Discussion

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The Present Situation

There now exist reports of a number of large scale studies dealing with the association of smoking and mortality. Starting with the observation that the reported death rate for lung cancer had increased markedly in recent years, Doll and Hill conducted a retrospective study which seemed to indicate a relationship between smoking and Cancer of the Lung. The special difficulties in the interpretation of the results of retrospective studies led Doll and Hill, and also Hammond and Horn, to do separate prospective studies, and again smoking seemed to be implicated.

However, serious questions were raised about the interpretation of these prospective studies also. First was the question of sampling technique. In the Hammond-Horn study the subjects were recruited by volunteers and the population sampled is difficult to define or, at any rate, to study. In the Doll-Hill study the population--all British physicians--was well defined, but the proportion of nonrespondents was about as large as the proportion of nonsmokers and, since nothing was known about the nonrespondents, there appeared to be appreciable possibilities for biased selection here also.

Second was the question of possible biases and inaccuracies in responses to the mailed questionnaire and in the diagnoses of cause of death.

Third, as Berkson has emphasized, the results of both prospective studies seemed to indicate that only a minor portion of the increase in death rate among smokers is attributed to lung cancer. It seems that almost all causes of death have elevated rates, and almost two-thirds of the increase is attributed to coronary artery disease, rather than to lung cancer. Berkson suggests that this phenomenon might be taken as evidence that there is something fishy in the methodology or, at least, that the effect of smoking is a general one and not specifically that of a cancer producer. Others, on the contrary, see no incompatibility between the general and the carcinogenic effect. In any event, however, we do seem to be getting more than we had originally bargained for.

At this point it may be well to expose my own prejudices. I suspect that smoking really is bad for one's health, and that people not already slaves to the habit ought to be advised not to take it up. On the other hand, I think that some of the questions raised about the interpretation of the Doll-Hill and Hammond-Horn studies are nontrivial. I don't consider the question settled beyond a reasonable doubt, and I would like to see more conclusive evidence on the subject, if it can be had.

The Problem

Now it seems to me that we can profitably divide the problem of interpretation into two parts.

First, is the association between smoking and mortality (lung cancer and over-all) found in the study populations simply a sampling artifact due to nonrandom selection?

Second, supposing that the observed association in the sample from the study population is not a sampling artifact, does it indicate causation? It might be, for example, that factory workers are subject to industrial hazards which cause cancer and other illnesses and, at the same time, but for quite independent reasons, they tend to be heavy smokers. A population consisting of factory workers and others might then show an association between smoking and mortality which does not represent causation. Indeed, R. A. Fisher urges us not to overlook the possibility that cancer "causes" smoking, in the sense that people in the early and possibly unrecognized stages of their illness might seek the mild narcotic effect produced by smoking. Finally, so far as lung cancer alone is concerned, by now one may have serious doubts about the independence of a lung cancer diagnosis from smoking history. A lung cancer occurring in a smoker may have an appreciably better chance of being diagnosed than one occurring in a nonsmoker.

Contribution of the V.A. Study

So far as the sampling problem is concerned, the V.A. study population has some outstanding advantages over the populations investigated in the previous prospective studies. The population is capable of precise definition, and many characteristics are ascertainable for it without having to contact each individual. Furthermore, the mechanism for learning about the event of death seems almost foolproof and, although the nonrespondents have unknown smoking histories, their deaths are as well followed up as are those of the respondents. If the advantages conferred by use of this

population are fully exploited, our confidence in the assertion that the association between smoking and mortality is not purely a sampling artifact may be greatly strengthened.

In some other respects, however, although the findings in this study agree well with those of Hammond and Horn, the interpretation of them seems open to much the same kind of question. The smoking histories were obtained by mailed questionnaire and, although the physician signing the death certificate was queried, the possibility that a diagnosis of lung cancer may have been directly influenced by the smoking history still remains. Furthermore, since the group as a whole was of higher socio-economic status and had a much more favorable survival experience than does the white male population generally, one may wonder whether the smokers are not economically worse off than the nonsmokers and have a higher mortality for reasons not related to smoking.

For the V.A. population it seems possible to settle the question of whether smokers do or do not have a higher over-all death rate than nonsmokers. Whether this is true for lung cancer as a specific cause is a separate question, and a different type of study might be helpful in resolving it. There seems to be a tendency at present in favor of large studies which depend on mailed questionnaires and routinely reported deaths. However, the effects of smoking appear to be so large that they should be distinguishable in a much smaller study in which smoking histories could be taken by trained interviewers, and subjects might be closely followed in the hope of getting more definitive diagnoses of cause of death.

Some Further Comments

on Dr. Dorn's Report

The study reported here represents a substantial addition to our knowledge of the association of smoking and mortality and was well worth the considerable effort required to carry it out. For this we are much indebted to Dr. Dorn and his colleagues. There are, however, some points which Dr. Dorn's paper does not cover and which I hope he will take up in his final report.

a) I'm not quite clear on just why he chose to define the study population as he did. I infer that the population consists of all subjects with government insurance, excluding certain categories, who were alive or for whom no claim had been filed by January 1, 1954. Those who died in the mailing period, January to June, were carried as nonrespondents. Would it not be more useful to deal with the population surviving at some date after the mailing had been completed?

b) I see that the number of nonrespondents is not negligible--it is about twice the number of nonsmokers. However, although medical information was obtained for them and, I imagine, their ages were known, they are not carried through the analysis as an additional smoking category. Their average death rate, even in the last year, is higher than that of all smokers. This indicates a bias of some kind--perhaps only that the nonrespondents are somewhat older--but this is a point that I should like to see discussed.

c) I hope that we may expect to see many more detailed tables of death rates in which the reader himself may hunt for interesting leads, and that we will find a greatly expanded discussion of the possible or probable magnitude of the inaccuracy and bias which may be present.

I realize that there is no end to the tabulations and discussion which a curious reader might demand, but I do hope that Dr. Dorn will go further than he has in meeting this demand.

In closing let me again congratulate Dr. Dorn for having conceived and carried out this extremely valuable study.