Chapter 8

Mortality

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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 ohtained 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 doetors 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.

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).

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	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).

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.*

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.

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.

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.

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 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

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

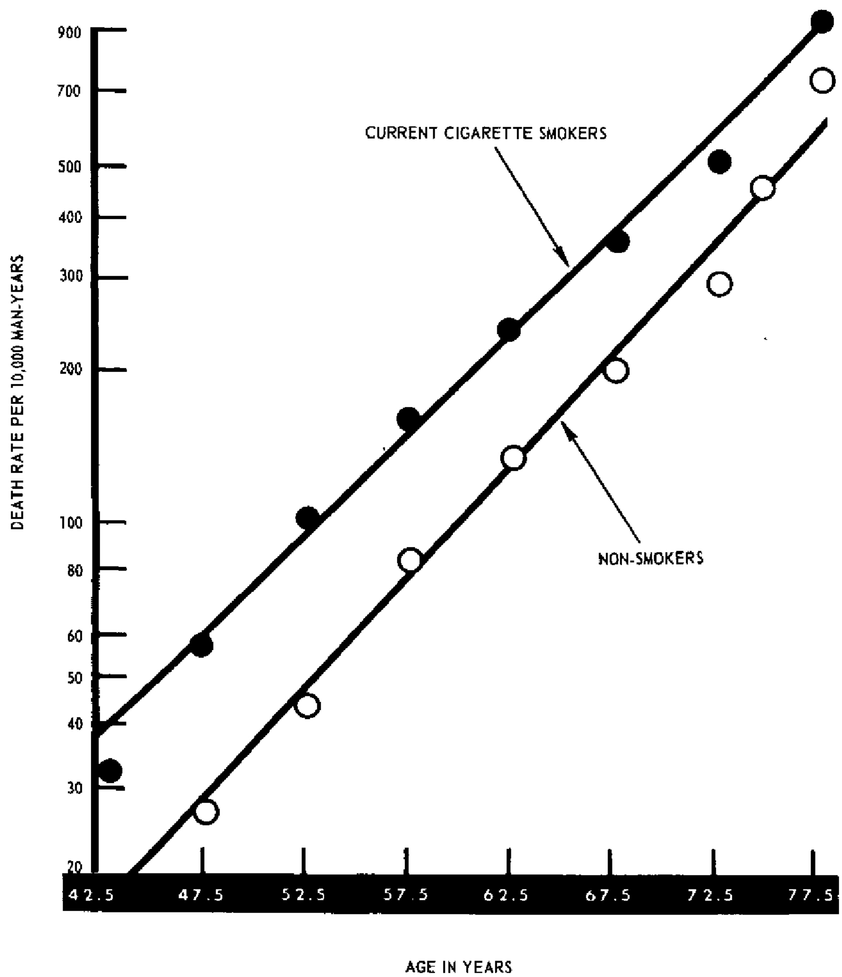

FIGURE 1.

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.

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 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.

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,

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 Rorn (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

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			

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. Tbe 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 l-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.

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 rep-

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	1.36	[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.

resented 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.

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

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.

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.

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 effec s of these amounts of non-response on the mortality ratios have received little discussion. Some pieces of information about

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

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 he 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 AR/(1+hR) where R is the true mortality ratio, *A* 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 he 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
	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.

higher for single than for married men. The size of the excess death rate for users of tranquilizers compared to men who do not use them is perhaps surprising (29.1 against 18.2 and 52.4 against 31.8). However, the tranquilizers in question required a doctor's prescription, so that some men in this group are presumably under medical attention for illness. The group of users is small, comprising only about 10 percent of those who answered this question. Death rates tend to decrease slightly as the educational level increases; this association may represent some facet of the association of death rates with socio-economic level. Degree of exercise displays an interesting association with mortality, the death rate declining steadily with additional degrees of exercise. In particular, the two "no exercise" groups show marked elevations in death rates. These groups, however, amount to only 2 percent of the respondents to this question.

From the same data, Ipsen and Pfaelzer (14) made a further analysis of seven variables that appeared to be related to mortality, in order to see whether any of the variables had a stronger association with mortality than did cigarette smoking. They concluded that apart from previous serious disease, none of the other variables examined had as high a correlation with mortality as smoking of cigarettes. Further, the correlation of any of these other variables with cigarette smoking was too weak to reduce markedly the correlation of cigarette smoking with mortality after adjustment for the other variable.

In the analyses above, smoking was matched against each variable separately. In addition, Hammond (11) carried out a "matched pair" analysis, in which pairs of cigarette smokers and non-smokers were matched on height, education, religion, drinking habits, urban-rural residence and occupational exposure. The percentage who had died in the 22 months was 1.64 for smokers and 0.88 for non-smokers.

These informative analyses are available, unfortunately, for only one of the studies. However, in order that the association of cigarette smoking with mortality should disappear when we adjust for another variable, the correlations of this variable with smoking and with the death rate must both be higher than the correlation between smoking and the death rate.

Except for the breakdowns by longevity of parents and grandparents, the analyses throw little light, however, on the objection that a part of the differences in death rates may be constitutional, psychological or behavioral; i.e., that regular cigarette smokers are the kind of men who would have higher death rates even if they did not smoke. Further discussion of this point appears in the next section.

MORTALITY BY CAUSE OF DEATH

In all seven studies the underlying cause of death, as specified in the International Statistical Classification of Diseases, Injuries and Causes of Death, was abstracted from the death certificate. In the two American Cancer Society studies, further confirmation of the cause of death, including histological evidence, was sought from the certifying physician for all cancer deaths; this procedure was also followed in the British doctors' study for all certificates in which lung cancer was mentioned as a direct or contributory cause. With these exceptions the data presented here represent the results of routine death certification.

For current smokers of cigarettes the total mortality, after adjustment for differences in age composition, was found previously (Table 2) to be about 70 percent higher than that of non-smokers in these studies. The primary objective in this section is to examine whether this percentage increase appears to apply about equally to all principal causes of death, or whether the relative increase is concentrated in certain specific causes or groups of causes.

RESULTS FOR CIGARETTE SMOKERS

For 24 causes of death, plus the "all other causes" category, Table 19 shows summary data over all seven studies.* In four of the studies the data are those for current smokers of cigarettes only, but in the two California studies and the 25-State study the cause-of-death breakdown was available for all cigarette smokers including "cigarette and other" smokers and current and ex-smokers.

For each listed cause, Table 19 shows the total numbers of expected and observed deaths of cigarette smokers summed over all seven studies, and

TABLE 19.—*Total numbers of expected and observed deaths and mortality ratios for smokers of cigarettes only* [1] *in seven prospective studies*

Underlying cause of death	Expected	Observed	Mortality ratio	Median mortality ratio	Non-smoker deaths
Cancer of lung (162-3)	170.3	1,833	10.8	11.7	123
Bronchitis and emphysema (502, 527.1) [2]	89.5	546	6.1	7.5	59
Cancer of larynx (161)	14.0	75	5.4	5.8	8
Cancer of oral cavity (140-8)	37.0	152	4.1	3.9	27
Cancer of esophagus (150)	33.7	113	3.4	3.3	19
Stomach and duodenal ulcers (540-1)	105.1	294	2.8	5.0	67
Other circulatory diseases (451-468)	254.0	649	2.6	2.3	170
Cirrhosis of liver (581)	169.2	379	2.2	2.1	96
Cancer of bladder (181)	111.6	216	1.9	2.2	92
Coronary artery disease (420)	6,430.7	11,177	1.7	1.7	4,731
Other heart diseases (421-2, 430-4)	526.0	868	1.7	1.5	398
Hypertensive heart disease (440-3)	409.2	631	1.5	1.5	334
General arteriosclerosis (450)	210.7	310	1.5	1.7	201
Cancer of kidney (180)	79.0	120	1.5	1.4	59
All other cancer	1,061.4	1,524	1.4	1.4	742
Cancer of stomach (151)	285.2	413	1.4	1.3	203
Influenza, pneumonia (480-493)	303.2	415	1.4	1.6	169
All other causes	1,508.7	1,946	1.3	1.3	1,036
Cerebral vascular lesions (330-4)	1,461.8	1,844	1.3	1.3	1,069
Cancer of prostate (177)	253.0	318	1.3	1.0	198
Accidents, suicides, violence (800-999)	1,063.2	1,310	1.2	1.3	627
Nephritis (592-4)	156.4	173	1.1	1.5	98
Rheumatic heart disease (400-416)	290.6	309	1.1	1.1	185
Cancer of rectum (154)	207.8	213	1.0	0.9	150
Cancer of intestines (152-3)	422.6	395	0.9	0.9	307
All causes	15,653.9	26,223	1.68	1.65	11,168

[1] Current cigarettes only for four studies: all cigarettes (current and ex-) for the two California studies and the study of men in 25 States.

[2] "Bronchitis and emphysema" includes "other bronchopulmonary diseases" for men in nine States and Canadian veterans.

*The individual results for the seven studies are shown for reference purposes in Table 26.

the resulting mortality ratios, arranged in order of decreasing ratios. The combination of the results of the seven studies in this way is open to criticism, since it gives more weight to the larger studies than may be thought advisable, and since the true mortality ratios for specific causes presumably differ somewhat from study to study. However, for some causes of death that are of particular interest the numbers of deaths are small in all studies, so that some procedure for combining the results is highly desirable. As an alternative measure of the combined mortality ratio, the median of the seven mortality ratios (obtained by arranging the seven ratios, in increasing order and selecting the middle one) is also shown for each cause in Table 19. The median, of course, gives equal weight to small and large studies. Although there are some changes in the ordering of the causes when medians are used instead of the ratios of the combined deaths, the general pattern in Table 19 is the same for both criteria.

Table 19 also presents the total numbers of non-smoker deaths on which the combined mortality ratios are based.

Lung cancer shows the highest mortality ratio in every one of the Seven studies, the combined ratio being 10.8. Other causes that exhibit substantially higher mortality ratios than the ratio 1.68 for all causes of death in Table 19 are bronchitis and emphysema, cancer of the larynx, cancer of the oral cavity and pharynx, cancer of the esophagus, stomach and duodenal ulcers, and a rather mixed category labeled “other circulatory diseases,” which includes aortic aneurysm, phlebitis of the lower extremities, and pulmonary embolism. For three of these causes--cancer of the larynx, oral cancer and cancer of the esophagus--the numbers of non-smoker deaths are small, so that the over-all mortality ratio cannot be regarded as accurately determined.

The U.S. veterans’ study and the 25-State study provide an additional breakdown for two of the causes listed in Table 19. For the rubric 527.1 (emphysema without mention of bronchitis), these studies give mortality ratios of 13.1 and 7.5, respectively. For ulcer of the stomach they give 5.1 and 4.3, whereas for ulcer of the duodenum their mortality ratios are 2.3 and 1.1. Bronchitis and emphysema also show a high rate, 12.5, in the British doctors’ study.

There follows a list of 14 causes whose mortality ratios are not greatly different from the ratio of 1.68 for all causes in Table 19. These causes range from cirrhosis of the liver, with a ratio of 2.2, down to a ratio of 1.2 for the miscellaneous class which contains accidents, suicides and violent deaths. This group includes the leading cause of death, coronary artery disease, with a ratio of 1.7, cerebral vascular lesions with a ratio of 1.3, and the “all other causes” group with a ratio of 1.3. For each of these 14 causes the mortality ratio differs from unity, by the approximate statistical test of significance.

Finally, there are four causes--nephritis, rheumatic heart disease, cancer of the rectum and cancer of the intestines--whose mortality ratios are close to unity.

For smokers of cigarettes and other, the data from four studies agree in general with the ordering of causes in Table 19, a lthough the mortality ratios for most causes are slightly lower than with smokers of cigarettes only. These and the corresponding data for ex-cigarette smokers are shown in Table 20.

Data on ex-cigarette smokers can be obtained from four studies. The causes of death with mortality ratios of 2.0 or higher are, in decreasing order, bronchitis and emphysema (7.6), cancer of the larynx (5.4), cancer of the lung (4.8), stomach and duodenal ulcers (3.1), oral cancer (2.0), and other circulatory diseases (2.0).

The group of 17 causes with mortality ratios below 2 in Table 19 requires discussion. If cancer of the bladder (mortality ratio 1.9) and coronary artery disease (mortality ratio 1.7) are omitted, since they receive detailed consideration elsewhere in this report, the numbers of expected and observed deaths for this group as a whole are as follows:

Expected	*Observed*	*Mortality Ratio*
8,241.3	10,789	1.31

If we exclude from this total the four causes at the foot of Table 19, for which the mortality ratios are 1 and smaller, the corresponding totals become:

Expected	*Observed*	*Mortality Ratio*
7,164.0	9,699	1.35

In either case the excess of observed over expected deaths is close to 2,500 or about 25 percent of the total excess in observed deaths in Table 19. Thus, although the mortality ratios for these groups are only moderately over 1, the group as a whole contributes substantially to the total number of excess observed deaths. The group consists mainly of a miscellaneous collection of chronic diseases.

Several tentative explanations of this excess mortality ratio can be put forward. Part may be due to the sources of bias previously discussed. It was indicated in the section on “Non-Response Bias” that the bias arising from non-response might account for a mortality ratio of 1.3. Relatively high mortality ratios in certain causes of death that have not yet been examined individually may also be a contributor, although as these causes are likely to be rare, the contribution from this source can hardly be large.

Part may be due to constitutional and genetic differences between cigarette smokers and non-smokers. Except for the breakdown mentioned previously by longevity of parents and grandparents in the men in 25 States study, there is no body of data available that provides a comparison of cigarette smokers and non-smokers on these factors as they affect longevity. But it is not unreasonable to speculate that the kind of men who become regular cigarette smokers are, to a moderate degree, less inherently able to survive to a ripe old age than non-smokers. We know of no way to make a quantitative estimate of the difference in death rates that might be attributable to such constitutional and genetic factors.

Studies reported in Chapters 14 and 15 indicate that some average differ; ences can be detected between smokers and non-smokers on behavioral, psychological and morphological characteristics. Nevertheless, the same comparisons show considerable overlap between the individual men in a group of smokers and a group of non-smokers. For what they are worth, these com-

TABLE 20.—*Expected and observed deaths and mortality ratios for current smokers of cigarettes and other (three studies)* [1] *and for ex-cigarette smokers (four studies)* [2]

Underlying cause of death	Cigarettes and other			Ex-cigarette		
	Number of deaths		Mortality ratio	Number of deaths		Mortality ratio
	Expected	Observed		Expected	Observed	
Cancer of lung (162–3)	60.9	510	8.4	30.4	145	4.8
Bronchitis and emphysema (502, 527.1) [3]	53.2	191	3.6	17.4	133	7.6
Cancer of larynx (161)	1.6	20	12.5	1.3	7	5.4
Cancer of oral cavity (140–8)	11.1	42	3.8	5.9	12	2.0
Cancer of esophagus (150)	13.1	57	4.4	5.4	6	1.1
Stomach and duodenal ulcers (540–1)	23.0	99	4.3	13.0	40	3.1
Other circulatory diseases (451–468)	99.0	227	2.3	45.8	93	2.0
Cirrhosis of liver (581)	57.3	85	1.5	22.4	27	1.2
Cancer of bladder (181)	58.2	73	1.3	29.8	31	1.0
Coronary artery disease (420)	2,335.0	3,262	1.4	1,245.0	1,731	1.4
Other heart diseases (421–2, 430–4)	225.9	321	1.4	124.1	178	1.4
Hypertensive heart disease (440–3)	144.4	174	1.2	93.0	133	1.4
General arteriosclerosis (450)	106.8	146	1.4	63.7	75	1.2
Cancer of kidney (180)	25.0	37	1.5	13.9	25	1.8
All other cancer	272.9	339	1.2	199.3	239	1.2
Cancer of stomach (151)	101.0	139	1.4	51.4	66	1.3
Influenza, pneumonia (480–493)	199.2	153	0.8	55.1	55	1.0
All other causes	769.3	790	1.0	308.1	357	1.2
Cerebral vascular lesions (330–4)	634.0	605	1.0	300.1	321	1.1
Cancer of prostate (177)	97.1	118	1.2	52.0	57	1.1
Accidents, suicides, violence (800–999)	287.1	316	1.1	169.6	159	0.9
Nephritis (592–4)	30.7	44	1.4	21.7	23	1.1
Rheumatic heart disease (400–416)	96.0	86	0.9	47.9	59	1.2
Cancer of rectum (154)	89.7	64	0.7	43.3	38	0.9
Cancer of intestines (152–53)	149.6	164	1.1	85.8	97	1.1
All causes	5,941.1	8,062	1.4	3,045.5	4,107	1.35

[1] British doctors, U.S. veterans and Canadian veterans.
[2] British doctors, men in nine States, U.S. veterans, and Canadian veterans.
[3] "Bronchitis and emphysema" includes "other bronchopulmonary diseases" for men in nine States and Canadian veterans.

parisons suggest by analogy that the differences in death rates from constitutional or genetic factors may be moderate or small rather than large.* Further, it seems unlikely that constitutional or genetic differences between cigar and pipe smokers and between these groups and non-smokers can have any substantial effect on their death rates, since the over-all death rates of these three groups differ only slightly.

Finally, part of the difference may represent a general debilitating effect of cigarette smoking in addition to marked effects on a few diseases. Pearl's hypothesis that smoking increases the "rate of living" is of this type, though there are difficulties in making this hypothesis precise enough to be subject to medical investigation. Hammond (13) has suggested that the explanation might lie in the effect of cigarette smoking in decreasing the quantity of oxygen per unit volume of blood, but there are numerous medical objections to this hypothesis. This Committee has no information that would lead it to favor one or another of the possible explanations put forward above.

*This question is discussed more fully in Chapter 9, p. 190.

MORTALITY RATIOS FOR CIGARETTE SMOKERS BY AMOUNT SMOKED

For coronary artery disease and lung cancer, the mortality ratios are given by amount smoked in Tables 21 and 22 for current smokers of cigarettes only.

In Table 21 an increasing trend with amount smoked appears in all five studies. The two California studies, in which the data are for all cigarette smokers (current and ex-smokers combined) show a less marked trend.

The trends in lung cancer mortality ratio with amount smoked are steep in all four studies. The two California studies also show marked trends for all cigarette smokers combined.

For the six causes of death (other than lung cancer) that were pointed out in Table 19 as having unusually high mortality ratios, the numbers of deaths permit a breakdown only into two amounts smoked. The results from six studies are shown in Table 23. Data were not available from the

Table 21.—*Mortality ratios for coronary artery disease for smokers of cigarettes only by amount smoked*

Number of packs per day	British doctors	Men in 9 States	U.S. veterans	Canadian veterans	Men in 25 States
<½	1.0	1.2	1.3	1.7	1.3
½-1	1.5	1.9	1.8	1.7	2.0
1-2	[1] 1.7	2.1	1.7	[1] 2.0	2.1
Over 2	----------	2.4	1.9	----------	2.5

[1] More than one pack.

Table 22.—*Lung cancer mortality ratios for current smokers of cigarettes only by amount smoked*

Number of packs per day	British doctors	Men in 9 States	U.S. veterans	Canadian veterans
<½	4.4	5.8	5.2	8.4
½-1	10.8	7.3	9.4	13.5
1-2	[1] 43.7	15.9	18.1	[1] 15.1
Over 2	----------	21.7	23.3	----------

[1] Over one pack.

Table 23.—*Expected and observed deaths and mortality ratios for current cigarette smokers, for selected causes of death, by amount smoked, in six studies*

Causes of death	One pack or less			More than one pack		
	Number of deaths		Mortality ratio	Number of deaths		Mortality ratio
	Expected	Observed		Expected	Observed	
Bronchitis and emphysema	44.6	225	5.0	17.2	147	8.5
Cancer of larynx	3.6	19	5.3	4.1	31	7.5
Cancer of oral cavity	16.8	53	3.2	14.8	60	4.1
Cancer of esophagus	13.2	40	3.0	9.7	48	4.9
Stomach and duodenal ulcers	32.5	110	3.4	31.2	91	2.9
Other circulatory	98.5	253	2.6	60.4	175	2.9
Cancer of the bladder	57.3	80	1.4	23.7	73	3.1

men in the 25-State study. Cancer of the bladder is included in Table 23 as background data for Chapter 9.

All causes except stomach and duodenal ulcers show some increase in the mortality ratio for the heavier smokers. The rate of increase cannot be regarded as accurately determined in view of the small numbers of deaths.

CIGARS AND PIPES

In view of the small numbers of deaths involved, the data for cigar and pipe smokers were combined in Table 24, which lists the total expected deaths, total observed deaths and mortality ratios from five studies (British doctors, U.S. Veterans, Canadian Veterans, and men in 9 and 25 States). Causes of death with relatively high mortality ratios are oral cancer (3.4), cancer of the esophagus (3.2), cancer of the larynx (2.8), cancer of the lung (1.7), cirrhosis of the liver (1.6), and stomach and duodenal ulcers (1.6). It should be noted that all these ratios are based on modest numbers of deaths.

Separate breakdowns by cause of death for cigar-only smokers and for pipe-only smokers are available in only three studies. The numbers of deaths are too few to throw any light on the question whether there are differences between cigar and pipe smokers in the causes of death for which mortality ratios are elevated.

TABLE 24.—*Numbers of expected and observed deaths and mortality ratios for cigar and pipe smokers, in five studies* [1]

Underlying cause of death	Number of deaths: Expected	Number of deaths: Observed	Mortality ratio
Cancer of oral cavity (140–8)	13.5	46	3.4
Cancer of esophagus (150)	10.2	33	3.2
Cancer of larynx (161)	3.2	9	2.8
Cancer of lung (162–3)	66.2	113	1.7
Cirrhosis of liver (581)	47.5	77	1.6
Stomach and duodenal ulcers (540–1)	35.2	56	1.6
Cancer of kidney (180)	30.8	39	1.3
Cancer of intestines (152–3)	174.6	219	1.3
Other circulatory diseases (451–468)	89.1	105	1.2
All other cancer	396.7	456	1.1
Cancer of prostate (177)	127.2	144	1.1
Cancer of stomach (151)	116.8	132	1.1
Cancer of rectum (154)	78.2	88	1.1
Hypertensive heart disease (440–3)	194.5	218	1.1
Other heart diseases (421–2, 430–4)	272.6	303	1.1
Bronchitis and emphysema (502, 527.1)	33.7	37	1.1
Cerebral vascular lesions (330–4)	685.3	720	1.1
Coronary artery disease (420)	2,721.5	2,842	1.0
All other causes	612.9	587	1.0
Influenza and pneumonia (480–493)	93.8	88	0.9
Accidents, suicides, violence (800–999)	347.1	318	0.9
Cancer of bladder (181)	63.1	56	0.9
General arteriosclerosis (450)	124.1	109	0.9
Nephritis (592–4)	63.6	55	0.9
Rheumatic heart disease (400–416)	100.5	69	0.7
All causes	6,500.9	6,919	1.06

[1] Includes British doctors, men in 9 States, U.S. veterans, Canadian veterans, and men in 25 States; includes ex-smokers for men in 9 States; excludes pipe smokers for Canadian veterans.

The Contribution of Different Causes to Excess Mortality

Several of the reports previously published on these studies have included a table showing how the excess number of deaths of cigarette smokers over non-smokers is distributed among the principal causes of death. For each cause, the difference between the observed and the expected number of deaths for cigarette smokers is divided by the total excess for all causes, and multiplied by 100 to express the figures on a percentage basis. Table 25 presents these percentages for the seven studies for 13 groups of causes. A negative percentage, which occurs in a few places in the table, implies that for this cause the observed smoker deaths were smaller than the expected deaths.

As previous writers have noted, all studies agree in showing coronary artery disease as the prime contributor to excess mortality, with lung cancer in second place. Other rubrics that show a substantial contribution in some studies, though not in all, are bronchitis and emphysema, cancers other than those of the mouth and lungs, and heart disease other than coronary.

SUMMARY

This report summarizes the results of the seven major prospective studies of the relative death rates of male smokers and non-smokers.

Total Mortality

Cigarette Smokers

The death rate for smokers of cigarettes only who were smoking at the time of entry is about 70 percent higher than that for non-smokers.

TABLE 25.—*Percentage of total number of excess deaths of cigarette smokers due to different causes* [1]

Underlying cause	British doctors	Men in 9 States	U.S. veterans	California occupational	California Legion	Canadian veterans	Men in 25 States
Coronary artery disease	32.9	51.9	38 6	43.5	43.5	44.2	51.7
Other heart disease	9.8	3.1	6.8	1.4	4.5	5.9	5.5
Cerebral vascular lesions	6.1	4.5	4.9	5.3	6.5	−1.8	3.3
Other circulatory diseases	1.9	2.7	7 1	1.7	0.2	5.6	4 4
Cancer of lung	24.0	13.5	14.9	20.2	16.8	18.3	13 6
Cancer of oral cavity, esophagus, larynx	3.3	2.9	2.7	0.2	3.0	2.2	2.2
Other cancer	−0.2	9.8	8.9	6.3	−2.2	7.2	7.6
Bronchitis and emphysema	9 6	1.1	4.0	1.3	5 6	8.2	3.8
Influenza and pneumonia	−2.4	1 6	0.4	2 4	1 5	1 5	1.5
Stomach and duodenal ulcers	2.7	3 1	1.4	−1.7	2.2	2 9	1.3
Cirrhosis of liver	2 9	1.6	2 5	6.9	2.2	0.8	0.9
Accidents, suicides, violence	0 2	1.2	2 0	8.3	3.7	4.6	0.8
All other causes	9.2	3.0	5.8	4.2	12.5	0.4	3.4
All causes	100.0	100.0	100.0	100.0	100.0	100.0	100.0

[1] All cigarette smokers (current and ex-) for the two California and men in 25 States studies; current cigarette smokers only for the remainder.

TABLE 26.—*Numbers of expected and observed deaths for smokers of cigarettes only, and mortality ratios, each prospective study and all studies*

Cause of death	British doctors			Men in 9 States			U.S. veterans			California occupational		
	Deaths		Mortality ratio	Deaths		Mortality ratio	Deaths		Mortality ratio	Deaths		Mortality ratio
	Expected	Observed		Expected	Observed		Expected	Observed		Expected	Observed	
Cancer of lung (162–3)	6.4	129	20.2	23.4	233	10.0	43.3	519	12.0	8 7	138	15.9
Bronchitis, emphysema (502, 527.1)	4.2	53	12.5	12.8	30	2.3	14.4	141	9.8	2 6	11	4.3
Cancer of larynx (161)	.0	7	---------	1.3	17	13.1	2.4	14	5.8	.0	3	---------
Cancer of oral cavity (140–8)	.0	6	---------	7.8	22	2.8	8.1	54	6.6	7.2	7	1.0
Cancer of esophagus (150)	3.3	7	2.1	2.7	18	6.6	5.2	33	6.4	5.5	4	.7
Stomach and duodenal ulcers (540, 541)	.0	14	---------	12.2	61	5.0	21.5	67	3.1	23.1	12	.5
Other circulatory diseases (451–68)	17.2	27	1.6	19 7	53	2 7	66.4	228	3.4	11.5	18	1.6
Cirrhosis of liver (581)	.0	15	---------	23 5	49	2 1	31.2	111	3.6	14.7	59	4.0
Cancer of bladder (181)	13.9	12	.9	17.2	41	2.4	31.4	55	1.8	2.2	13	6.0
Coronary artery disease (420)	366.9	535	1.5	927.7	1,734	1.9	1,803 3	3,037	1.7	273.9	551	2.0
Other heart diseases (421-2, 430–4)	78.8	115	1.5	72.5	108	1.5	122 2	244	2.0	23.8	24	1.0
Hypertensive heart disease (440–3)	21.0	32	1.5	89.7	107	1.2	138.7	223	1.6	27.2	28	1.0
General arteriosclerosis (450)	21.2	21	1.0	9.1	18	2.0	97.0	163	1.7	.0	5	---------
Cancer of kidney (180)	.0	8	---------	14.0	21	1.5	23.1	34	1.5	.0	10	---------
All other cancer	81.7	73	.9	132 9	230	1.7	315 8	457	1.4	72.1	105	1.5
Cancer of stomach (151)	28.3	31	1.1	33.7	76	2.3	61.5	90	1.5	31.4	24	8
Influenza, pneumonia (480–93)	47.0	35	.7	15.6	41	2.6	22.6	36	1.6	10.3	25	2 4
All other causes	144.0	182	1.3	209.5	263	1.3	354.8	530	1.5	68.9	101	1 5
Cerebral vascular lesions (330–4)	161.1	192	1.2	208.8	279	1.3	309.1	467	1.5	42.2	76	1.8
Cancer of prostate (177)	29.0	15	.5	32.4	51	1.6	53.7	106	2 0	8.6	4	.5
Accidents, suicides, violence (800–999)	89.2	90	1.0	174.1	192	1.1	241.5	306	1 3	108.4	161	1.5
Nephritis (592–4)	8.1	17	2 1	43.3	34	.8	18.6	30	1.6	16.0	10	.6
Rheumatic heart disease (400-16)	10 2	13	1 3	48.4	43	.9	67.4	77	1.1	22.9	31	1.4
Cancer of rectum (154)	4.2	15	3.6	29.8	25	8	68.7	62	.9	13 6	14	1.0
Cancer of intestines (152–3)	26.1	28	1.1	65 6	35	5	121.2	152	1.3	23 7	22	.9
All causes	1,161.8	1,672	1.44	2,227.7	3,781	1.70	4,043.1	7,236	1.79	818.5	1,456	1.78

TABLE 26.—*Numbers of expected and observed deaths for smokers of cigarettes only, and mortality ratios, each prospective study and all studies*—Continued

Cause of death	California Legion			Canadian veterans			Men in 25 States			Total, all studies			Median mortality ratio
	Deaths		Mortality ratio	Deaths		Mortality ratio	Deaths		Mortality ratio	Deaths		Mortality ratio	
	Expected	Observed		Expected	Observed		Expected	Observed		Expected	Observed		
Cancer of lung..................(162-3)	19.9	98	4.9	27.1	317	11.7	41.5	399	9.6	170.3	1,833	10.8	11.7
Bronchitis, emphysema..(502, 527.1)	3.6	30	8.4	36.5	166	4.6	15.4	115	7 5	89.5	546	6.1	7.5
Cancer of larynx..................(161)	4.0	6	1.5	.0	5	----	6.3	23	3.7	14.0	75	5.4	5.8
Cancer of oral cavity..........(140-8)	5.2	10	1.9	5.1	20	3.9	3.6	33	9.2	37.0	152	4.1	3.9
Cancer of esophagus.............(150)	1.8	9	5.1	6.8	22	3.3	8.4	20	2.4	33.7	113	3.4	3.3
Stomach and duodenal ulcers (540, 541)	1.8	12	6.8	7.9	54	6.9	38 6	74	1.9	105.1	294	2 8	5.0
Other circulatory diseases...(451-68)	16 7	37	2.2	41 5	96	2.3	81.0	190	2.5	254.0	649	2.6	2 3
Cirrhosis of liver..................(581)	13.1	23	1.8	37.6	50	1.3	49.1	72	1.5	169 2	379	2 2	2.1
Cancer of bladder.................(181)	1.8	7	4.0	22.3	38	1 7	22.8	50	2.2	111.6	216	1.9	2.2
Coronary artery disease..........(420)	312.8	515	1.7	882.5	1,582	1.8	1,863.6	3,223	1.7	6,430.7	11,177	1.7	1.7
Other heart diseases...(421-2, 430-4)	13.1	26	2.0	75.3	156	2 1	140.3	195	1.4	526.0	868	1.7	1.5
Hypertensive heart disease...(440-3)	24.9	29	1.2	36.2	58	1.6	71.5	154	2.2	409.2	631	1.5	1.5
General arteriosclerosis..........(450)	39.1	20	.5	14.7	48	3 3	29.6	35	1 2	210.7	310	1.5	1.7
Cancer of kidney..................(180)	8.3	6	.7	9.5	13	1.4	24.1	28	1.2	79.0	120	1.5	1.4
All other cancer........................	75.4	84	1.1	104.1	149	1.4	279.4	426	1.5	1,061.4	1,524	1.4	1.4
Cancer of stomach.................(151)	20.5	25	1.2	41.2	76	1.9	68.6	91	1,3	285.2	413	1.4	1.3
Influenza, pneumonia........(480-93)	14.7	22	1.5	135.0	159	1 2	58.0	97	1.7	303.2	415	1.4	1.6
All other causes........................	39.1	94	2.4	361.5	360	1.0	330.9	416	1.3	1,508.7	1,946	1.3	1.3
Cerebral vascular lesions......(330-4)	57.1	87	1.5	294.1	266	.9	389.4	477	1.2	1,461.8	1,844	1.3	1.3
Cancer of prostate.................(177)	22.1	19	9	32.3	48	1.5	74.9	75	1.0	253.0	318	1.3	1 0
Accidents, suicides, violence (800-999)	45.0	62	1.4	101.3	174	1.7	303.7	325	1.1	1,063.2	1,310	1.2	1.3
Nephritis ....(592-4)	.0	3	----	11.6	17	1.5	58.8	62	1.1	156 4	173	1.1	1.5
Rheumatic heart disease.....(400-16)	14.2	18	1.3	48.1	39	.8	79.4	88	1.1	290.6	309	1.1	1.1
Cancer of rectum..................(154)	12.0	9	.8	41.3	24	.6	38.2	64	1.7	207.8	213	1.0	.9
Cancer of intestines............(152-3)	33.2	13	.4	46.6	64	1.4	106.2	81	.8	422.6	395	.9	.9
All causes..............................	799.4	1,264	1.58	2,420.1	4,001	1.65	4,183.3	6,813	1,63	15,653.9	26,223	1.68	1.65

The death rates increase with the amount smoked. For groups of men smoking less than 10, 10-19, 20-39, and 40 cigarettes and over per day, respectively, the death rates are about 40 percent, 70 percent, 90 percent and 120 percent higher than for non-smokers.

The ratio of the death rates of smokers to that of non-smokers is highest at the earlier ages (40-50) represented in these studies, and declines with increasing age. The same effect appears to hold for the ratio of the death rate of heavy smokers to that of light smokers.

In the studies that provided this information, the mortality ratio was substantially higher for men who started to smoke under age 20 than for men who started after age 25. In general, the mortality ratio was increased as the number of years of smoking increased, although the pattern of increase was irregular from study to study.

In two studies which recorded the degree of inhalation, the mortality ratio for a given amount of smoking was greater for inhalers than for non-inhalers.

Cigarette smokers who had stopped smoking prior to enrollment in the study had mortality ratios about 1.4 as against 1.7 for current cigarette smokers. Two studies reported the number of years since smoking was stopped. In these, the mortality ratio declined in general as the number of years of cessation increased. The mortality ratio of ex-cigarette smokers increased with the number of years of smoking and was higher for those who stopped after age 55 than for those who stopped at an earlier age. (These results were available in one study only.)

Taken as a whole the seven studies offer a substantial breadth of sampling of the type of men and environmental exposures to be found in North America and Britain, although none of the groups studied was planned as a random sample of the U.S. male population. All the studies had death rates below those of the U.S. white male population in 1960. To some extent this is to be expected, since men in poor health were likely to be under-recruited in these studies. Only a minor part of these differences in death rates can be attributed to a failure to trace all deaths or to higher death rates among non-respondents in these studies.

The data on smoking status and on amount smoked were subject to errors of measurement, particularly since smoking status was measured only once and some men presumably changed their status after entry into the study. For men designated as current smokers of cigarettes only, our judgment is that the net effect of such errors of measurement is to make the observed mortality ratios relative to non-smokers underestimates of the true mortality ratios.

The studies suffered from a failure to obtain substantial portions of the study populations selected for investigation. For a non-response rate of 32 percent in the prospective studies, calculations based on the available information about the non-respondents indicate that reported mortality ratios lying between 1 and 2 might overestimate the corresponding figure for the complete study population by 0.2 or 0.3. In our judgment these biases can account for only a part of the elevation in mortality ratios found for cigarette smokers (see Appendix I).

In three studies in which the data could be subdivided by size of city, the mortality ratios differed little in the four sizes of communities studied.

In one study numerous other variables that might influence the death rate, such as longevity of parents and grandparents, use of alcohol, occupational exposure and educational level, were recorded. Adjustment for each of these variables individually produced little change in the mortality ratios.

Although similar information from other studies would have been welcome, it is our judgment that the mortality ratios are unlikely to be explained by such environmental, social class, or ethnic differences between cigarette smokers and non-smokers.

Except for the analyses reported above by longevity of parents and grandparents and by previous serious disease, no direct information is available on whether there are basic constitutional differences between cigarette smokers and non-smokers that would affect their longevity. As described elsewhere in this report, differences have been found between cigarette smokers and non-smokers on certain psychological and behavioral variables. However, even for these variables the distributions for cigarette smokers and non-smokers show considerable overlap. It seems a reasonable opinion that the same situation would apply to the constitutional hardiness of cigarette smokers and non-smokers, if it were possible to measure such a variable. This implies that constitutional differences, if they exist, are likely to express themselves in only a moderate difference in death rates.

Cigar Smokers

Death rates are about the same as those of non-smokers for men smoking less than five cigars daily. For men smoking five or more cigars daily, death rates were slightly higher (9 percent to 27 percent) than for non-smokers in the four studies that gave this information. There is some indication that this higher death rate occurs primarily in men who have been smoking for more than 30 years and in men who stated they inhaled the smoke to some degree.

Death rates for ex-cigar smokers were higher than those for current smokers in all four studies in which this comparison could be made.

Pipe Smokers

Death rates for current pipe smokers were little if at all higher than for non-smokers, even with men smoking 10 or more pipefuls per day and with men who had smoked pipes for more than 30 years.

Ex-pipe smokers, on the other hand, showed higher death rates than both non-smokers and current smokers in four out of five studies. The epidemiological studies on ex-cigar and ex-pipe smokers are inadequate to explain this puzzling phenomenon. According to Hammond and Horn (10) and Dorn (6) the explanation may be that a substantial number of cigar and pipe smokers stop smoking because of illness.

MORTALITY BY CAUSE OF DEATH

In the combined results from these seven studies, the mortality ratio of cigarette smokers was particularly high for a number of diseases: cancer of the lung (10.8), bronchitis and emphysema (6.1), cancer of the larynx (5.4), oral cancer (4.1), cancer of the esophagus (3.4), stomach and duodenal ulcers (2.8), and the rubric, 451-468, "other circulatory diseases" (2.6). For coronary artery disease, the mortality ratio was 1.7.

There is a further group of diseases, including some of the most important chronic diseases, for which the mortality ratio for cigarette smokers lay between 1.2 and 2. The explanation of the moderate elevations in mortality ratios in this large group of causes is not clear. Part may be due to the sources of bias previously mentioned or to some constitutional and genetic difference between cigarette smokers and non-smokers. There is the possibility that cigarette smoking has some general debilitating effect, although no medical evidence that clearly supports this hypothesis can be cited. The substantial number of possibly injurious agents in tobacco and its smoke also may explain the wide diversity in diseases associated with smoking.

In all seven studies, coronary artery disease is the chief contributor to the excess number of deaths of cigarette smokers over non-smokers, with lung cancer uniformly in second place.

For cigar and pipe smokers combined, the data suggest relatively high mortality ratios for cancers of the mouth, esophagus, larynx and lung, and for cirrhosis of the liver and stomach and duodenal ulcers. These ratios are, however, based on small numbers of deaths.

APPENDIX I

Appraisal of Possible Biases Due to Non-response

The non-response rates in the prospective studies were approximately as follows: 15 percent for the California occupational study; 15 percent for the U.S. veterans' study during the 3-year period 1957-1959 and 32 percent during the 3-year period 1954-1956: 32 percent for the British doctors' study; and about 44 percent for the California Legion study and the Canadian veterans' study. In forming a judgment about the size of the bias that may be due to non-response, we have concentrated on a non-response rate of 32 percent, since this represents roughly an average figure for these five studies. The objective is to estimate by how much the mortality ratio for the whole population might differ from that found in the respondents.

The only useful information in any detail about the non-respondents comes from the U.S. veterans' study. Table 27 shows data on death rates in 1958 and 1959 (16).

For the present purpose the 1957 respondents will be regarded as a part of the 32 percent of non-respondents to the original questionnaire for whom we are fortunate to have some data.

Table 27 indicates that the non-respondents in 1954 have higher death rates than respondents for both non-smokers and smokers. For non-smokers the ratio of the death rate of 1957 respondents to 1954 respondents was 1.35 in

1958 and 1.27 in 1959. For smokers the corresponding figures are 1.18 in 1958 and 1.14 in 1959.

If the adjusted death rates in Table 27 are weighted by the proportions of men in the population, it is found that the over-all 1958 death rate for 1954 respondents was 17.77 as compared with 19.05 for the complete study population. The ratio 19.05/17.77 is 1.07, so that in 1958 the death rate for the study population was 7 percent higher than for the 1954 respondents. In 1959 the corresponding death rates were 17.46 for 1954 respondents and 18.31 for the complete population, the ratio being 1.05. These ratios agree with Doll's judgment (4) that in the British doctors' study the death rate in the complete population may exceed that in his 68 percent of respondents by from 5 percent to 10 percent.

Comparison of the 1954 and 1957 respondents also suggests that the non-respondents in 1954 contain a higher proportion of smokers than the respondents. In the 1954 respondents,non-smokers contributed 183,094 person-years of experience during 1957-1959 as compared with 179,750 person-years for current smokers of cigarettes only, non-smokers representing 50.6 percent of the total of the two groups. Among the 1957 respondents the corresponding figure was 46.8 percent. A further decline may have occurred in the non-respondents to the 1957 questionnaire.

From these data the following assumptions were made in investigating the non-response bias as it affects the mortality ratio of current smokers of cigarettes only.

1. The proportions of the relevant groups in the complete population are as follows:

This assumes that in the 68 percent of respondents, non-smokers constitute 50 percent of non-smokers plus cigarette smokers, but in the non-respondents this figure has dropped to 44 percent.

TABLE 27.—*Age-adjusted death rates (per 1,000 person-years) for 1954 respondents, 1957 respondents, and non-respondents in U.S. veterans study*

Groups		Proportion in population	Death rates	
			1958	1959
1954 respondents	Non-smokers	0.17	13.29	12.84
	All smokers	.51	19.26	19.00
1957 respondents	Non-smokers	.04	17.96	16.37
	All smokers	.13	22.67	21.61
Non-respondents	All	.15	21.99	19.84

Groups	Non-smokers	Cigarette smokers	Total
Non-respondents	0.14	0.18	0.32
Respondents	.34	.34	.68
Complete population	.48	.52	1.00

2. The death rate in the complete population is 10 percent higher than in the respondents.

3. One further numerical relationship is needed in order to obtain concrete results. For this, the computations were made under two different sets of assumptions. The more extreme (3a) is that cigarette smokers have no higher death rates among non-respondents than among respondents. The alternative (3b) is that the death rate of cigarette smokers was 10 percent higher among non-respondents than among respondents. Both sets of assumptions seem more extreme than the indications from the U.S. veterans' study in which, as already noted, the smoker death rates were 18 percent and 14 percent higher among 1957 respondents than among 1954 respondents.

For total mortality, the calculations of most interest are those for a mortality ratio of 1.7 among the respondents, since this is the average ratio found in the prospective studies for smokers of cigarettes only. For individual causes of death, however, the mortality ratios among respondents range from 1 to 10, so that calculations were made for a series of different mortality ratios among respondents. Table 28 illustrates the calculations made on assumptions (3a) and (3b) for a mortality ratio of 1.7 among respondents.

Thus, the mortality ratio drops from 1.7 to 1.36 in the complete population under assumption (3a) and to 1.48 under assumption (3b). One consequence of assumption (3a) is that the mortality ratio of cigarette smokers among the non-respondents is less than 1.

Table 29 shows the results obtained for a range of mortality ratios in the respondent population.

For the high mortality ratios the assumptions may appear unduly extreme. For instance, under assumption (3a) with mortality ratio 10.0 in the respondents, the non-smoker death rate in the non-respondents has to be 3.6 times

TABLE 28.—*Illustration of calculation of non-response bias*

Assumption (3a)

	Mortality ratios		
	Non-smokers	Cigarette smokers	
Non-respondents	[4] (1.865)	1.700	[3] (1.772)
Respondents	1.000	1.700	[1] (1.350)
Complete population	[5] (1.252)	[6] (1.700)	[2] (1.485)
M.R.	[7] (1.36)		

Assumption (3b)

	Mortality ratios		
	Non-smokers	Cigarette smokers	
Non-respondents	[4] (1.646)	1.870	[3] (1.772)
Respondents	1.000	1.700	[1] (1.350)
Complete population	[5] (1.188)	[6] (1.759)	[2] (1.485)
M.R.	[7] (1.48)		

The figures without parentheses in the mortality ratio tables represent the start of the computations. The indexes ([1] [2] etc.) show the order in which other figures are computed. For assumption (3a):

(1.350) [1] $=[(0.34)(1.000)+(0.34)(1.700)]/(0.68)$
(1.485) [2] $=(1.1)(1.350)$
(1.772) [3] $=[(1.485)-(0.68)(1.350)]/(0.32)$
(1.865) [4] $=[(0.32)(1.772)-(0.18)(1.700)]/(0.14)$
(1.252) [5] $=[(0.14)(1.865)+(0.34)(1.000)]/(0.48)$
(1.700) [6] $=[(0.18)(1.700)+(0.34)(1.700)]/(0.52)$
(1.36) [7] $=1.700/1.252$

that in the respondents, although the smoker death rates are assumed the same in respondents and non-respondents.

It may be of interest to quote Berkson's (1) example in the same form (Table 30).

In their general direction, Berkson's assumptions are similar to those made in this Appendix, but the differences in death rates between respondents and non-respondents were more extreme in his example. The death rate in the complete population (3.000) was 42 percent higher than the respondent death rate. The non-smoker death rate was over 38 times as high among non-respondents as among respondents (60.121 / 1.553), whereas among the smokers it was only 1.8 times as high. His calculations referred to the early years of a study, in which the effects of differential entry of ill persons among smokers and non-smokers are likely to be most marked. Further, as we interpret his writing, the example was intended as a warning against the type of subtle bias that can arise whenever a study has a high proportion of non-respondents, rather than a claim that this numerical estimate of the bias actually applied to these studies.

To summarize, the amounts of non-response in prospective studies could have produced sizable biases in the estimated mortality ratios. Taking assumption 3b in Table 29, as representing fairly extreme conditions, it appears that a reported mortality ratio between 1 and 2 might overestimate by 0.3, a ratio of 5.0 by 1.0 and a ratio of 10.0 by 3.0.

TABLE 29.—*Mortality ratios in respondents and computed values for the complete population*

In respondents (68 percent)	In complete population	
	Assumption (3a)	Assumption (3b)
1.2	1.00	1.06
1.4	1.14	1.23
1.6	1.28	1.40
1.8	1.43	1.56
2.0	1.57	1.73
5.0	3.43	4.07
10.0	5.65	7.41

TABLE 30.—*Proportions and death rates for Berkson's example*

Group	Proportions			Death rates		Total
	Non-smokers	Smokers	Total	Non-smokers	Smokers	
Non-respondents	0.00494	0.28360	0.28854	60.121	4.217	5.174
Respondents	.19506	.51640	.71146	1.553	2.332	2.118
Total	.20000	.80000	1.00000	3.000	3.000	3.000

APPENDIX II

STABILITY OF MORTALITY RATIOS

In computing the mortality ratio of a group of smokers to a group of non-smokers, each group is subdivided into age-classes (usually 5-year). For the ith age-class let y_i denote the number of smoker deaths and x_i the number of non-smoker deaths. The "expected" number of smoker deaths in the ith class (expected on the assumption that smokers have the same age-specific death rates as non-smokers) is

summed over the age-classes.

In the interpretation of the values of R found in the seven studies, much weight has been given to the consistency of the values from one study to another, on the grounds that if the values of R for a particular cause of death are high in all seven studies, this evidence is more impressive than R values that are high in say, three studies but show no elevation in the remaining four studies. As a consequence, the question whether the value of $\hat{R}$ in an individual study is significantly above unity, in the technical sense of this term, becomes less important. Nevertheless, an answer to this question is occasionally useful in the analysis. Moreover, for some causes of death the total numbers of deaths, even when all seven studies are combined, are small enough so that a measure of the stability of the combined $\hat{R}$ is needed.

Assumptions

In attempting to get some idea of the stability of $\hat{R}$ without too much complexity, the following assumptions will be made.

1. The numbers of deaths y_i and x_i are distributed as Poisson variables. As Chiang (3) has shown, a more accurate assumption is to regard y_i and x_i as binomial numbers of successes. But with causes of death for which the probability of dying in a 5-year age span is very small the Poisson assumption, which is slightly conservative, is reasonable.

2. The quantities λ_i can be regarded as known constants. This is not quite correct. Initially, the λ_i are the ratios of the numbers of smokers to non-smokers in the age-classes, which can reasonably be regarded as given. In subsequent years, however, the numbers are depleted by deaths, and the number of deaths is a random variable. When death rates are small, however, this assumption should introduce little error.

3. The variates y_i and y_j are uncorrelated. An error in the age assigned to a death, putting it in the wrong age-class, induces a negative correlation between y_i and y_j. The existence of such errors should have no effect on

$$\frac{\text{(Person-years for smokers in class i)}}{\text{(Person-years for non-smokers in class i)}} x_i = \lambda_i x_i \qquad \text{(say)}$$

The estimated mortality ratio $\hat{R}$ is defined as

$$\hat{R} = \frac{\Sigma y_i}{\Sigma \lambda_i x_i} \tag{1}$$

the variance ascribed to Σy_i on the assumption of independence. The same remarks apply to the assumption that x_i and x_j are uncorrelated.

4. The variates x_i and y_i are uncorrelated. An error in assigning a death to the correct smoking category would induce a negative correlation between x_i and y_i. Such errors should of course not be allowed to happen, since they vitiate the comparison of the death rates that is the main point of the study, but occasional errors of this type may have occurred.

With these assumptions the numerator Σy_i of $\hat{R}$ follows a Poisson distribution. The denominator $\Sigma \lambda_i x_i$ is a linear function of independent Poisson variates, and numerator and denominator are independent of one another. The exact distribution of a ratio of this type has not been worked out. Two approximate methods of obtaining confidence limits for the true mortality ratio $\hat{R}$ will be given. Confidence limits are presented rather than the standard error of $\hat{R}$ because the distribution of $\hat{R}$ is skew when the numbers of deaths are moderate or small, so that the standard error is harder to interpret.

The Binomial Approximation

If the λ_i can be regarded as approximately constant ($=\lambda$, say) then $\hat{R}$ becomes of the form $y/\lambda x$, where y and x are independent Poisson variates. Since λx then represents the expected number of deaths of the smokers, the quantity λ is estimated as the ratio of the expected number of smoker deaths to the number of non-smoker deaths.

By a well-known result it follows that $x/(y+x)$, the ratio of non-smoker deaths to smoker plus non-smoker deaths, is distributed as a binomial proportion with

where R is the true mortality ratio. Confidence limits for R are found from those for p.

Example. For the study of men in 25 States, the figures for lung cancer for cigar and pipe smokers are as follows:

Hence, $\lambda = 9.71/16 = 0.607$ and the binomial ratio is $16/31 = 0.516$. Hald's (9) table of the 95 percent two-tailed confidence limits of the binomial distribution gives 0.331 and 0.698 as the confidence limits for p. Those for R are given by the relation

This yields 0.7 and 3.3 as the 95 percent limits for R. Since the lower limit, 0.7, is less than unity, the estimated $\hat{R}$, 1.5, is not significantly above unity.

n = number of trials = $y + x$
p = probability of success = $1/(1+\lambda R)$

	Non-smokers	Smokers	
	Observed	Observed	Expected
Number of deaths	16(x)	15(y)	9.71(λx)

$$R = (1-p)/\lambda p$$

Unfortunately the assumption that λ_i is constant is not true in these studies. For instance, in the study of men in 25 States λ_i has the value 3.85 for cigarette smokers aged 45-49 and declines steadily with increasing age to a value of 0.96 for men aged 75-79. For cigar and pipe smokers the fluctuation in γ_i with age is less drastic but is still noticeable.

The Normal Approximation

This approach avoids the assumption that the λ_i are constant, but makes other assumptions that are shaky with small numbers of deaths. If R is the true mortality ratio, the quantity

$$y - Re$$

where $e = \Sigma\lambda_i x_i$ is the expected number of smoker deaths, will follow a distribution that has mean zero. If μ_i, m_i, denote the true means of y_i and x_i, respectively, the variance of (y-Re) is

The basis of this approximation is to regard the quantity

as normally distributed with zero mean, since y_i and x_i are regarded, as previously, as independent Poisson variates. The 95 percent confidence limits for R are then obtained, by a standard device, by setting the absolute value of this quantity equal to 1.96 and solving the resulting quadratic equation for R.

Since the μ_i and the m_i are unknown, a further approximation is to substitute y as an estimate of $\Sigma\mu_i$ and $\Sigma\lambda_i^2 x_i$ as an estimate of $\Sigma\lambda_i^2 m_i$.

Example. For the example previously discussed the data are as follows:

On squaring (2), the quadratic equation becomes

The roots are found to be 0.7 and 3.4, in good agreement with the limits 0.7 and 3.3 given by the binomial approximation. This agreement is better than will usually be found with small numbers of deaths.

The following are 4 comparisons of the confidence limits for cigarette smokers in the same study.

$$\Sigma(\mu_i + R^2\lambda_i^2 m_i)$$

$$\frac{y - Re}{\sqrt{\Sigma(\mu_i + R^2\lambda_i^2 m_i)}} \quad (2)$$

$$y=15: e=9.71: \Sigma\lambda_i^2 x_i=6.059$$

$$(15-9.71R)^2=3.84(15+6.059R^2)$$

Cause of death	Number of deaths: Non-smokers observed	Cigarette smokers: Observed	Cigarette smokers: Expected	Mortality ratio	95 percent limits: Binomial	95 percent limits: Normal
Cancer of lung	16	399	41.20	9.7	(5.0, 14.5)	(5.0, 21.4)
Emphysema	7	115	15.31	7.5	(3.5, 18.1)	(4.0, 40.0)
Cancer of rectum	16	64	38.42	1.7	(1.0, 3.3)	(1.0, 3.6)
Influenza and pneumonia	29	97	58.01	1.7	(1.1, 2.6)	(1.1, 2.9)

The lower confidence limits agree well, but the upper limit runs higher for the normal approximation. For cigarette smokers the normal method is perhaps more accurate. The binomial method has some advantage in simplicity.

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