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 only 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, although 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 differences 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.

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.

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 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.

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		Mortality ratio
	Expected	Observed	
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)	65.2	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.

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.

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.

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.

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 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

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

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:

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

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.

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.

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):

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

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 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).

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

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 the 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.

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

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

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

$$\hat{R} = \frac{\Sigma y_i}{\Sigma \lambda_i x_i} \qquad (1)$$

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

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

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

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:

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

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

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

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.

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

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

The basis of this approximation is to regard the quantity

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

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:

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

On squaring (2), the quadratic equation becomes

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

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.

Cause of death	Number of deaths			Mortality ratio	95 percent limits	
	Non-smokers observed	Cigarette smokers			Binomial	Normal
		Observed	Expected			
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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