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Chapter 8

Mortality

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Chapter 8

PROSPECTIVE STUDIES OF MALE POPULATIONS

The principal data on the death rates of smokers of various types and of nonsmokers come from seven large prospective studies of men. In such studies, information about current and past smoking habits, as well as some supplementary information (e.g., on age), is first obtained from the members of the group to be studied. Provision is also made to obtain death certificates for all members of the group who die during subsequent years. From these data, over-all death rates and death rates by cause are computed for the different types of smokers, usually in five-year age classes.

These seven studies comprise all the large prospective studies known to us. The first started in October 1951: the latest, in October 1959.

In brief, the seven groups of men are as follows:

(1) British doctors, a questionnaire having been sent to all members of the medical profession in the United Kingdom by Doll and Hill, 1956 (5).

(2) White American men in nine states. These men were enrolled by a large number of American Cancer Society volunteers, each of whom was asked to have the questionnaire filled in by 10 white men between the ages of 50 and 69. Hammond and Horn, 1958 (10).

(3) Policyholders of U.S. Government Life Insurance policies, available to persons who served in the armed forces between 1917 and 1940. Dorn, 1958 (6).

(4) Men aged 35–64 in nine occupations in California who were suspected of being subject to a higher than usual occupational risk of developing lung cancer. Dunn, Linden and Breslow, 1960 (7).

(5) California members of the American Legion and their wives. Dunn, Buell and Breslow (8).

(6) Pensioners of the Canadian Department of Veterans Affairs, i.e., veterans of World Wars I and II and the Korean War. Best, Josie and Walker, 1961 (2).

(7) American men in 25 states, enrolled by volunteer researchers of the American Cancer Society, each of whom was asked to enroll about 10 families containing at least one person over 45. Hammond, 1963 (11).

It will be noted that the studies cover different types of population groups in three countries. Study (2), often referred to as the Hammond and Horn study, terminated after 44 months' follow-up, and the data discussed here for this study are essentially the same as those already published (10). All other studies have accumulated substantial amounts of data beyond that which has been published. The authors and agencies responsible for the studies supplied their latest available data for this report. The tables in this Chapter are based on the new compilations.

Table I shows for each study the approximate number of subjects from whom usable replies about smoking habits were obtained, the date of enrollment, age range, number of months followed, total number of deaths, and the number of person-years of exposure. The number of subjects studied (usable replies) ranged from around 34,000 in the British doctors study to 448,000 in the new American Cancer Society study. The number of months of follow-up varied from about 22 to 120.

Although several of the studies obtained some data on women, only the California Legion study (8) and the new American Cancer Society study (11) include large numbers of women. No tabulations on women are as yet available from these prospective studies.

Data on Smoking History

The exact description of the type of smoking and the amount smoked at all times throughout a man's past life would necessitate an amount of detail and an accuracy of memory that was not considered practicable in these studies. While the information collected on smoking habits varied from study to study, all studies asked for data on the *current* amount and type of smoking as of the date of answering the questionnaire. These amounts were usually expressed as the number of cigarettes, cigars or pipes per day. In the case of subjects who had stopped smoking previous to the date of enrollment (ex-smokers), most studies obtained data on the maximum amount previously smoked per day. The category described as *non-smokers* sometimes included also those men who had smoked an insignificant total amount during their whole previous lifetime.

As regards type of smoking, cigarettes, cigars and pipes appear in all seven combinations. Since results for the "mixed" categories are difficult to interpret and sometimes involve relatively small numbers of subjects, the analysis here concentrates on the following types:

Cigarettes only
Cigarettes and other
Cigars only
Pipes only

In some instances the last two categories have been combined when the numbers of subjects are too small to give reliable data for the separate types.

Adjustment for Differences in Age Distribution

Since the death rate of any group of men is markedly affected by their age distribution, it is essential, when comparing the death rates of two groups of men, to ensure that their age distributions are comparable. A standard measure for this purpose is the *age-specific* death rate, in which the rate is computed for a group of men whose ages all lie within a relatively narrow span, say 50–54 years. This measure is particularly appropriate when it is desired to examine how the relative death rates in two groups change with age.

TABLE 1.—*Outline of prospective studies of smoking and mortality*

Authors	Doll & Hill (5)	Hammond & Horn (10)	Dorn (6)	Dunn, Linden, Breslow (7)	Dunn, Buell, Breslow (8)	Best, Josie, Walker (2)	Hammond (11)
Subjects	British doctors	White men in 9 States	U.S. veterans	California occupational groups	California American Legion members	Canadian pensioners (veterans and dependents)	Men in 25 States
Number of usable replies	34,000	188,000	248,000	67,000	60,000	78,000	448,000
Date of enrollment	Oct. 1951	Jan.-Mar. 1952	Jan. 1954 and Jan. 1957.	Nov. 1953 and May 1957.	May-Nov. 1957	Sept. 1955-July, 1956	Oct. 1959-Feb. 1960.
Age range	35-75+	50-69	30-75+	35-69	35-75+	35-75+	35-89
Months followed	120	44	78	About 48	About 24	72	About 22
Number of deaths	4,534	11,870	24,519	1,714	1,704	9,070	11,612
Person-years of exposure	269,000	668,000	1,312,000	222,000	119,000	383,000	820,000

Several methods of adjustment for differences in age distribution are available for populations that have a wide range of ages. For comparing the death rate of a group of smokers with that of the non-smokers in the study, the measure most frequently used in previous publications is a type of *mortality ratio*, obtained as follows: In each five-year age class, the age-specific death rate for non-smokers is multiplied by the number of person-years in the group of smokers. This product gives an expected number of deaths, which represents the number of deaths of smokers that would be expected to occur if the age-specific death rate were the same as for non-smokers. These expected numbers of deaths are added over all age classes, and their total is compared with the total number of observed deaths in the smokers. The mortality ratio is the ratio (total observed deaths in the smokers)/(total expected deaths). A mortality ratio of 1 implies that the over-all death rates are the same in smokers and non-smokers after this adjustment for differences in age distribution. It does not imply that the death rates of smokers and non-smokers were the same at each specific age. A mortality ratio higher than 1 implies that the group of smokers has a higher over-all death rate than the non-smokers.

Another common method of adjustment for age is to use some age-distribution as a standard, for instance the combined age-distribution of all persons in the study or the age-distribution of the U.S. male population as of a certain Census year. The age-specific death rates for a certain group (e.g., smokers) are multiplied by the number of persons of that age in the standard distribution. These products are added and finally divided by the total standard population to obtain an *age-adjusted* rate for the group. A mortality ratio of smokers to non-smokers is then computed as the ratio of the age-adjusted rates for smokers and non-smokers. Mortality ratios computed in different ways will of course give somewhat different results and experts in this field do not regard any one method as uniformly best. In this report we have used the ratio of observed to expected deaths, as described in the previous paragraph, primarily because this measure is the most common one in previous publications from these studies. Both methods of adjustment run the risk of concealing a change in the relative death rate with age. For instance, the over-all mortality ratio might be unity if smokers had higher death rates than non-smokers prior to age 60, but lower death rates thereafter.

Smokers and non-smokers may differ with regard to variables other than age that are known or suspected to influence death rates, such as economic level, residence, hereditary factors, exposure to occupational hazards, weight, marital status, and eating and drinking habits. In the summary results to be presented in subsequent sections, as in most results previously published, the death rates of smokers and non-smokers have not been adjusted so as to equalize the effects of these disturbing variables. This issue will be discussed later in this chapter.

A further complexity in interpreting the results comes from interrelationships among the variables that describe the habit of smoking. As will be seen, the death rates of a group of cigarette smokers vary with the amount smoked, the age at which smoking was started, the duration of smoking, and the amount of inhalation. In trying to measure the "net" effect of one of these variables, such as the number of cigarettes smoked per day, we should make adjustments so that the different groups of smokers being compared are equalized on all other relevant aspects of the practice. This can be done at best only partially. Most studies measured only some of the variables on which adjustment is desirable. When the data are subclassified in order to make the adjustments, the numbers of deaths per subclass are small, with the consequence that the adjusted death rates are somewhat unstable.

Consequently, like previous reporters on these studies, we have used our judgment as to the amount of subclassification and adjustment to present. The possibility that part of the differences in death rates may be associated with smoking variables other than the one under discussion cannot be excluded.

RESULTS FOR TOTAL DEATH RATES

Mortality Ratios for Current Smokers

Table 2 shows the mortality ratios to non-smokers for men who were smoking regularly at the time of enrollment.

For males smoking cigarettes only, the over-all death rate is higher than that for non-smokers in all studies, the increase ranging from 44 percent for the British doctors to 83 percent in the men in 25 states. For smokers of other forms of tobacco as well as cigarettes the increases in death rates are in all cases lower than for the smokers of cigarettes only.

For smokers of cigars only or of pipes only, three of the studies show small increases in over-all death rates, ranging from 5 percent to 11 percent. The study of men in 25 states, however, gives slight decreases for both types, as does the British study for the two types combined.

TABLE 2.—*Mortality ratios of current smokers by type of smoking*

Type of smoking	Study group[1]				
	British doctors	Men in 9 States	U.S. veterans	Canadian veterans	Men in 25 States
Cigarettes only	1.44	1.70	1.79	1.65	1.83
Cigarettes and other	1.05	1.45	1.46	1.23	1.54
Cigars only	0.95 (cigars and pipes combined)	1.10	1.07	1.11	0.97
Pipes only		1.05	1.06	1.10	0.86

[1] The California occupational and Legion studies give mortality ratios of 1.78 and 1.58 respectively, for all cigarette smokers (current and ex-smokers).

Mortality Ratios by Amount Smoked

For smokers of cigarettes only who were smoking at the time of entry, the mortality ratio increases consistently with the amount smoked in each of the seven studies, with one exception for the California occupational study, which includes ex-cigarette smokers as well as current smokers (Table 3).

For smokers of cigars only who were smoking at the time of entry, four of the studies give a breakdown into two amounts of smoking (Table 4).

Men smoking less than five cigars per day have death rates about the same as non-smokers. For men smoking higher amounts there is some elevation of the death rate. When the results are combined by adding the observed and expected deaths over all four studies, an over-all mortality ratio of 1.20 is obtained for the five-or-more group. This over-all increase is statistically significant at the 5 percent level.*

TABLE 3.—*Mortality ratios for current smokers of cigarettes only, by amount smoked*

Cigarettes per day	British doctors	Men in 9 States	U.S. veterans	California occupational* [1]	California Legion*	Canadian veterans	Men in 25 States
Less than 10	1.06	1.33	1.35	1.44	[2] 1.30	1.55	1.45
10–20	1.31	1.66	1.76	1.79		1.68	1.75
21–39	[3] 1.62	1.93	1.99	2.27	[6] 1.64	[5] 1.84	1.90
40 and over	[4] 2.50	2.20	2.22	1.83	[7] 1.85		2.20

*Current and ex-cigarette smokers combined.
[1] "Less than 10" is "less than 5" plus "about ½"; "10–20" is "about 1"; "21–39" is "about 1½".
[2] Less than 1 pack.
[3] 20–34.
[4] 35 plus.
[5] More than 1 pack.
[6] About 1 pack.
[7] More than 1 pack.

TABLE 4.—*Mortality ratios for current smokers of cigars only, by amount smoked*

Number per day	Men in 9 States	U.S. veterans	Canadian veterans	Men in 25 States	Over-all results
1–4	1.06	0.99	[1] 1.12	0.93	1.00
5 or more	1.20	1.24	[2] 1.26	1.10	1.20

[1] 1–2.
[2] 3 or more.

For current pipe smokers (Table 5), men smoking less than 10 pipefuls per day have death rates very close to those of non-smokers. For heavy pipe smokers (10 or more per day) two studies show increases of 15 and 12 percent in death rates, but the other two studies show little or no increase. The over-all mortality ratio of 1.05 does not differ statistically from unity. The

*Statistical significance throughout this report refers to the 5 percent level unless otherwise specified. In testing whether an observed mortality ratio of smokers relative to non-smokers is greater than unity, the probability is calculated that a ratio as large as or larger than the observed ratio would occur by chance if the smokers and non-smokers were drawn from two populations having the same death rate. If this probability is less than 0.05 (5 percent) the observed increase in the death rate of smokers relative to non-smokers is said to be statistically significant at the 5 percent level. The results of significance tests will be quoted only for mortality ratios in which the number of deaths raises a doubt as to whether the difference from unity could be due to sampling errors.

British doctors study gives a mortality ratio of 0.91 for cigar and pipe smokers together (presumably mostly pipe smokers) who consume more than 14 gms. of tobacco daily.

TABLE 5.—*Mortality ratios for current smokers of pipes only, by amount smoked*

Pipes per day	Study				Over-all ratio
	Men in 9 States	U.S. veterans	Canadian veterans	Men in 25 States	
1-9	1.00	1.03	1.07	0.92	1.01
10 or more	1.15	1.12	1.01	0.76	1.05

Mortality Ratios at Different Ages

As indicated previously, the mortality ratios presented in previous tables for different groups of smokers represent a kind of average over the age-distribution of the smokers concerned, and do not necessarily apply to smokers of any specific age. For cigarette smokers, the studies show that the mortality ratio declines with increasing age, being higher for men aged 40–50 than for men over 70. This effect is illustrated in Table 6 from the study of men in 25 states, which gives the mortality ratio computed separately for five age classes.

The drop in mortality ratio with each increase in age appears fairly consistently for every amount of smoking. For smokers of cigarettes only as a whole, the death rate is more than double that for non-smokers in the age range 40–49, but only about 20 percent higher for men over 80. The picture is, of course, different if we look at the *absolute* excess in death rates at different ages. Owing to the marked increase in death rates with age, the absolute excess also increases steadily with increasing age.

A more thorough investigation of the relation between death rates and age for different groups of smokers has been made by Ipsen and Pfaelzer (14). If the logarithm of the age-specific death rate is plotted against age, the resulting points lie reasonably close to a straight line. For the U.S.

TABLE 6.—*Mortality ratios by age group for current smokers of cigarettes only, men in 25 States*

Number of cigarettes per day	Age at start of study				
	40–49	50–59	60–69	70–79	80–89
1-9	2.27	1.44	1.40	1.40	1.08
10-19	2.12	1.94	1.69	1.50	1.65
20-39	2.22	2.05	1.78	1.48	1.16
40+	3.06	2.37	1.68	1.28	0.58
All amounts	2.33	2.06	1.70	1.47	1.22

veterans study, Figure 1 shows the points and fitted lines for non-smokers and for current smokers of cigarettes only. (The lines were fitted by the standard method of least squares, weighting each point by the number of deaths involved.)

If the lines for cigarette smokers and non-smokers were parallel, this would imply that the mortality ratio of the smokers to the non-smokers was constant at all ages, because the vertical distance between the two lines at any age is the log of the mortality ratio for that age. In Figure 1, however,

DEATH RATE (logarithmic scale) PLOTTED AGAINST AGE, PROSPECTIVE STUDY OF MORTALITY IN U.S. VETERANS

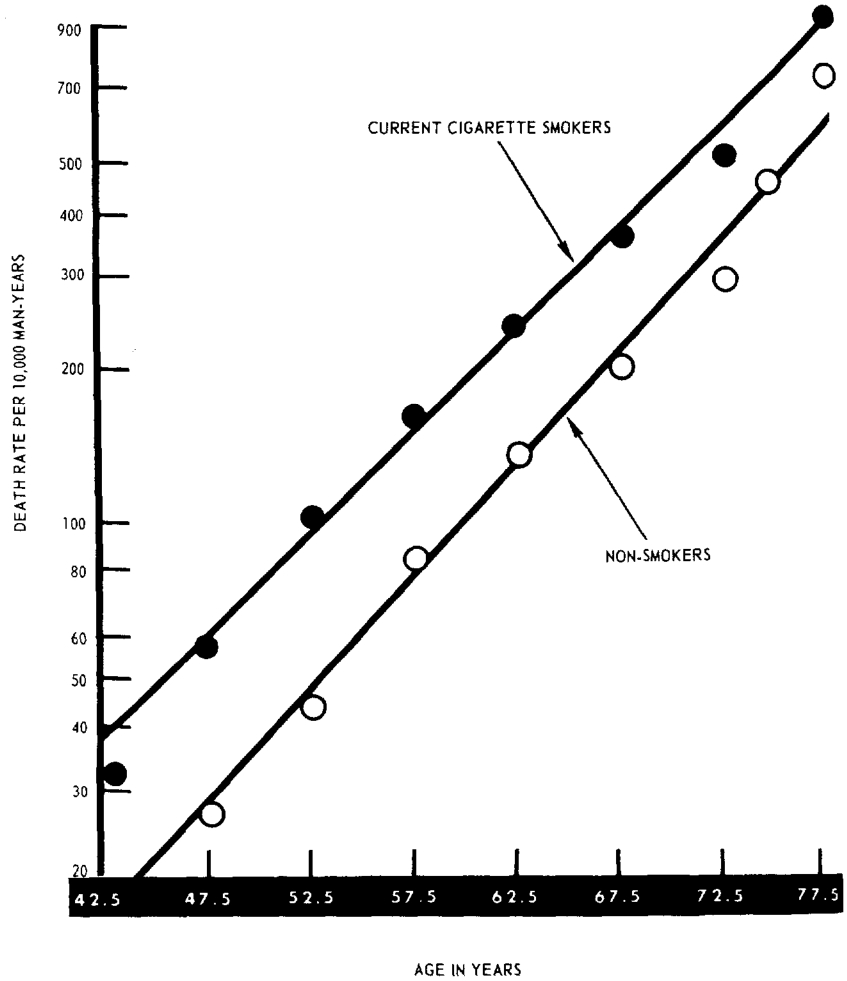

FIGURE 1.

the slope is slightly less steep for the cigarette smokers than for the non-smokers. This indicates that the mortality ratio is declining with increased age.

Table 7 shows these slopes (increase in the *natural* logarithm of the death rate for each 5-year increase in age) computed from six of the studies. The salient features are as follows: (1) In each study the slope for cigarette smokers is smaller than the slope for non-smokers; (2) Within the cigarette smokers the slope tends to decline, with some inconsistencies, as the amounts smoked become greater; (3) for cigar or pipe smokers the slopes are closer to those for non-smokers.

TABLE 7.—*Increase in natural logarithm of death rate per 1,000 man-years for each 5-year increase in age, 6 prospective studies*

Type of smoking	British doctors	Men in 9 States	U.S. veterans	California occupational [1]	California Legion [1]	Men in 25 States [2]
Non-smokers	.593	.474	.499	.489	.502	.490
Cigarettes by amount per day	.492	.427	.448	.436	.476	.438
1–9	.536	.484	.490	.401	.567	.445
10–20	.551	.457	.454	.461	.471	.441
21–39	.477	.420	.467	.447	.449	.401
40+	.401	.345	----------	----------	----------	.401
Cigars	.598	.466	.483	----------	----------	.457
Pipes		.521	.458	----------	----------	.458

[1] "Cigarettes" includes "cigarettes and other" and current and ex-smokers.
[2] First 10 months' experience.

AGE AT WHICH SMOKING WAS STARTED

The study of U.S. veterans and the study of men in 25 states provide data on the death rates of current smokers of cigarettes only, classified by the age at which the person started to smoke. Since in both studies the men who start to smoke early tend to smoke greater amounts per day than men who start later in life, the mortality ratios to non-smokers are presented separately for different amounts of smoking (Table 8).

TABLE 8.—*Mortality ratios by age at which smoking was started and by amount smoked for current smokers of cigarettes only*

Age started to smoke	Number of cigarettes per day				Over-all ratio
	1–9	10–20	21–39	40+	
U.S. veterans:					
Under 20	1.60	1.89	2.16	2.45	1.98
20–24	1.40	1.72	1.87	2.23	1.72
25 or over	1.15	1.50	1.47	1.11	1.39
Men in 25 States:					
Under 15	1.79	[1] 2.23	[2] 2.21	2.15	2.17
15–19	1.75	[1] 1.83	[2] 2.01	2.38	1.99
20–24	1.25	[1] 1.52	[2] 1.62	1.93	1.58
25 or over	1.03	[1] 1.36	[2] 1.45	1.56	1.34

[1] 10–19 cigarettes per day.
[2] 20–39 cigarettes per day.

For a fixed amount of smoking, the mortality ratios (with one exception) exhibit a consistent and rather striking increase as the age at which smoking was started decreases. This increase appears in all smoking groups of Table 8. For men who started smoking cigarettes under the age of 20, the over-all death rate was about twice that for non-smokers, whereas for those who did not start until they were over 25 the death rate was only about 35 percent higher.

Mortality Ratios by Duration of Smoking

Three studies have some data available on the number of years during which the subjects had smoked. The comparison of mortality ratios for different lengths of time smoked is of interest in relation to two questions raised by Dorn (6) in an earlier analysis of the U.S. veterans' data. Is there a minimum period of use during which no effect on the death rate is noticeable? Is there a maximum period after which no increase in the relative death rate is perceptible?

For current cigarette smokers the results (Table 9) are not clear-cut. In the U.S. veterans study, men smoking for less than 15 years had death rates about the same as non-smokers. There is a rise of about 50 percent in the mortality ratio for those who had smoked 15–35 years, with a further rise for those smoking longer than 35 years. The study of men in nine states shows a rise from under 25 years to 25–34 years duration, but no further rise thereafter. In the Canadian study the mortality ratio with cigarette smokers is just as high for durations less than 15 years as for durations of 15–29 years, though there is a rise (to 1.73) for smokers of cigarettes only who have been smoking more than 30 years.

TABLE 9.—*Mortality ratios for current smokers by type of smoking and by length of time smoked*

Type of smoking	Number of years smoked									
	U.S. veterans				Canadian veterans			Men in 9 States		
	<15	15–24	25–34	35+	<15	15–29	30+	<25	25–34	35+
Cigarettes only	0.92	1.52	1.50	1.88	1.52	1.41	1.73	1.46	1.74	1.78
Cigarettes and other	1.07	1.41	1.33	1.49	1.24	1.27	1.22			
Cigars only	0.92	0.94	0.95	1.12	1.06	0.81	1.31			
Pipes only	1.01	1.34	0.97	1.07	1.36	0.93	1.09			

Thus, all three studies show some increase in the mortality ratios with longer duration of smoking, but the pattern is irregular. In a further breakdown of the data by amount smoked, Hammond and Horn (10) found no trend with duration for men smoking more than a pack a day, but the other two studies show an upward trend for this group of smokers.

For cigar smokers the only groups showing an increase in death rates over non-smokers are those smoking for the longest period (Table 9). The increases of 12 percent for the 35 years or over group in the U.S. study and of

31 percent for the 30 years or over group in the Canadian study are both statistically significant.

For pipe smokers no trend with duration of smoking is discernible. The two figures which stand out (1.34 in the U.S. study and 1.36 in the Canadian study) are both based on relatively small numbers of deaths.

Inhalation of Smoke

In two of the studies the subjects were questioned as to whether they inhaled. In the study of men in 25 states each subject was asked to place himself in one of the four classes: do not inhale, inhale slightly, inhale moderately, inhale deeply. In the Canadian veterans study the subject simply classified himself as an inhaler or non-inhaler.

For current smokers of cigarettes only in the U.S. study, 6 percent of the subjects stated that they did not inhale, 14 percent inhaled slightly, 56 percent moderately and 24 percent deeply. In the Canadian study 11 percent classified themselves as non-inhalers.

Since inhalation practices may vary with the amount smoked, the results for cigarette smokers (Table 10) are given separately for different amounts. For the men in 25 states an increase in the degree of inhaling for a fixed amount of smoking is in general accompanied by an increase in the mortality ratio. The relation of inhalation to mortality appears quite marked: for instance, non-inhalers who smoke 20–39 cigarettes daily have mortality ratios no higher than moderate or deep inhalers who smoke 1–9 cigarettes daily. With the very heavy smokers (40+) the figures in Table 10 suggest that the mortality ratio may remain the same for non-, slight, and moderate inhalers. The ratios of 2.05 (non-) and 1.97 (slight) are, however, based on only 26 and 41 deaths, respectively.

TABLE 10.—*Mortality ratios for smokers of cigarettes only by inhalation status and amount of smoking*

Degree of inhalation	Cigarettes per day				Over-all ratio
	1–9	10–19	20–39	40+	
Men in 25 States:					
None	1.29	1.46	1.56	2.05	1.49
Slight	1.29	1.68	1.84	1.97	1.68
Moderate	1.61	1.82	1.84	2.01	1.83
Deep	1.88	1.76	2.18	2.50	2.20
Canadian veterans: [1]					
None	1.05	[2] 1.11	[3] 1.03	----------	1.08
Some	1.35	[2] 1.50	[3] 1.71	----------	1.52

[1] Amounts are lifetime maximum amounts smoked.
[2] 10–20 cigarettes per day.
[3] Over 20 cigarettes per day.

Looking along the rows of the U.S. veterans study it will be seen that for each degree of inhalation the mortality ratio increases with the amount smoked. Ipsen and Pfaelzer (14) have shown that the logarithms of the 16 death rates at age 61 (approximately the average age) can be adequately represented as an additive function of the amount of smoking and the degree of inhalation (although other types of mathematical relationship would also fit the data). In their analysis, the average change in logarithm of death rate from "no inhalation" to "deep inhalation" is as great as the difference between consumption of less than 10 cigarettes and consumption of more than 40 cigarettes daily.

In the Canadian data the inhalers have higher mortality ratios than the non-inhalers for each amount of smoking. No trend with amount of smoking appears for the non-inhalers, but the ratios in this row are based on rather small numbers of deaths.

For cigar smokers (current and ex-smokers) in the 25-state study 19 percent stated that they inhaled to some extent. The mortality ratio is 0.89 for non-inhalers and 1.37 for inhalers. The latter increase of 37 percent (based on 91 deaths) is statistically significant, but as the data have not been subclassified by amount of smoking the result may be partially a reflection of the increase in death rates noted in Table 4 for heavy cigar smokers. In the Canadian study, 13 percent of the cigar smokers classified themselves as inhalers, but the number of deaths is insufficient to present a breakdown of the mortality ratio by inhalation status.

Among the pipe smokers there were 28 percent who inhaled in the U.S. study and 18 percent in the Canadian study. The U.S. mortality ratios are 0.8 for non-inhalers and 1.0 for inhalers; the Canadian data contain too few deaths to allow a breakdown by inhalation.

Ex-Cigarette Smokers

For men who had stopped smoking prior to the date of enrollment, Table 11 gives the mortality ratios from five studies for "cigarette only" smokers and "cigarette and other" smokers. The corresponding results for current cigarette smokers (from Table 2) are given for comparison. The distinction between current and ex-smokers is not of course clear cut, since some current smokers may have stopped after enrolling in the study and some ex-smokers may have later resumed smoking.

With one exception, the mortality ratios for ex-smokers lie consistently below those for current smokers and above those for non-smokers. In interpreting comparisons of ex-smokers and current smokers there are at least three relevant factors. If smoking is injurious to health, cessation of smoking would be expected to reduce the mortality ratio. Secondly, some men stop smoking because of illness. In the 25-State study, over 60 percent of the men who had stopped smoking within a year prior to entry stated that a disease or physical complaint was one of the reasons for stopping (12). This factor would tend to make mortality ratios for ex-smokers higher than those for current smokers. Finally, ex-smokers may have previously smoked smaller amounts than current smokers. This factor is not the explanation of the drops in mortality ratios in Table 11. In a further breakdown by amount of smoking, made for the three largest studies, the mortality ratio for ex-smokers is consistently below that for current smokers for each amount smoked.

TABLE 11.—*Mortality ratios for ex-smokers and current smokers of cigarettes*

	British doctors	Men in 9 States	U.S. veterans	Canadian veterans	Men in 25 States
Ex-cigarettes	1.04	1.40	1.41	1.42	1.50
Current cigarettes	1.44	1.70	1.79	1.65	1.83
Ex-cigarettes and other	1.21	1.29	1.21	1.18	1.51
Current cigarettes and other	1.05	1.45	1.46	1.23	1.54

TABLE 12.—*Mortality ratios for ex-smokers of cigarettes only by number of years since smoking was stopped and by amount smoked*

Study	Cigarettes per day	Number of years stopped					Current smokers
		<1	1–4	1–9	5–9	10+	
Men in 9 States [1]	<19	2.04	----------	1.30	----------	1.08	1.61
	20+	2.69	----------	1.82	----------	1.50	2.02
Men in 25 States	<19	1.60	1.62	----------	1.46	0.81	1.73
	20+	2.80	2.01	----------	1.51	1.22	2.01

[1] These data are from Hammond and Horn, 1958.

TABLE 13.—*Mortality ratios for ex-cigarette smokers by number of years of smoking, U.S. veterans study*

Cigarettes per day	Number of years of smoking			
	<15	15–24	25–34	35+
1–20	1.05	1.08	1.25	1.58
20+	1.12	1.18	1.41	2.00
	Age at which smoking was stopped			
	<45	45–54	55+	
1–20	1.09	1.24	1.51	----------
20+	1.12	1.59	1.86	----------

Some supplementary analyses throw a little further light on this topic. In the two American Cancer Society studies (Table 12) a breakdown is given by the number of years since smoking was stopped.

Except for the smokers of under one pack a day in the 25-State study, the mortality ratio for men who had stopped less than a year is higher than that for current smokers. Thereafter the ratio drops steadily as the interval since smoking was stopped increases.

In the U.S. veterans study, further breakdowns are available by the numbers of years during which the ex-smokers were smoking and by the age at which smoking was stopped (Table 13), as well as by the amount of smoking. The mortality ratios are about the same for those smoking less than 15 years as for those smoking 15–24 years. Thereafter the ratios rise with longer durations of smoking. Table 13 also shows that mortality ratios were higher for those who stopped smoking at later ages.

Ex-Cigar and Pipe Smokers

Mortality ratios for smokers of cigars only and pipes only who had stopped smoking prior to the date of entry are given in Table 14, the corresponding ratios for current smokers being included for comparison.

For ex-cigar smokers the mortality ratios are higher than those for nonsmokers and higher than those for current smokers in all four studies presented. The same is true for ex-pipe smokers with the exception of the Canadian study.

The interpretation of this result is not clear to us. According to Hammond and Horn (10) and Dorn (6), the explanation may be that a substantial number of cigar and pipe smokers give up because they become ill: some data from cigarette smokers that support this explanation have recently been analyzed by Hammond (12). Further analysis of the U.S. veterans data indicates that mortality ratios run highest in ex-smokers who smoked heavily and for a long time.

TABLE 14.—*Mortality ratios for ex-smokers of cigars only and pipes only and for current cigar and pipe smokers*

Type of smoker	British doctors	Men in 9 States	U.S. veterans	Canadian veterans	Men in 25 States
Ex-cigar	----------	1.65	1.30	1.17	1.24
Current cigar	----------	1.10	1.07	1.11	0.97
Ex-pipe	[1] 1.12	1.29	1.38	1.01	1.23
Current pipe	[1] 0.95	1.05	1.06	1.10	0.86

[1] Pipe and cigar combined.

EVALUATION OF SOURCES OF DATA

The Study Populations

Various reasons dictated the particular choices made of the seven study populations, considerations of feasibility playing an important role. None of the populations was designed, in particular, to be representative of the U.S. male population. Any answer to the question "to what general populations of men can the results be applied?", must involve an element of unverifiable judgment. However, three of the studies have populations with widespread geographic distribution within the United States, as do the British and Canadian studies within their respective countries. Taken as a whole, the seven populations offer a substantial breadth of sampling of the type of men and environmental exposures to be found in North America and Britain, as well as providing some variation in methodological approach, although the basic plan was similar in all studies.

The seven studies differ considerably in size. They vary also in the extent to which they are free from methodological weakness. The studies of men in nine states and men in 25 States, for instance, suffer from the difficulties that the populations studied are hard to define, that the smokers and non-smokers were recruited by a large number of volunteer workers, and that completeness in the reporting of deaths was hard to achieve, since this depends on reports from the volunteers. On the other hand these studies have the advantage of being large and of having a broad geographic representation of the U.S. male population, while the second study is the only one that attempts to investigate many other relevant variables in which smokers and non-smokers may differ. In the California occupational study the focus of interest is occupational differences in lung cancer mortality, smoking history being recorded primarily in order to be able to adjust comparisons among different occupational groups for differences in amount smoked. In the analysis we have not attempted to rate the studies as to over-all quality or to assign differential weights to their results, except that in the smaller studies it is recognized that mortality ratios are subject to larger sampling errors. Our attitude is to attach importance only to results that appear to be generally confirmed by the studies.

Some idea of the relative death rates in these studies as compared with the 1960 white male population of the United States is given in Table 15, which shows the age-adjusted death rates for ages 35 and over, using the age distribution of the U.S. white male population as a standard. (The choice of 1960 for the comparison is arbitrary, but the white male rate changed little between 1955 and 1960.)

In all studies the death rates for non-smokers are markedly below those of U.S. white males in 1960. Even the smokers of one pack of cigarettes or more daily have death rates that average slightly below the U.S. white male figure. To some extent this is to be expected, since hospitalized and other seriously ill persons are not recruited in such studies. The sizes of the differences appear, however, surprising for the studies with United States populations. Hammond and Horn (10), in a special investigation on this question, concluded that the discrepancy in their study was due to the screening out of sick persons in recruiting plus probably a selection towards men of higher economic levels. They point out that their death rates are substantially above those for males who had held ordinary life insurance policies for from

TABLE 15.—*Age-adjusted death rates per 1,000 man-years for current smokers of cigarettes only (aged 35 and over), by amount smoked, in seven studies and for U.S. white males*

Study	Non-smokers	Current smokers of cigarettes only		U.S. white males, 1960
		Less than 1 pack	1 pack or more	
British doctors	15.8	19.2	23.2	22.9
Men in 9 States	[1] 14.4	[1] 22.4	[1] 27.1	[1] 22.6
U.S. veterans	12.0	18.1	23.9	22.9
California occupational	[1] 10.5	[1] 14.2	[1] 18.0	[1] 22.6
California legion	11.3	16.4	16.3	22.9
Canadian veterans	14.1	22.1	24.2	22.9
Men in 25 States	[2] 12.8	[2] 18.5	[2] 19.2	22.9

[1] Ages 50–69.
[2] These figures may be too low by about 1.7 percent, since the person-years used in the computation included some contribution by men who had not been fully traced.

5 to 15 years. The U.S. veterans' study population also came mainly from the middle and upper socio-economic classes (6).

Another reason might be a failure to trace all deaths. In mass studies it is almost impossible to devise infallible provisions for recording every death. The study directors were, however, experienced in handling this problem and it seems unlikely that more than, say, 5 percent of the deaths would be missed. (Moreover, in the studies of veterans it is to the family's advantage to report the death.)

Another contribution probably came from the failure to obtain data for some members of the population. Evidence on this point is available from the British doctors and the U.S. veterans' studies, in which death rates for the complete population (respondents and non-respondents) are available. In these studies the death rate for the whole population exceeded that in the respondents, but by only 5 percent to 10 percent, so that non-response appears unlikely to be a major cause of the discrepancy.

So far as interpretation of results is concerned, the discrepancy raises two points. It is clear that the seven prospective studies involve populations which are healthier than U.S. males as a whole. Secondly, the low death rates for non-smokers suggest the possibility that the studies recruited unusually healthy groups of non-smokers. In the case of the five studies which had clearly defined populations, this selection would arise only if the non-smokers who refused to enter the study had death rates much higher than those who were enrolled. This point is discussed in the next section.

Non-Response Bias

In all five studies that had a clearly defined target population, sizeable proportions of the population were omitted. The major reason was failure to answer the questionnaire; in addition, certain replies were rejected as too incomplete. The percentages of the populations for which usable replies were obtained were approximately as shown in Table 16.

TABLE 16.—*Percentages of usable replies in five studies*

British doctors	U.S. veterans	California occupational	California Legion	Canadian veterans
68	68, 85	85	56	57

In the U.S. veterans study, 68 percent replies were obtained from the 1954 questionnaire. A second questionnaire, sent in 1957, enrolled an additional 17 percent, for whom data are available during the period 1957–60. In the two American Cancer Society studies it is not possible to present meaningful percentages, since each research volunteer selected her own small part of the study population from among her acquaintances.

The possible effects of these amounts of non-response on the mortality ratios have received little discussion. Some pieces of information about non-respondents are available in two studies. From a recent sample, Doll (4) states that (a) the death rate of non-respondents in the British doctors study is higher than that of respondents; (b) consequently the death rate for respondents is lower than that of British doctors as a whole, perhaps by as much as 5 percent to 10 percent; (c) there are relatively more smokers among the non-respondents than among the respondents. In the U.S. veterans' study, the death rate for the whole study population exceeded that for the original 68 percent responders by 7 percent in 1958 and 5 percent in 1959. From this study one can also calculate mortality ratios separately, during 1957–60, for the 1954 respondents and the 1957 respondents. The results for smokers of cigarettes are as follows:

	1954 respondents (68 percent)	*1957 respondents (17 percent)*	*Non-respondents (15 percent)*
Current cigarettes only	1.87	1.71	?
Current cigarettes and other	1.56	1.33	?

Those who did not respond in 1954 but did respond in 1957 show lower mortality ratios than the original set of men giving usable replies. By making guesses about the mortality ratios in the 15 percent of non-responders, one can compare the resulting mortality ratio in the whole population with that found in the original 68 percent. To consider how much of an overestimate the ratios of 1.87 and 1.56 might be, we might suppose, to illustrate the method, that the mortality ratio is unity for the non-respondents. The mortality ratio for the whole population then turns out to be 1.71 for cigarettes only and 1.44 for cigarettes and other. Thus, with a non-response rate of 30 percent, the computed mortality ratio might overestimate by 0.1 or 0.2.

Berkson (1) produced a set of assumptions under which, with a mortality ratio of 1 in the whole population and a response rate of 71 percent, the mortality ratio in the respondents is found to be 1.5. Non-respondents are assumed to be of two types. One group, destined to have a high death rate, refuses because they don't feel well. This group has a high refusal rate (50 percent) for both smokers and non-smokers, since the reason for refusal is illness and not smoking. In the remainder of the non-respondents, the refusal rate is higher among smokers than non-smokers. Qualitatively, these assumptions are not unreasonable and agree in direction with the results quoted previously for the British doctors and U.S. veterans' studies. Korteweg (15) worked further examples of Berkson's model as applied to individual causes of death in the first report of the study of men in nine states. He concluded that the response bias in the mortality ratio might be as high as 0.3. Both Berkson and Korteweg, had, of course, to make some arbitrary assumptions about the sizes of biases from different sources.

Further discussion of the non-response bias and computations as to its magnitude are given in Appendix I. The computations indicate that reported mortality ratios lying between 1 and 2 might overestimate by as much as 0.3, a mortality ratio of 5.0 might overestimate by 1.0, and one of 10.0 might overestimate by 3.0. Thus, under assumptions that are rather extreme, although consistent with the available data about non-respondents, the mortality ratios of cigarette smokers would still remain substantially higher than unity after adjustments for these amounts of over-estimation.

MEASUREMENT OF SMOKING HISTORY

Measurement of the type and amount of smoking, being based on a single mail questionnaire, was admittedly crude. Consider men recorded as current smokers of cigarettes only. Subsequent to enrollment, some of these presumably stopped smoking, at least temporarily, and some took up other forms, with or without cigarettes.

Similarly, some men recorded as non-smokers may have begun to smoke cigarettes subsequently. Consequently, the group designated as "current smokers of cigarettes only" presumably contained men who were, for some period of time "ex-smokers" or "cigarette and other" smokers, while men designated as "non-smokers" contained some who smoked cigarettes for a time. It seems likely that this dilution of the contrast between the two groups would make the mortality ratio of cigarette smokers, as reported in previous tables, underestimate the mortality ratio of unchanging cigarette smokers relative to unchanging non-smokers, particularly when we note that the groups labeled "ex-smokers of cigarettes" and "cigarette and other" smokers both had mortality ratios lower than the group labeled "current smokers of cigarettes only".

As regards number of cigarettes per day, two types of errors of measurement may occur. There will be "random" errors of measurement (some men overestimate the amount and others underestimate it) that tend to cancel out over all men in the study. The effect of such errors is that the reported data underestimate the increase in the mortality ratio per additional cigarette smoked daily, the computed increase being an estimate of $B/(1+h)$, where B is the true increase and h is the ratio of the variance due to errors of measurement in the amount smoked to its total variance, Yates (17). There may also, however, be systematic errors in reporting the amount smoked. Heavy smokers may tend to underestimate the amount smoked. If this happens, the reported increase in mortality ratio per additional cigarette smoked will be an overestimate of the true increase, although the upward trend of mortality ratio with increasing amount smoked will remain.

On balance, we are inclined to agree with the opinion expressed by the authors of several of the studies to the effect that the general result of errors in reporting smoking history is to depress the mortality ratios of smokers relative to non-smokers, so that reported ratios will tend to be underestimates so far as this source of error is concerned.

STABILITY OF THE MORTALITY RATIO

The sampling distribution of the mortality ratio has not to our knowledge been at all thoroughly investigated and appears to be complicated. As a rough approximation (Appendix II), the ratio of smoker deaths to smoker plus non-smoker deaths may be regarded as a binomial proportion with mean $\lambda R/(1+\lambda R)$ where R is the true mortality ratio, λ is the ratio of the expected smoker deaths to the observed non-smoker deaths and the sample size is the number of smoker plus non-smoker deaths. From this approximation, confidence limits for R may be derived. This approximation requires that (1) the age distributions of smokers and non-smokers do not differ greatly and (2) all age-specific death rates are small. An alternative normal approximation that avoids assumption (1) is also given in Appendix II.

The sampling variation of the estimate of R is seldom of major import in this part of the report, since the ratios for total mortality are mostly based on relatively large numbers of deaths. The estimate has a positive mathematical bias, negligible with large but not with small numbers of deaths. In another sense the particular mortality ratio used in this report has a different kind of bias. Since the standard age-distribution used in this ratio is the age-distribution of the smokers, who are somewhat younger than the non-smokers, the mortality ratios apply to populations slightly younger than the combined population of the study. This is not in our opinion a serious objection, but may sometimes be relevant in questions of interpretation.

OTHER VARIABLES RELATED TO DEATH RATES

As mentioned previously, the smokers and non-smokers in these studies may differ with respect to other variables that might influence the death rate. Except in the new 25-State study, no attempt was made to measure these variables apart from urban-rural residence, and previous reports on these studies give little discussion of this problem. For urban-rural residence, Doll and Hill (5) found that the proportions of smokers of different amounts in the study population were about the same in rural areas, small cities and large cities. In three studies the mortality ratios of cigarette smokers were computed separately by size of city (6, 10, 11). In the study of men in 25 States, the data refer to men who smoked 20 or more cigarettes a day and said that they inhaled moderately or deeply. In all three studies the mortality ratios show little change with size of community (Table 17).

In the 25-State study, over 20 other variables that may be associated with death rates were recorded. The study population was broken down into subgroups for many of these variables separately: for instance, into smokers who have long-lived parents and grandparents and those whose parents and

TABLE 17.—*Mortality ratios for cigarette smokers by population-size of city*

Study	Population-size			
	Over 50,000	10,000–50,000	Small towns	Rural
Men in 9 States	1.48	1.62	1.50	1.52
U.S. veterans	1.54	1.51	1.42	1.59
Men in 25 States	1.89	[1] 2.02		1.74

[1] Includes towns of less than 10,000.

grandparents were short-lived. Included among these variables were religion, educational level, native or foreign birth, residence by size of town and occupational exposure, use of alcohol, use of fried food, amount of nervous tension, use of tranquilizers, and presence or absence of prior serious disease. For cigarette smokers who smoked more than a pack a day and inhaled moderately or deeply, the mortality ratio was computed within each subgroup. For example, the mortality ratio was 1.99 for men with long-lived parents and 2.30 for men with short-lived parents. In every subgroup the mortality ratio was well above unity, the lowest among 71 computed ratios being 1.57 (for men with a history of previous serious disease).

These data provide information on the association of the other variables with mortality as well as on the association of smoking with mortality. For six of the most relevant variables, Table 18 gives age-adjusted death rates, using the combined populations of non-smokers and cigarette smokers as the standard population. The death rates apply to a period of roughly 22-months follow-up. As already mentioned, the cigarette smokers (of more than a pack per day who inhaled moderately or deeply) have higher death rates than the non-smokers in every cell of Table 18. Since not all respondents answered these supplementary questions, the results may be subject to some additional non-response bias.

As would be expected, death rates are relatively high for men with previous serious disease and for men from short-lived families, and are somewhat

TABLE 18.—*Age-adjusted death rates per 1,000 men (over approximately 22 months) for variables that may be related to mortality*

Type of smoking	Long-lived parents and grandparents	Short-lived parents and grandparents	No previous serious disease	Previous serious disease
None	14.8	21.1	11.5	42.5
Cigarettes [1]	27.1	44.8	22.3	65.0

Type of smoking	Single	Married	Use tranquilizers	Do not use tranquilizers
None	26.0	18.9	29.1	18.2
Cigarettes [1]	50.1	33.0	52.4	31.8

Type of smoking	Educational level				
	No high school	Some high school	High school graduate	Some college	College graduate
None	22.7	20.0	16.9	18.3	15.8
Cigarettes [1]	35.2	34.5	35.5	34.2	29.4

Type of smoking	Degree of exercise [2]			
	None	Slight	Moderate	Heavy
None	23.8	14.7	11.0	9.5
Cigarettes [1]	34.1	25.5	20.8	19.7

[1] Smokers of more than a pack per day who inhaled moderately or deeply.
[2] Confined to men with no history of heart disease, stroke, high blood pressure or cancer (except skin) who were not sick at the time of entry.