DISCUSSION
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I would first like to congratulate Dr. Dorn on an excellent study well presented. My discussion will be confined to his statistical findings rather than to an interpretation in terms of possible cause and effect relationships.

The two major variables in the study were: 1) status of subjects in successive periods of time (i.e., alive or dead), and 2) past and current smoking habits as ascertained at the start of the study. There was little chance of recording a living man as dead since deaths were verified by death certificate. Some under-reporting of deaths may have occurred due to failure of beneficiaries to make a claim. This would result in an artificially low apparent death rate but there is no reason to suppose that it would bias the findings in respect to smoking. Men who dropped their life insurance policies after the start of the study may be somewhat different from those who retained them, and it is not stated whether all such persons were traced. However, it seems unlikely that this could have had much influence on the findings.

It is more difficult to estimate the amount of error in reporting of smoking habits. The most serious error would be confusion between smokers and non-smokers. However, the subjects certainly knew the answer to this simple question and the only problem is how many of them deliberately or inadvertently gave a false answer. Conceivably, a few smokers claimed to be non-smokers because they were afraid that it might affect their insurance status. Unless confined to the healthiest subjects, an error in this direction would tend to reduce the apparent relationship between smoking habits and death rates. The possibility of errors in the other direction seems less likely considering the detailed questions asked of smokers. Incidental to our prospective study,[1] we questioned 45,000 subjects about their smoking habits in 1952 and again in 1954. Of those who in 1952 said that they had never smoked, less than 1% said that they were smoking cigarettes regularly when questioned in 1955. This suggests that it is rare for a non-smoker to record himself as a smoker.

Finkner[2] and his associates have studied the accuracy of reporting daily amount of cigarette smoking, making use of lighters with counters attached and cans in which individuals were asked to deposit their cigarette butts. An analysis of the basic data they present for 76 regular cigarette smokers among workers in a research laboratory showed the following: 80% were classified in the same amount category by lighter counts as by questionnaire answers and all the remainder were in adjacent categories when classified independently by the two methods. A similar study of 52 regular cigarette smokers among office workers showed essentially the same thing.

Todd and Laws[3] made a study for the Tobacco Manufacturers' Standing Committee of Great Britain on the accuracy of information on current smoking habits obtained by questionnaires. They came to the following conclusion:

"......since in most tables in this paper informants are classified into broad groups consisting of non-smokers of cigarettes and of smokers of 0-4, 5-14, 15-24, and 25 or more cigarettes a day, the percentage of smokers, particularly in view of the proportion smoking 10 or 20 cigarettes a day, likely to be classified wrongly even with a 15% error is negligible."

Considering this evidence, it seems unlikely that errors in either of the two major variables could have introduced much error in the apparent association between current smoking habits and total death rates reported by Dr. Dorn. Estimates of past smoking habits are probably less reliable than are estimates of current smoking habits.

The population chosen for study was well defined, namely the 291,800 veterans who held United States Government Life Insurance at the end of 1953. Almost all of them were traced but 31.8% of them failed to answer the questionnaire on smoking habits in 1954. About half of the non-responders of 1954 who were still living in 1957 answered a smoking questionnaire at that time.

The responders of 1954 had a death rate far below that of the general white male population of the United States. This was due to two factors: 1) The insured veterans as a whole (responders and non-responders together) had a death rate only about 70% of that of the general white male population, and 2) the responders were self-selected in such a way that their death rate was considerably less than that of the non-responders. Dr. Dorn reasonably postulates that the difference in death rates between responders and non-responders was due to failure of critically ill persons to answer his questionnaire. The rapid drop in the death rate of the non-responders during the subsequent few months gives strong support to this explanation. However, there is no way of knowing for sure whether this selective factor operated differentially on smokers and non-smokers. If such a differential did exist, it would bias the findings at least temporarily. The bias would have been maximum during the first few months of the study and then would have diminished rather rapidly thereafter. I imagine that this was one of the reasons that Dr. Dorn omitted the first six months of experience from the data he presented today. The trend in mortality ratios during the first several years of the study will provide a good indication of the degree and direction of this

bias if indeed any such bias existed. I should add that there is no reason to suspect that a serious bias of this type occurred.

From the standpoint of possible selective bias, Dr. Dorn's analysis of death rates in relation to duration of cigarette smoking and age at which smoking began presents an interesting problem. Candidates for the armed services are screened by medical examinations which eliminate those with impairments. Some of these impairments (e.g., cardio-vascular fitness,[4] chronic severe cough,[5] etc.) may be associated with smoking habits. Subjects who started smoking at an early age were smoking prior to the time of medical screening, while most of those who started smoking later in life were non-smokers at the time of medical screening. This raises a question as to the validity of the comparison of later death rates in these two groups. In all probability, the selective bias would have worn off long before the start of Dr. Dorn's study. However, some evidence on this point would be most interesting.

It is of interest to compare Dr. Dorn's findings with the findings in two other prospective studies on smoking in relation to death rates.

Doll and Hill[6] mailed questionnaires to all physicians registered in Great Britain and 68% of them replied. The subjects have been traced ever since 1951. A direct comparison cannot be made with Dr. Dorn's findings because Doll and Hill used a different method of classifying smoking habits. Nevertheless, the findings in relation to smoking and death rates were essentially the same in all major aspects, taking sampling variation into consideration. That is, they found that death rates increased with amount of smoking. This was true not only for lung cancer but for many other diseases including coronary artery disease, lung diseases other than lung cancer, peptic ulcers, and cancer of several sites.

Hammond and Horn[1] studied death rates in a sample of 187,783 white American males who were in age group 50 to 69 at the time of selection in 1952, and were followed for 44 months. The subjects were friends and relatives of volunteer workers of the American Cancer Society. Obviously ill men were deliberately excluded. We have reason to believe that very few men (probably less than 3%) refused to fill out a questionnaire when asked to do so. Thus, there was very little self-selection on the part of the subjects. The death rate in the last year of the study was about 81% of that of the general white male population of the United States as compared with 70% for the total group of veterans and less than 70% for the responders studied by Dr. Dorn. The very lowest socio-economic groups were somewhat under-represented and the institutionalized segment of the general population was almost entirely excluded.

Table 1 shows mortality ratios by type of smoking history for Dorn's study and for the Hammond and Horn study. I think that it is fair to say that the two sets of figures are in essential agreement. The major difference is that the mortality ratios tend to be a bit lower in Dorn's study than in our study. It would have indeed been surprising if they had agreed any more closely considering that the subjects were selected in different ways, the age distributions were not the same, and the subjects were followed for different lengths of time. The fact that all veterans were originally selected on the basis of medical examinations which screened out those with serious impairments and the factor of self-selection of the subjects may have had some influence on Dr. Dorn's findings. The deliberate exclusion of obviously ill persons probably had some influence on our findings.

Table 2 shows mortality ratios by current amount of cigarette smoking. Again the figures from the two studies are in essential agreement although not identical.

Table 1

MORTALITY RATIOS OF SMOKERS AND NON-SMOKERS
DORN STUDY COMPARED WITH HAMMOND AND HORN STUDY

Smoking History	Current Use					
	Total		Smokes		Does Not Smoke	
	Dorn	H.& H.	Dorn	H.& H.	Dorn	H.& H.
Never Smoked	1.00	1.00	-	-	-	-
Occasional Only	.98	1.09	-	-	-	-
Cigarette Only	1.58	1.68	1.65	1.74	1.39	1.43
Cigarette & Other	1.29	1.43	1.35	1.50	1.21	1.32
Cigar Only	1.07	1.22	.94	1.09	1.44	1.68
Pipe Only	1.10	1.12	1.05	1.09	1.25	1.32

Table 2

MORTALITY RATIOS OF CIGARETTE SMOKERS BY CURRENT AMOUNT SMOKED
DORN STUDY COMPARED WITH HAMMOND AND HORN STUDY

Current Cigarettes Per Day	History of Cigarettes Only		History of Cigarettes and Other	
	Dorn	H.& H.	Dorn	H.& H.
1-9	1.29	1.34	.95	1.27
10-20	1.66	1.70	1.37	1.49
21-39	1.77	1.96	1.72	1.70
40+	1.99	2.23	1.79	1.83

Now let us turn to a consideration of death rates by cause of death as reported by physicians. Table 3 shows mortality ratios for men with a history of regular cigarette smoking by broad categories of underlying causes of death. In other words, each death shown here was classified according to the cause which in the opinion of the physician was the major factor leading to death. The figures from the two studies are in fairly good agreement. There appears to be no association between cigarette smoking and death rates from violence, accidents, and suicide. In each of the other categories, the mortality ratios are appreciably greater than 1.00 in both studies.

Table 4 shows mortality ratios for men with a history of regular cigarette smoking only for a number of specific diseases. While doctors are required to name one disease or injury as the underlying cause of each death, additional diseases are often specified as contributing to death. Dr. Dorn chose to classify each death according to every disease mentioned, thereby putting many deaths into two, three, or more categories. In our original study, we chose to classify each death by underlying cause only. These figures are shown in the last column of this table. For this presentation, I had our cases reclassified according to the procedure used by Dr. Dorn and the figures are shown in the middle column. Except for pneumonia (which frequently occurs in the terminal stages of other diseases) and peptic ulcer (which is a common chronic disease with a low case fatality rate), the two methods of classification yielded about the same mortality ratios.

The finding which is likely to attract the greatest attention is the very high mortality ratio for lung cancer. This has now been found in such a large number of independent studies and has been discussed so often that it is pointless for me to say anything more about it at this time.

In my opinion, much more attention should be given to the findings in relation to other diseases. Mortality ratios, as shown here, only tell a part of the story. A table showing differences in observed and expected number of deaths would give a very different impression of the findings. The association between cigarette smoking and lung cancer accounts for only a small part of the excess deaths among cigarette smokers as compared with non-smokers. In our study, 52% of the excess deaths associated with cigarette smoking were

Table 3

MORTALITY RATIOS OF MEN WITH A HISTORY OF REGULAR CIGARETTE SMOKING
DORN STUDY COMPARED WITH HAMMOND AND HORN STUDY

Underlying Cause of Death	Dorn	Hammond and Horn
Cancer of Lung	8.32	10.73
Other Cancer	1.30	1.51
Respiratory	2.24	2.85
Cardiovascular	1.40	1.57
Accidents, Violence, Suicide	.91	.94
Other	1.48	1.29

Table 4

MORTALITY RATIOS OF MEN WITH A HISTORY OF REGULAR CIGARETTE SMOKING ONLY
DORN STUDY COMPARED WITH HAMMOND AND HORN STUDY

Disease	Underlying & Contributory		Underlying Only
	Dorn	Hammond & Horn	Hammond & Horn
Cancer of Lung	9.85	12.75	12.45
Cancer of Mouth, etc.	2.18	5.00	4.76
Cancer of Prostate	2.17	1.85	1.73
Cancer of Bladder	1.93	2.33	2.37
Cancer of Stomach	1.86	2.19	2.19
Cancer of Rectum, Colon	1.09	0.74	0.70
Coronary	1.63	1.84	1.83
Rheumatic Heart	0.84	1.13	0.98
Cerebral Vascular	1.33	1.38	1.36
Bronchitis, Emphysema	3.27	3.27	3.25
Pneumonia	1.61	2.76	3.77
Peptic Ulcer	2.83	3.94	4.64
Cirrhosis of Liver	2.95	1.97	2.21
Diabetes	1.18	0.84	0.84

accounted for by cases in which coronary artery disease was specified as the underlying cause of death by the certifying physicians. The corresponding figure for Dr. Dorn's study is 45%.

To me, the most striking finding in all three of the prospective studies is that death rates attributed to a number of diverse diseases were found to be higher among cigarette smokers than among non-smokers. The question is whether this can be attributed to errors of some sort which occurred in roughly the same way in all three studies. Faulty diagnosis of cause of death appears to be the most likely source of serious error.

If we accept the evidence that total death rates are higher among smokers than among non-smokers, then it follows that death rates from at least one specific disease must be higher among smokers than among non-smokers. Considering the number of cases involved, lung cancer cannot possibly account for all of the difference, so one or more other diseases must be involved. If, because of errors in diagnosis, Dr. Dorn's figures give an over-estimate of the mortality ratio for certain diseases, it follows that they give an under-estimate for some other diseases.

The diagnosis of cancer is seldom wrong since it is microscopically proved in 80% or more of the cases so reported. An unknown number of cases are missed. The greatest chance for error here is erroneous diagnosis of primary site of the disease which is sometimes little more than a guess. Conceivably, lung cancer occurring in cigarette smokers is often diagnosed as primary cancer of some other site. If so, it is possible that cigarette smoking is not associated with cancer of primary sites other than the lungs. In that event,

the figures presented are an under-estimate of the degree of association between cigarette smoking and lung cancer. More evidence will be required to test this hypothesis.

Pneumonia can occur secondary to lung cancer and the symptoms of lung cancer can be confused with symptoms produced by bronchitis and other lung diseases. If confusion of this type accounts for the apparent association between cigarette smoking and pneumonia, bronchitis, and emphysema, it follows that the death rate from lung cancer is badly under-reported in general mortality statistics and that the association between cigarette smoking and lung cancer is greater than shown by Dr. Dorn's figures.

Evidence from a well controlled experiment on human subjects[7] as well as evidence from animal experiments [8] supports Dr. Dorn's findings of an association between cigarette smoking and death rates from peptic ulcer.

Perhaps the most interesting finding is the apparent association between cigarette smoking and death rates from coronary artery disease. While the mortality ratio is only moderately high, the absolute difference in death rates is very large. If correct, this finding is extremely important since coronary artery disease is reported to account for about 37% of all deaths among white males in the United States over the age of 50.

Many people who have studied the problem are under the impression that recording of coronary artery disease is one of the least reliable diagnoses reported on death certificates in the United States today. It is often put down in cases of sudden death when the certifying physician has had little or no opportunity to make a proper diagnosis. If

erroneous diagnosis entirely accounts for the apparent association between cigarette smoking and this disease, then the association between cigarette smoking and some other disease or diseases is grossly under-estimated in the figures presented here. This is necessarily so because of the large number of cases involved.

In closing, I would like to make a comment on the use of the mortality ratio as an index of association in studies of this type.

The probability of a person dying from a particular disease at a particular moment depends upon a multiplicity of factors operating at various times during the entire life span of the individual. There are two reasons for believing this to be true. First, there is reason to suppose that many causes of death are selective as to type of individual; so a high death rate from any one cause may alter the composition of the surviving population. Second, and aside from this, a number of factors (including susceptibility, exposure, treatment, etc.) influence the probability of death from any particular disease. At least this appears to be true of almost every disease so far studied.

Now let us assume that a particular factor can have an influence upon death rates from a particular disease. In the exposed population, the death rate from that disease is dependent not only upon that factor but upon other factors as well. The same is true of the unexposed population (provided the factor in question is not necessary for death from the disease). If this be true, then the mortality ratio for a particular disease and a particular factor depends upon the total set of conditions and will vary under other sets of conditions. For example, it is virtually certain that long exposure to a heavy concentration of uranium dust results in lung cancer in a very large proportion of people so exposed whether or not they smoke. Therefore, if a study such as Dr. Dorn's were to be carried out among uranium miners, it is virtually certain that the mortality ratio (smokers compared with non-smokers) would be far smaller than he has reported.

Assuming that a causal relationship actually exists, it seems to me that the mortality ratio is a reasonably good index of the contribution of a particular factor to the variance in death rates under a particular set of conditions. If the mortality ratio is small, it simply means that the factor contributes little to the variance under that set of conditions; it might make a much larger contribution under some other set of conditions. In other words, a mortality ratio of any size greater than 1.00 may reflect a causal relationship.

Now suppose that it is unknown whether a causal relationship exists. A mortality ratio above 1.00 suggests the possibility of a causal relationship but it is necessary to rule out other possible explanations before arriving at that conclusion. It seems to me that

if the mortality ratio is very large, then it should be relatively easy, with appropriate studies, to determine whether some other associated factor or selective bias accounts for the relationship. This is more difficult if the mortality ratio is small.

In the case of smoking and lung cancer, we have evidence of an extremely high mortality ratio but a relatively small absolute difference in death rates (cigarette smokers compared with non-smokers). In the case of coronary artery disease we have the appearance of a much smaller mortality ratio but a very large difference in death rates (cigarette smokers compared with non-smokers). The latter may be as truly a reflection of a causal relationship as the former. Furthermore, if we had more accurate information on diagnosis and greater knowledge of the total situation, we might find that in a particular segment of the population the mortality ratio for coronary artery disease (cigarette smokers compared with non-smokers) is as high as the mortality ratio for lung cancer. I do not assert that this is so, but considering the magnitude of the difference in death rates I suggest that it is an important field for further investigation.

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