this show a causal relation? *b*) Consider promiscuity. Nuns are not promiscuous; prostitutes are. For other women, there is also a positive correlation between promiscuity and cervical cancer. Is there a causal relation? *c*) Promiscuity is highly correlated with smoking. Either may be causally involved; the other would necessarily be statistically related and might in a univariate analysis be considered a causal element. *d*) Both, or neither, might be causally implicated. Both are correlated with extraversion as a style of life and, through it, with a plethora of possibly causal factors. It is obvious that here are ample opportunity for error and incorrect attribution of causality. Multivariate analysis is an essential, although it, too, may run into difficulties unless all major risk factors are considered simultaneously (12). This is the crucial warning that Fisher had to give, and it is as applicable today as it was in his time. Let us forget about his eccentric presentations and failure to look at all the evidence; orthodoxy has unfortunately followed his example as far as his faults are concerned, rather than in taking seriously his real contribution (29).

CONCLUSIONS

Where does all this leave us? The problem of cancer and coronary heart disease, and their relation to smoking, is a serious one, affecting millions of people. What is needed is not confrontation, as practiced by Fisher and the Surgeon General, one-sided argumentation and disregard of facts inimical to one's cause, and idle projection of imaginary mortality rates into the future but, rather, rational debate, careful analysis of the data, and restrained and cautious statement of conclusions: in fact, science rather than propaganda. Where Fisher erred was not so much in his doubts about orthodoxy but, rather, in his manner of presentation. It is regrettable that this has set a precedent that many others have followed. Perhaps we can all agree that both sides have sinned and resolve that, in the future, we will all abide by the rules of scientific objectivity, avoidance of overstatement, and careful consideration of anomalies. As Huxley said, the great tragedy in science is the slaying of a beautiful hypothesis by an ugly fact; that is the lesson we ought to learn from Fisher.

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