Mortality in Relation to Smoking: Ten Years' Observations of British Doctors

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In previous papers (Doll and Hill, 1954, 1956) we have described how at the end of October 1951 we sent a short and simple questionary to the 59,600 men and women whose names were on the current British *Medical Register* and who were then resident in the United Kingdom. In addition to giving name, address, and age, they were asked to say whether (*a*) they were, at that time, smokers of tobacco, (*b*) they had previously smoked but had given up, or (*c*) they had never smoked regularly (which we defined as having never smoked as much as one cigarette a day, or its equivalent in pipe tobacco or cigars, for as long as one year). The smokers and ex-smokers were asked the age at which they had started smoking, the amount that they smoked, and the method by which they smoked either at the time of reply or when they last gave up, and, when appropriate, the age at which they had stopped.

We deliberately limited our inquiries to these very few questions, partly to encourage a large number of answers and partly because we believed that these were questions that could be answered with reasonable accuracy. For such reasons we did not ask for a life-history of smoking habits nor did we, at that time, inquire into the habit of inhaling.

Data

To this request we had 40,637 replies sufficiently complete to be used—34,445 from men and 6,192 from women. From a 1 in 10 random sample of the register that we subsequently drew and analysed we estimate that these figures represent answers from 69% of the men and 60% of the women alive at the time of the inquiry.[1] (These numbers differ slightly from those we published in 1956 ; from answers to our second questionary (see below) we learned that we had allotted the wrong sex to a few subjects and had included a few forms that had come from relatives who were not doctors.)

Selective Sample

We may feel sure that the doctors who chose to answer were not representative of the total. The seriously ill would have been unable to respond, and thus, as we showed in our previous paper, the mortality of the group who replied would be, at least for a time, abnormally low. In fact, using the 1 in 10 sample as a basis, we calculated that the standardized death rate of those who replied to us had been only 63% of the death rate for all doctors in the second year of the inquiry, and 85% in the third year. In the fourth to tenth years the proportion varied about an average of 93%, and there was no evidence of any regular change with the further passage of years. Evidently the effect of selection did not entirely wear off, but after the third year it had become slight.

One factor in this favourable mortality is the presence among those who replied of a relatively large number of non-smokers and a relatively small number of heavier cigarette smokers. This feature, which we previously suspected, can now be shown from a small inquiry we undertook in 1961. We then drew two small samples of (*a*) those who *had* replied to us in 1951 and (*b*) those who had *not*. Eliminating those who had died between 1951 and 1961 we had 267 previous "answerers" and 213 previous "non-answerers." We asked them their smoking habits in 1961, and 261 (98%) of the answerers and 179 (84%) of the non-answerers responded. Comparison of these two groups shows 21% (answerers) and 6% (non-answerers) as non-smokers and 15% (answerers) and 28% (non-answerers) as moderate or heavy cigarette smokers (15 or more daily). While these differences are large and must contribute measurably to the continuing favourable mortality of the group that replied in 1951, they are unlikely to account for it wholly. As a further factor we suspect (but obviously cannot prove) that there may be some more general association between mortality and the tendency not to reply to such an inquiry—whether the tendency be due to a deliberate refusal (which is rare) or a mere neglect of these things (which is frequent). In this respect it is perhaps not too fanciful to note that one non-replier died of smallpox and another of diabetic coma.

Second Questionary

According to the doctors' replies in 1951 we allocated them to the appropriate non-smoking or smoking groups (subdivided by manner and amount, continuing or stopped). Our previous calculations of their subsequent death rates were based upon the number of persons in each of those groups at that time. We knew nothing about any subsequent change of smoking habits, either in the dead or in the living, and the further we moved from 1 November 1951 the more likely it was that changes in habits had occurred. In particular, it was probable that a large number of doctors had given up cigarette smoking. We therefore decided to approach again all the survivors of those who had previously replied, and, taking advantage of this opportunity, we added questions on: (1) the past use of cigarettes by pipe and cigar smokers, and (2) inhaling (a factor that had since become prominent in argument). Allowing for repeated inquiries, we sought answers from men between

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[1] This sample was not quite representative of the total to whom we wrote, since we drew it some months later and by then some of the original population would have been removed from the *Register* by death and other causes ; no other names had, however, been added and the error is small.

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1 November 1957 and 31 October 1958, and from women between 1 November 1960 and 31 October 1961.

Between the issue of our first and second questionaries 2,579 of the men and 320 of the women had died ; seven men had been struck off the *Register,* and these we omitted. Of the remaining 31,859 men and 5,872 women, all but 2% replied to our second approach. Of the 651 men and 122 women who did not do so, 182 (28%) and 24 (20%) died within the year of inquiry or were reported to be too ill ; 433 (67%) and 90 (74%) could not be traced or would make no reply ; and a very small number (36 men and 8 women) refused to answer.

Fortunately, these 2% are not wholly lost to us as they would be in a first approach. We can retain them under their 1951 habits, and, in view of their small number, do so without appreciable error.

Deaths

Through the courtesy of the Registrars-General in the United Kingdom, a form with particulars of the cause of death has been provided to us for every death since November 1951 identified as referring to a medically qualified person. We have also obtained lists of deaths notified to the General Medical Council and of those recorded by the British Medical Association, and we have sought information from the records of the fighting Services and from other sources at home and abroad. A few deaths came to light from our second questionary. As a result of these several approaches we believe that very few deaths can have been missed. In fact, combining their total numbers appropriately with our 10% sample of non-repliers gives us a mortality rate for all British doctors which is 93% of the corresponding mortality of all males in England and Wales. This figure compares well with the standardized mortality ratio of 89% that the Registrar-General gives for doctors aged 20–64 and 65–74 years in his Occupational Mortality Supplement for 1949–53.

In total, in the ten years to which this paper relates (1 November 1951 to 31 October 1961) there have been 4,597 deaths of men and 366 deaths of women. (Preliminary data for the eleventh year give another 472 deaths of men and 48 deaths of women, and these will also be used for analyses where the numbers would otherwise be too few.) Except for deaths attributed to cancer of the lung, we have accepted without further inquiry the certified cause of death, and (unless otherwise mentioned) have classified these deaths according to the specified underlying causes. In only one case have we failed to obtain any evidence of the cause of death.

Cancer of the lung was given as the underlying cause in 216 men and 7 women and as a contributory cause in 6 men. For each of these deaths we sought confirmation of the diagnosis from the doctor who certified the death, and, when necessary, from the consultant to whom the patient had been referred. We thus obtained information on the nature of the evidence in all but one case. As a result we have accepted 212 deaths from carcinoma of the lung in men (5 being contributory causes) and 6 in women, and we have rejected 10 in men and 1 in a woman.[2] The 10 deaths of men we have reclassified, on the information given, to cancer of the stomach, cancer of the bladder, cancer of the rectum, cancer of the trachea, peripheral neuritis, atheroma of the aortic valves, collapse of lung, heart failure, and (in two cases) cancer primary site unknown ; while these last two may have been primary carcinomas of the lung, the evidence was lacking. With the woman, the histological report was sarcoma of the lung (the specimen had been lost and could not be reviewed). All these reclassifications were made on the advice of a colleague (Dr. J. R. Bignall), who had no knowledge of the smoking history of the patient.

A further 16 deaths of men and 1 of a woman were attributed to cancer of the lung in the 11th year of the study: in each case further information was obtained and the diagnosis was accepted.

Method of Analysis

Use of Questionaries

It is important to remember that we can use the information given by our second questionary only prospectively from 1 November 1958. For example, we may find that a doctor cut down from the 30 cigarettes a day he reported at 1 November 1951 to 10 a day soon after and remained at that level. We can use that information to see what happens to him (and similar persons) *after 1 November 1958* ; but we cannot change his group from the earlier date when he changed his habits, since we have no such information for doctors who died between 1951 and 1958. We cannot adjust the denominators of the death rates when we are unable to adjust the numerators. In particular we can study the effects of inhaling only in the events that reveal themselves after 1 November 1958. On the other hand, the increase in the number of doctors who reported giving up smoking is immediately valuable in that if we know that a doctor stopped smoking in 1952 we can at 1 November 1958 begin to measure the effects of having stopped for six years.

As a result of these features we can analyse the data in three ways: (A) we can relate the deaths of the whole ten years to the smoking habits as recorded in the 1951 questionary ; (B) we can relate the deaths reported during the first seven years to the smoking habits recorded on the first questionary (1951) and the deaths of the last three years, 1958 to 1961, to the smoking habits recorded on the second questionary (1957 to 1958) ; and (C) we can relate the deaths of the last three years, 1958 to 1961, to the information recorded *only* on the second questionary.

In considering whether to adopt the simplicity of method A or the slightly more complex method B we have studied the changes reported in smoking habits (Tables 1, 2, and 3). Table 1 shows the changes in the *method* of smoking ; the main features are: (1) 75% of the population had not changed ; (2) only 3% of non-smokers had started smoking but 12% of ex-smokers had restarted ; (3) 19% of smokers had given up, and the proportion is much the same for the various methods of smoking.

TABLE 1.—*Method of Smoking in* 1951 *and* 1958. *Men*

Habits in 1951	Habits in 1958					Total
	Non-smokers	Ex-smokers	Current Smokers			
			Pipe or Cigar	Cigarette and Other	Cigarette Only	
Non-smokers ..	5,272	—	54	13	100	5,439
Ex-smokers ..	—	4,247	207	65	293	4,812
Current smokers : Pipe or cigar ..	—	707	2,575	213	118	3,613*
Cigarette and other ..	—	520	629	2,083	570	3,802
Cigarette only	—	2,840	641	787	9,274	13,542
Total ..	5,272	8,314	4,106†	3,161	10,355	31,208

* Including 153 cigar. † Including 608 cigar.

In examining changes in the *amount* of smoking (Table 2) we may regard a smoker's change of 1 to 4 cigarettes a day (or the equivalent in pipe tobacco) as being a negligible movement, probably well within the error of reporting. On this basis 69% of the men had not changed their habits, 23% had reduced their smoking (including those who gave up entirely), and 8% had increased it (including those who started or recommenced).

Of *pure cigarette smokers* in 1951 (men who were smoking only cigarettes and were not known to have smoked pipes or cigars regularly in the past), 64% were still smoking approximately the same—that is, remained in the same or an adjacent category—2% had increased their smoking, 29% had decreased

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TABLE 2.—*Amount of Smoking in* 1951 *and* 1958. *Men (all Forms of Smoking)*

Habits in 1951	Habits in 1958									
	No Tobacco	Some Tobacco (g./Day)								Total
		Reduced by				No Change	Increased by			
		15 or More	10–14	5–9	1–4		1–4	5–9	10–14	15 or More	
Non-smokers	5,272						67	47	24	29	5,439
Ex-smokers	4,247						135	144	122	164	4,812
Smokers of (g./day):											
1–4	591				139	473	242	68	21	35	1,569
5–9	808			115	487	938	322	154	53	32	2,909
10–14	854		60	436	569	1,439	376	289	98	38	4,159
15–19	629	27	190	427	394	1,504	289	244	67	31	3,802
20–24	677	131	290	453	300	1,991	160	216	128	39	4,385
25+	508	392	336	373	162	1,832	153	183	116	78	4,133
Total	13,586	550	876	1,804	2,051	8,177	1,744	1,345	629	446	31,208

TABLE 3.—*Pure Cigarette Smokers in* 1951 *and Their Smoking Habits in* 1958. *Men*

Habits in 1951 (No. Smoked per Day)	Habits in 1958									Total
	Stopped Smoking	Changed to Pipes and/or Cigars	Continued Smoking Cigarettes No. per Day							
			1–4	5–9	10–14	15–19	20–24	25+	Total	
1–4	328	31	301	65	18	11	8	3	406	765
5–9	481	72	171	495	101	25	19	5	816	1,369
10–14	550	120	125	280	920	188	88	23	1,624	2,294
15–19	438	101	59	156	240	1,056	191	79	1,781	2,320
20–24	557	163	54	87	268	213	1,753	316	2,691	3,411
25+	397	130	31	43	90	149	222	2,027	2,562	3,089
Total	2,751	617	741	1,126	1,637	1,642	2,281	2,453	9,880	13,248*

* This total is less than the total of men smoking only cigarettes shown in Table I since it excludes 294 men who were known to have smoked pipes or cigars regularly at some previous time.

(including those who had given up), and 5% had changed to pipes and/or cigars (Table 3).

We have, secondly, to consider that we have seven years of deaths to place against the 1951 habits and only three years of deaths against the revised 1958 habits. When this and the magnitude of the changes in habits are both taken into account it is not surprising to find that the principal results of the inquiry are practically the same irrespective of whether we use method A or method B. We have therefore used the simpler method A throughout except (1) for the analysis of the effects of giving up smoking when method B is the method of choice, and (2) for the analysis of the effects of inhaling when method C must be employed.

Calculation of Rates

For each of the subgroups defined by smoking habits, sex, and age we have calculated the number of person-years of exposure between 1951 and 1961 (as described in our 1956 paper). On this basis we have calculated sex and age specific death rates from the different causes of death. By applying these specific rates to the 1956 male population of England and Wales (as given by the Registrar-General) we have calculated standardized death rates at all ages.

Mortality Among Male Doctors

Principal Comparisons

By such means we can compare the mortality from all causes and from separate causes among: (1) smokers and lifelong non-smokers, (2) cigarette smokers and pipe smokers, (3) smokers who had given up before 1 November 1951 and those who were continuing to smoke at that date, and (4) those who smoked different daily numbers of cigarettes or different quantities of pipe tobacco. The results for male doctors are presented in Tables 4 to 24. Study of the mortality among men who had stopped smoking for different lengths of time and among men with different inhaling habits is made later (see p. 1407). Analysis of the mortality among women is also deferred (see p. 1409), since the deaths (366) are too few to allow similar detailed comparisons.

All Causes

The total mortality rate was 19% higher among smokers (*14.32*[3]) and 28% higher among cigarette smokers (*15.38*) than among non-smokers (*12.06*). In contrast, the mortality among men who had smoked only pipes or cigars and were not known to have smoked cigarettes (*12.23*) was only 1% greater than among the non-smokers. As would be anticipated from these data the mortality among men who were known to have smoked cigarettes as well as pipes or cigars—referred to subsequently as mixed smokers—was intermediate between the figures for the two separate types (*13.34*). Very few doctors in Britain have smoked only cigars, and the rate for men in this category in 1951 (*10.78*) is based on the experience of only 127 men and may therefore not be very accurate (95% confidence limits 6.57 and 14.99).

Among cigarette smokers the rate was substantially higher among those who were still smoking at 1 November 1951 (*16.32*) than among those who had given up (*12.68*), and among the continuing smokers there was a progressive increase in mortality from those smoking 1–14 a day (*14.44*) to those smoking 15–24 a day (*15.47*) and to those smoking 25 or more cigarettes a day (*19.67*). Among the last group the mortality was 63% greater than that of the lifelong non-smokers and 55% greater than that of men who had smoked cigarettes but, at 1 November 1959, had given up. (The rates quoted above can be found in the bottom lines of Tables 23 and 24.)

The numbers of deaths in most of these categories are so large that tests of statistical significance are hardly necessary.

[3] All the mortality rates referred to are rates per 1,000 persons per year and are standardized for age unless stated otherwise.

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As would be expected, there are highly significant differences ($P<0.001$) between non-smokers and all smokers, non-smokers and all cigarette smokers, cigarette smokers and pipe and/or cigar smokers, ex- and continuing cigarette smokers, and light and heavy cigarette smokers. In contrast the differences between non-smokers and pipe or cigar smokers and between non-smokers and ex-cigarette smokers are not significant ($P>0.05$).

While the simplest interpretation of these differences is that cigarette smoking is an important factor contributing to death, it is not the only possible explanation. We must consider whether smoking habits may be determined by the presence of disease or whether they are not associated with some other factor, environmental or constitutional, to which the cause of death is more directly related. For example, a man who suspects that he has developed a fatal disease is unlikely to quit smoking; therefore men who have recently given it up may form a relatively healthy group. Again, men who drink heavily tend also to be heavy smokers, and any mortality attributable to alcoholism will accordingly tend to raise the mortality of heavy smokers above that of non-smokers.

These figures for total mortality should not, therefore, be interpreted until the mortality of each of its principal disease components has been separately studied.

Cancer of the Lung

Mortality from cancer of the lung is examined in Tables 4 to 11, where we have included the five deaths for which cancer of the lung was mentioned on the death certificate as contributory with the 207 in which it was given as the underlying cause.[4] Many of the rates, however, are based on small numbers, and although they may contribute usefully to the general picture they cannot be relied on individually. In spite of this there is a steadily rising death rate with increasing consumption of cigarettes at every age above 45 years (Table 4). For all ages a more detailed analysis in Fig. 1 indicates a linear relationship, the death rate rising step by step from the *0.07* per 1,000 in non-smokers to *3.15* per 1,000 per annum in men smoking 35 or more cigarettes daily.

TABLE 4.—*Age and Number of Cigarettes Smoked: Death Rates Per 1,000 Per Annum from Cancer of the Lung (Numbers of Deaths in Parentheses)*

Age	Non-smokers	Cigarettes per Day*		
		1–14	15–24	25+
35–44	0·05 (1)	0·07 (1)	0·00	0·11 (1)
45–54	0·00	0·31 (3)	0·62 (9)	0·75 (8)
55–64	0·00	0·48 (3)	2·31 (20)	3·88 (26)
65–74	0·00	2·69 (9)	5·16 (17)	6·48 (14)
75 and over	1·11 (2)	2·68 (6)	7·27 (8)	16·33 (8)
All ages	0·07 (3)	0·57 (22)	1·39 (54)	2·27 (57)

* Number reported at 1 November 1951 for men continuing to smoke cigarettes only at that time.

In examining the effect of the *method* of smoking (Table 5), we are dependent upon the smoking habits reported at the time of our first questionary, and we did not, in that inquiry, ask whether pipe smokers had ever previously smoked cigarettes. We have learnt subsequently, from the response to the second questionary, that 40% of the pipe smokers had regularly smoked cigarettes at some time previously, so that the excess death rate of pipe and/or cigar smokers over that of non-smokers (*0.43* against *0.07*) may be partly due to this previous consumption of cigarettes. We cannot yet test this directly by examining the mortality of the 60% of pipe smokers who never smoked cigarettes regularly, since their number is small and we have not observed them for long enough to obtain a reliable estimate of their death rate. However, although the numbers of deaths are very few the rates in Table 5 do show an increase in lung cancer mortality with increasing amounts of pipe tobacco consumed. On these data, together with the total rate, we could hardly exonerate the pipe from all risk.

[4] Ten certified deaths were excluded because additional evidence suggested that the diagnosis was incorrect (see p. 1400).

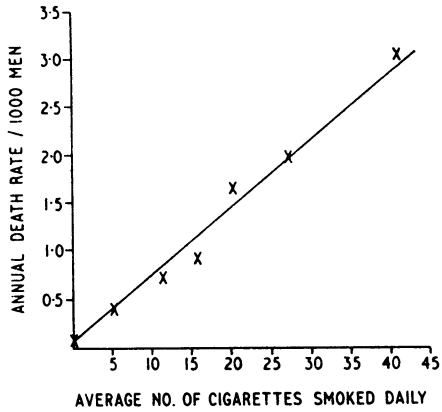

FIG. 1.—Death rate from lung cancer, standardized for age, among men smoking different daily numbers of cigarettes at the start of the inquiry (men smoking pipes or cigars as well as cigarettes excluded).

TABLE 5.—*Method of Smoking: Standardized Death Rates from Cancer of the Lung*

Method of Smoking	Death Rate per 1,000 (No. of Deaths)
Cigarette (current and ex*) ..	0·96 (143)
Mixed (current and ex*)	0·53 (42)
Pipe and/or cigar (current and ex*)	0·43 (24)
Pipe and/or cigar (current*):	
1–14 g. daily	0·42 (12)
15–24 „ „	0·45 (6)
25+ „ „	0·96 (3)

* At 1 November 1951.

We are still less inclined to do so after examining the data in Table 6, which show the death rates of men who were continuing to smoke at 1 November 1951 and of those who had stopped. For each type of smoking (cigarettes alone, mixed, pipe and/or cigar alone) the rate of continuing smokers is higher than that of those who had stopped, and the rate in ex-cigarette smokers (*0.24*) is notably less than that in current pipe smokers (*0.47*).

The difference between the ex-smokers and the continuing smokers is most marked for those who smoked cigarettes, where the rate for those who had given up is only 19% of the rate for those who continued. This difference, moreover, may well underestimate the true difference, since in this analysis we take no account of the changes in habits in the years following 1951. (See p. 1407, where allowance has been made for some of the changes in habits which took place and where comparison is made between men who have given up smoking for different lengths of time.)

TABLE 6.—*Continuity of Smoking: Standardized Death Rates from Cancer of the Lung*

Continuity of Smoking	Death Rate per 1,000 (No. of Deaths)		
	Cigarette Smokers	Mixed Smokers	Pipe and/or Cigar Smokers
Continuing at 1/11/51 ..	1·25 (133)	0·59 (36)	0·47 (21)
Stopped before 1/11/51 ..	0·24 (10)	0·48 (6)	0·23 (3)

In Table 7 we consider the nature of the evidence available to the doctors who certified cancer of the lung as the cause of death (excluding the one case for which this information was refused to us). In more than half of the deaths (56%) there was histological, cytological, or necropsy evidence together with *x*-ray or bronchoscopic confirmation of the site of the primary growth. In another 38% an *x*-ray picture or bronchoscopy

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supported the clinical evidence. In both these groups the various associations of mortality with smoking are quite distinct. On the other hand, it is of interest that for the 12 cases in which the diagnosis rested on history and physical examination there is no clear evidence of association. In other words, these figures show that doctors are not diagnosing cancer of the lung in their colleagues without adequate evidence, and that in the few less definite cases they are not making such a diagnosis merely because the sick person was a heavy cigarette smoker.

TABLE 7.—*Standard of Diagnosis: Standardized Death Rates from Cancer of the Lung*

Standard of Diagnosis* (No. of Deaths)	Death Rate per 1,000						
	Non-smokers	All Smokers	Cigarette Smokers†				
			Continuing	Given Up	1–14 Daily	15–24 Daily	25+ Daily
Grade 1 (118)	0·01	0·41	0·68	0·17	0·37	0·76	1·02
„ 2 (81) ..	0·03	0·28	0·52	0·05	0·15	0·60	1·21
„ 3 (12) ..	0·03	0·04	0·04	0·03	0·02	0·03	0·05
All grades (211)	0·07	0·73	1·24	0·24	0·54	1·39	2·27

* Grade 1 = Necropsy evidence *or* histological *or* cytological together with evidence of primary from *x*-ray picture or bronchoscopy. Grade 2 = Clinical evidence together with evidence of primary from *x*-ray picture or bronchoscopy. Grade 3 = Evidence from history and physical examination alone.
One case for which information was refused has been excluded (a man aged 74 smoking 14 cigarettes a day).
† At 1 November 1951.

Similarly Table 8 shows no marked associations with smoking in the 13 cases of adenocarcinoma, whereas they are distinct with both the squamous and the oat and anaplastic growths. Taking the death rate of the continuing cigarette smokers in each histological group as standard (100), we have ratios for those smoking 1 to 14, 15 to 24, and 25 or more daily, of 68, 104, and 139% in the squamous group, and 44, 91, and 169% with the oat celled and anaplastic group.

TABLE 8.—*Histological Type: Standardized Death Rates from Cancer of the Lung*

Histological Type (No. of Deaths)	Death Rate per 1,000						
	Non-smokers	All Smokers	Cigarette Smokers				
			Continuing	Given Up	1–14 Daily	15–24 Daily	25+ Daily
Squamous (55)	0·00	0·19	0·32	0·09	0·22	0·33	0·45
Oat and anaplastic (40)	0·01	0·14	0·22	0·05	0·10	0·20	0·38
Adenocarcinoma (13) ..	0·00	0·05	0·07	0·03	0·03	0·12	0·07

The rise in lung cancer mortality with increasing number of cigarettes smoked occurred in all types of area, and the rates in Table 9 provide no reason to suppose that the association

TABLE 9.—*Place of Residence: Standardized Death Rates from Cancer of the Lung*

Place of Residence	Death Rate per 1,000				No. of Deaths
	Non-smokers	Cigarettes per Day*			
		1–14	15–24	25+	
Conurbation ..	0·03	0·48	1·31	1·90	49
Large towns ..	0·00	0·32	1·88	4·43	34
Small „	0·11	0·87	1·06	2·20	32
Rural areas	0·12	0·52	1·15	1·17	18

* For men continuing to smoke cigarettes only at 1 November 1951.

was any closer in big towns than in small towns or in the countryside. It is, however, possible that the rural mortality is affected by the retirement there of men who have passed their active lives in towns. We therefore consider in Table 10 doctors under 65 years of age. The number of deaths in the different areas is then small, but they do suggest that there is a lower lung cancer mortality in the rural, and possibly the small town, areas which is not due to differences in amounts smoked.

TABLE 10.—*Place of Residence: Standardized Death Rates* at Ages 25–64 Years*

Place of Residence	Death Rate per 1,000		
	Non-smokers	Cigarette Smokers†	No. of Deaths
Conurbation	0·04	0·62	31
Large towns	0·00	0·65	17
Small „	0·00	0·52	16
Rural area	0·00	0·40	8

* Standardized for age and amount smoked.
† Men continuing to smoke cigarettes only at 1 November 1951.

Table 11 shows the mortality in the principal smoking categories for two periods of time—1 November 1951 to 31 October 1956 and 1 November 1956 to 31 October 1961. The first of these quinquennia followed immediately after the questionaries were sent out. Although the majority were returned within a few weeks, there were some which were not returned for several months, so that the first year of observation was biased by the inclusion of some months of observation for which there could not be any corresponding mortality. A much more important type of bias is the differential selection of healthy men among the repliers, and we have shown that the total mortality rate was lower during the early years of follow-up than in any subsequent period. Clearly, therefore, we would expect the mortality from lung cancer to be higher in the second quinquennium and that the effect of any selective bias would show itself most markedly during the first. In fact, the association with smoking was similar in both periods—though somewhat closer in the second period than in the first. Few, if any, of the doctors who died of lung cancer in the second period could have suspected that they had the disease in November 1951, and it is thus impossible to attribute this association to a selective bias in answering the questionary.

TABLE 11.—*Period After Start of Inquiry: Standardized Death Rates from Cancer of the Lung*

Period (No. of Deaths)	Death Rate per 1,000							
	All Men	Non-smokers	All Cigarette Smokers	Cigarette Smokers		Current Cigarette Smokers		
				Current	Ex-	1–14/d	15–24/d	25+/d
1951–6 (102)	0·69	0·05	0·98	1·22	0·41	0·64	1·20	2·25
1956–1 (110)	0·64	0·08	0·95	1·28	0·09	0·50	1·53	2·32

It is notable also that the mortality of ex-smokers decreased in the second quinquennium, when—on average—they had given up smoking for a longer time, and that it also decreased among the doctors as a whole. This last decrease was not large (from *0.69* to *0.64* per 1,000 men per year), but it took place in spite of an increase in the mortality from all causes (from *13.46* to *14.56*) and despite a steady increase during these years in the mortality from lung cancer in the male population of the whole country.

Other Cancers

Data for cancers other than cancer of the lung are shown in Tables 12 to 15. The number of deaths attributed to each type is small—in some cases very small—but we have given the results separately to enable them to be compared with other series.

Table 12 shows the mortality from cancer of (1) the mouth, pharynx, or nose; (2) the larynx or trachea; and (3) the oesophagus. In each case the rates are higher in smokers than in non-smokers (columns 4 and 5), but they are not specifically higher in cigarette smokers than in other smokers (columns 6, 7, and 8). In Table 13, therefore, the rates are examined only for all smokers classed together, equating 1 g. of pipe or cigar tobacco with 1 cigarette. The most marked feature is a substantially increased death rate for each type of cancer in the heavily smoking men (25 g. or more a day), and it is evidently

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to this group that the excess mortality of smokers over non-smokers is largely due. Only cancer of the oesophagus shows a progressive increase in mortality with an increase in the amount smoked, and only this type of cancer shows any important difference in the death rates between men who have stopped smoking and those who have continued. It must be remembered, however, that the numbers of deaths attributed to cancer of the mouth, pharynx, or nose (19) and to cancer of the larynx or trachea (16) are very small. If all these cancers of the upper respiratory and digestive tracts are grouped together the combined results show significant differences between smokers and non-smokers ($P=0.02$) and between heavy smokers and light smokers ($P<0.001$), but not between continuing smokers and men who have stopped ($P>0.1$).

TABLE 12.—*Standardized Death Rates from Cancers of the Upper Respiratory and Digestive Tracts*

Site	No. of Deaths*	Death Rate per 1,000					
		All Men	Non-smokers	All Smokers†	Cigarette Smokers†	Mixed Smokers†	Pipe or Cigar Smokers†
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Mouth, pharynx, or nose	19 (2)	0·06	0·00	0·06	0·05	0·10	0·04
Larynx or trachea ..	16 (5)	0·05	0·00	0·06	0·05	0·03	0·10
Oesophagus	29 (1)	0·09	0·04	0·10	0·06	0·19	0·08
Total	64 (8)	0·20	0·04	0·22	0·16	0·32	0·22

* The numbers in parentheses are of deaths (included in the total figure) in which cancer of the specified site was certified as being associated with the death but not its direct or underlying cause.
† Currently smoking or past smokers in 1951.

TABLE 13.—*Standardized Death Rates from Cancer of the Upper Respiratory and Digestive Tracts in Relation to the Amount Smoked*

Site	Death Rate per 1,000				
	Amount of Tobacco Smoked Daily (g.)*				Given Up Smoking
	1–14	15–24	25+	All Amounts	
Mouth, pharynx, or nose ..	0·04	0·01	0·21	0·07	0·06
Larynx or trachea ..	0·02	0·02	0·15	0·06	0·05
Oesophagus ..	0·08	0·14	0·20	0·12	0·02
Total ..	0·13	0·17	0·56	0·24	0·13

* Continuing smokers at 1 November 1951.

TABLE 14.—*Standardized Death Rates from Cancer of Other Sites*

Site	No. of Deaths	Death Rate per 1,000					
		All Men	Non-smokers	All Smokers	Cigarette Smokers	Mixed Smokers	Pipe or Cigar Smokers
Bladder ..	38*	0·11	0·17	0·11	0·13	0·12	0·07
Stomach ..	84	0·26	0·27	0·25	0·30	0·14	0·30
Bowel ..	97	0·30	0·31	0·30	0·26	0·32	0·39
Rectum ..	35	0·11	0·05	0·11	0·12	0·12	0·08
Prostate ..	69	0·21	0·33	0·20	0·18	0·16	0·26
Other sites	194	0·61	0·64	0·61	0·68	0·52	0·51
Primary site unknown	27	0·08	0·09	0·08	0·05	0·09	0·15
Total ..	542	1·67	1·87	1·65	1·72	1·45	1·77

* Two deaths from other causes in which cancer of the bladder was mentioned as contributory are included in this category, but are excluded from the total cancer deaths.

TABLE 15.—*Standardized Death Rates from Cancer of Other Sites in Relation to the Amount Smoked*

Site	Death Rate per 1,000				
	Amount of Tobacco Smoked Daily (g.)*				Given Up Smoking
	1–14	15–24	25+	All Amounts	
Bladder	0·10	0·11	0·13	0·12	0·08
Stomach	0·28	0·28	0·26	0·28	0·18
Bowel	0·37	0·22	0·44	0·32	0·23
Rectum	0·10	0·06	0·22	0·11	0·12
Prostate	0·16	0·19	0·12	0·17	0·28
Other sites	0·57	0·59	0·83	0·63	0·54
Primary site unknown	0·10	0·07	0·06	0·09	0·05
Total ..	1·67	1·52	2·03†	1·71	1·49

* Continuing smokers at 1 November 1951. † See footnote to Table 14

Tables 14 and 15 show no clear evidence of an association for any of the other forms of cancer, either with method of smoking or with amount. As would be expected with eight groups, the individual figures show considerable variation, but in no case is this more than can reasonably be attributed to chance. Moreover, the total mortality from all these cancers is closely similar among non-smokers (*1.87*), cigarette smokers (*1.72*), and pipe or cigar smokers (*1.77*).

Other respiratory diseases

Mortality from respiratory diseases other than cancer of the lung is given in Tables 16 and 17. For chronic bronchitis there is a close—and statistically highly significant—association with smoking. While this was most marked when chronic bronchitis was described as the underlying cause of death, it was also clearly present when chronic bronchitis served as a contributory cause in cardiovascular mortality. For pulmonary tuberculosis the evidence is much less clear. The mortality was higher in cigarette smokers than in non-smokers, in continuing cigarette smokers compared with those who had stopped, and in heavy cigarette smokers compared with light. The deaths were, however, few, and none of these differences was statistically significant. Moreover, the few additional deaths for which pulmonary tuberculosis was described as a contributory cause tend to diminish the relationship rather than reinforce it. In other words, the data suggest that *death* from pulmonary tuberculosis may be associated with smoking, while the disease itself is not.

All other respiratory diseases (including 116 deaths due to pneumonia, 21 deaths due to influenza and other acute infections and 44 deaths due to other causes) show no association with smoking. In our previous report (Doll and Hill, 1956) we suggested that some of the excess mortality attributed to chronic bronchitis among heavy cigarette smokers might be due to a tendency to diagnose chronic bronchitis rather than some other respiratory disease in patients with a chronic cough. With the present greater numbers the evidence for a negative association between other respiratory diseases and smoking has disappeared and it is clear that such a bias (if it exists at all) could not account for the results with chronic bronchitis.

TABLE 16.—*Standardized Death Rates from Respiratory Diseases*

Cause of Death	No. of Deaths	Death Rate per 1,000					
		All Men	Non-smokers	All Smokers	Cigarette Smokers	Mixed Smokers	Pipe or Cigar Smokers
Chronic bronchitis	111	0·34	0·05	0·37	0·51	0·33	0·15
Chronic bronchitis as associated cause* ..	55	0·17	0·03	0·18	0·20	0·21	0·12
Pulmonary tuberculosis ..	42	0·13	0·06	0·14	0·15	0·11	0·11
Pulmonary tuberculosis as associated cause ..	14	0·04	0·05	0·04	0·05	0·02	0·04
Other respiratory diseases ..	181	0·54	0·63	0·53	0·55	0·49	0·47

* In association with cardiovascular disease.

TABLE 17.—*Standardized Death Rates from Respiratory Diseases in Relation to the Number of Cigarettes Smoked*

Cause of Death	Death Rate per 1,000				
	No. of Cigarettes Smoked Daily				Given Up Smoking Cigarettes
	1–14	15–24	25+	All Amounts	
Chronic bronchitis ..	0·34	0·64	1·06	0·58	0·38
Chronic bronchitis as associated cause*	0·15	0·20	0·30	0·21	0·16
Pulmonary tuberculosis	0·10	0·16	0·26	0·17	0·12
Pulmonary tuberculosis as associated cause	0·05	0·09	0·02	0·06	0·11
Other respiratory diseases	0·41	0·68	0·40	0·51	0·61

* In association with cardiovascular disease.

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Cardiovascular disease

In Tables 18 and 19 we set out the data relating to mortality from cardiovascular diseases—including under this heading deaths certified as due to nephritis. With the deaths attributed to cardiovascular accidents or to coronary disease we have separately considered those in which reference was made on the death certificate to the presence of hypertension, for these deaths might be related to the causes of hypertension more closely than to any other factor.

For the 138 deaths in which hypertension was given as the primary cause there is no association with smoking habits—neither with method (Table 18) nor with the amount of cigarette smoking (Table 19). This is equally true for the 143 cerebrovascular accidents and for the 89 coronary disease deaths in which hypertension was also mentioned. Adding the three hypertensive groups together gives, with one exception, remarkably similar rates in all the smoking categories, varying only between *1.26* per 1,000 in non-smokers and *1.10* per 1,000 in men who had given up smoking (the final lines of Tables 18 and 19). The exception lies in the rather low death rate of *0.81* per 1,000 in pipe and/or cigar smokers, a figure which is based upon only 53 deaths, and has 95% confidence limits of 0.69 and 0.93.

We can also conclude from these tables that there is no association with smoking habits in the 135 deaths from "other heart diseases" (rheumatic heart 35, other valvular disease 22, other diseases 78) nor in the 135 from "other cardiovascular diseases" (general arteriosclerosis 64, dissecting and atherosclerotic aneurysm of the aorta 47, and other vascular diseases 24). With the larger group of cerebrovascular accidents without reference to hypertension, there also seems to be no association. Though the death rate of all smokers at *1.41* per 1,000 is a trifle above that of the non-smokers (*1.24*), this small excess is not related specifically to one method of smoking (Table 18), and there is no clear gradient with number of cigarettes smoked nor fall in the death rate on giving up smoking (Table 19).

With the 337 deaths attributed to myocardial degeneration and the 43 deaths attributed to nephritis there is some suggestion of an association, but the evidence is slight. With myocardial degeneration there is a substantial—and statistically significant ($P<0.01$)—difference between smokers (*1.02*) and non-smokers (*0.59*), but there is no difference between the different methods of smoking (Table 18) and no gradient with the number of cigarettes smoked. With nephritis the maximum mortality falls on the heaviest smoking category and mortality declines with giving up smoking, but the differences are small; none of them is statistically significant.

In short, we would conclude from these data that the only cardiovascular cause of mortality to show any association with smoking habits is coronary disease, unrelated to hypertension, and that even here the differences in rates are not very marked. The death rate of all smokers (*4.08*) is 23% higher than that of non-smokers (*3.31*), and this excess appears to be limited to the cigarette smokers (*4.39*, or 33% above the non-smokers, Table 18). There is certainly no clear gradient with number of cigarettes smoked, but the highest mortality is found among the heaviest smokers and there appears to be a fall in mortality on giving up smoking (Table 19). We examine these findings more closely in Table 20, which shows the age-specific death rates from coronary disease. These figures show that a rising gradient of mortality from non-smokers to heavy cigarette smokers is clearly present at ages under 65, doubtful at ages 65–74, and absent at age 75 years and over.

We have not sought clinical information about the large number of deaths in this cardiovascular group and consequently have not felt justified in trying to separate a group of deaths which might be ascribed to "cor pulmonale." We noted earlier that 55 cardiovascular deaths included a reference to chronic bronchitis on the death certificate (coronary thrombosis 24, myocardial degeneration 15, hypertension 2, other heart disease 4, and cerebrovascular accidents 10), and it was shown in Tables 16 and 17 that these deaths were closely associated with smoking. It is possible that in a few of them the primary cause was really chronic bronchitis—particularly perhaps among those attributed to myocardial degeneration or "other heart disease"—and that these constitute another cardiovascular group which is also associated with smoking. On the evidence available, however, this group would not appear to be large enough to have materially affected the results. Possibly most such deaths among doctors are attributed directly to chronic bronchitis.

TABLE 18.—*Standardized Death Rates from Cardiovascular Diseases*

Cause of Death		No. of Deaths	Death Rate per 1,000					
			All Men	Non-smokers	All Smokers	Cigarette Smokers	Mixed Smokers	Pipe or Cigar Smokers
Cerebrovascular accidents	(a)*	462	1·39	1·24	1·41	1·48	1·27	1·44
	(b)†	143	0·45	0·51	0·44	0·50	0·44	0·23
	All	605	1·84	1·76	1·85	1·98	1·71	1·67
Coronary disease	(a)*	1,287	3·99	3·31	4·08	4·39	3·87	3·18
	(b)†	89	0·28	0·30	0·28	0·26	0·37	0·21
	All	1,376	4·26	3·61	4·36	4·65	4·25	3·39
Myocardial degeneration		337	0·97	0·59	1·02	1·01	0·98	1·00
Hypertension		138	0·42	0·45	0·42	0·45	0·36	0·37
Other heart diseases		135	0·41	0·41	0·41	0·42	0·43	0·33
Other cardiovascular diseases		135	0·41	0·41	0·41	0·46	0·38	0·35
Nephritis		43	0·13	0·09	0·14	0·14	0·13	0·12
Total		2,769	8·44	7·32	8·61	9·11	8·24	7·23
Total hypertensive		370	1·15	1·26	1·14	1·22	1·17	0·81

* (a) Without reference to hypertension on the death certificate.
† (b) Hypertension referred to on the death certificate.

TABLE 19.—*Standardized Death Rates from Cardiovascular Diseases in Relation to the Number of Cigarettes Smoked*

Cause of Death		Death Rate per 1,000				
		No. of Cigarettes Smoked Daily				Given Up Smoking Cigarettes
		1–14	15–24	25+	All Amounts	
Cerebrovascular accidents	(a)*	1·46	1·43	1·69	1·49	1·42
	(b)†	0·46	0·48	0·54	0·51	0·51
	All	1·93	1·91	2·23	2·00	1·93
Coronary disease	(a)*	4·35	4·28	4·97	4·57	3·73
	(b)†	0·29	0·29	0·18	0·28	0·19
	All	4·65	4·57	5·16	4·86	3·92
Myocardial degeneration		1·10	0·94	0·97	1·07	0·87
Hypertension		0·44	0·45	0·45	0·46	0·40
Other heart diseases		0·32	0·59	0·21	0·41	0·41
Other cardiovascular diseases		0·41	0·45	0·62	0·54	0·25
Nephritis		0·16	0·14	0·29	0·17	0·08
Total		9·01	9·05	9·93	9·51	7·86
Total hypertensive		1·20	1·22	1·17	1·25	1·10

* (a) Without reference to hypertension on the death certificate.
† (b) Hypertension referred to on the death certificate.

TABLE 20.—*Death Rate from Coronary Thrombosis by Age**

Age in Years	No. of Deaths	Death Rate per 1,000				
		Non-smokers	Current Cigarette Smokers Smoking Daily			All Cigarette Smokers, Ex and Current
			1–14	15–24	25+	
35–44	38	0·11	0·41	0·49	1·50	0·61
45–54	149	1·12	1·66	3·40	2·73	2·40
55–64	319	4·90	6·81	7·03	8·81	7·20
65–74	389	10·83	16·44	13·04	17·59	14·69
75–84	314	21·20	21·22	15·04	17·30	19·18
85+	78	32·35	33·06	58·54	—†	35·93
All ages	1,287	3·31	4·36	4·28	4·97	4·39

* Includes all deaths attributed to coronary thrombosis, except those for which hypertension was mentioned as a contributory cause (89).
† Very small total number of man-years at risk (27½)—no deaths due to coronary thrombosis.

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Other diseases

Finally, in Tables 21 and 22 we set out the mortality observed in all other diseases. Some associations with smoking are seen in peptic ulcer, in cirrhosis of the liver and alcoholism, and in "other digestive diseases," but none in genito-urinary diseases other than nephritis, deaths due to violence, indefinite causes, and a miscellaneous group of other causes to which many diseases each contribute a handful of cases.

The 54 deaths ascribed to peptic ulcer include 15 in which peptic ulcer was referred to only as a contributory cause and two deaths attributed to haematemesis (a man of 64 smoking 30 cigarettes a day and a man of 82 smoking 16 g. a day in a pipe who have been included here rather than with the group of indefinite causes as peptic ulcer is most likely to have been the correct diagnosis). For these deaths the association with smoking is not close—for example, the mortality is higher among men smoking 15 to 24 cigarettes a day (*0.31*) than among heavier smokers (*0.22*)—but the difference between the mortality rates for smokers (*0.18*) and non-smokers (*0.03*) is sufficiently great to be unlikely to be due to chance ($P=0.05$).

With alcoholism (6 deaths) and cirrhosis of the liver (27 deaths) the association is strong. No deaths from these causes occurred among non-smokers, and, like cancers of the mouth, pharynx, and larynx, the mortality fell almost wholly on the heaviest smokers.

The evidence relating to other digestive diseases is inconclusive. This is a heterogeneous group, the major components of which were 11 deaths from appendicitis, 12 from hernia, 18 from obstruction, 9 from diverticulitis, and 17 from gall-stones or cholecystitis. Several of these conditions are normally treated by surgery, and it would be reasonable to assume that their fatality rate was related to smoking, because of the resulting chest complications, rather than the incidence of the conditions themselves. The numbers of deaths, however, are too few to justify separate examination of the various diseases. The difference in mortality between smokers and non-smokers for the group as a whole is statistically significant ($P=0.03$), but there is very little trend with the amount smoked and no difference between continuing smokers and ex-smokers. Until further evidence is obtained, we have tentatively classified the group as unrelated to smoking.

TABLE 21.—*Standardized Death Rates from Other Diseases*

Cause of Death	No. of Deaths	Death Rate per 1,000					
		All Men	Non-smokers	All Smokers	Cigarette Smokers	Mixed Smokers	Pipe or Cigar Smokers
Peptic ulcer ..	54*	0·17	0·03	0·18	0·21	0·16	0·12
Cirrhosis of liver and alcoholism	33	0·10	0·00	0·11	0·12	0·11	0·05
Other digestive diseases ..	87	0·26	0·07	0·28	0·32	0·20	0·25
Genito-urinary diseases† ..	82	0·24	0·33	0·24	0·27	0·21	0·22
Indefinite causes	50	0·15	0·17	0·14	0·13	0·12	0·20
Violence ..	248	0·77	0·94	0·75	0·79	0·68	0·64
All remaining causes of death	150	0·46	0·50	0·47	0·49	0·48	0·45

* Including 15 deaths in which peptic ulcer was certified as being associated with the death but not its direct or underlying cause.
† Excluding nephritis.

TABLE 22.—*Standardized Death Rates from Other Diseases in Relation to the Number of Cigarettes Smoked*

Cause of Death	Death Rate per 1,000				
	No. of Cigarettes Smoked Daily				Given Up Smoking Cigarettes
	1–14	15–24	25+	All Amounts	
Peptic ulcer* ..	0·07	0·31	0·22	0·21	0·16
Cirrhosis of liver and alcoholism ..	0·05	0·08	0·43	0·15	0·03
Other digestive diseases	0·26	0·33	0·36	0·32	0·32
Genito-urinary diseases*	0·28	0·29	0·29	0·29	0·21
Indefinite causes ..	0·21	0·12	0·12	0·16	0·08
Violence	0·85	0·57	1·15	0·83	0·65
Allfremaining causes of death	0·53	0·34	0·53	0·45	0·55

* See footnotes to Table 21.

Related and Unrelated Causes

From this examination of the mortality rates by cause we believe that we can now reasonably and usefully divide them into two groups: (*a*) those that have revealed associations with smoking, and (*b*) those that have not. Thus we reach the death rates summarized in Tables 23 and 24. (In these tables we have ignored the contributory causes of death and have included each death once only under that condition given on the death certificate as the underlying cause.)

Causes of death that we have regarded as related to smoking account, it will be seen, for 39% of all deaths (1,775 of 4,597). In this group the mortality among smokers (*5.74*) is 63% more than in non-smokers (*3.53*) and that among cigarette smokers (*6.39*) 81% more; and the mortality in continuing cigarette smokers (*7.01*) is 50% more than in ex-cigarette smokers (*4.67*). The mortality in men who smoke 25 or more cigarettes a day (*9.56*) is 74% more than in those who smoke under 15 a day (*5.48*) and 171% more than in non-smokers (*3.53*). In contrast, the mortality in pipe or cigar smokers (*4.17*) is only 18% more than in non-smokers.

In contrast, the remaining 2,822 deaths (61% of the total) provide mortality rates that are closely similar in all the smoking categories. Among smokers as a whole the mortality from these causes (*8.58*) is 1% more than in non-smokers (*8.53*) and the mortality among cigarette smokers (*8.99*) is raised by only 5%. There is a somewhat greater difference—16%—between men who continued to smoke cigarettes (*9.31*) and those who stopped (*8.02*), but, as will appear later, this may be an artifact due to the self-selection of men who stop smoking (see p. 1408). The mortality in pipe and/or cigar smokers (*8.06*) is 6% less than

TABLE 23.—*Standardized Death Rates from Causes Related to Smoking and from Causes Unrelated to Smoking*

Cause of Death	No. of Deaths	Death Rate per 1,000					
		All Men	Non-smokers	All Smokers	Cigarette Smokers	Mixed Smokers	Pipe or Cigar Smokers
Related causes :							
Cancer of lung	207	0·65	0·07	0·71	0·93	0·52	0·43
Other upper respiratory and digestive cancers ..	56	0·17	0·04	0·20	0·15	0·28	0·16
Chronic bronchitis ..	111	0·34	0·05	0·37	0·51	0·33	0·15
Coronary disease without hypertension ..	1,287	3·99	3·31	4·08	4·39	3·87	3·18
Peptic ulcer (including haematemesis)	39	0·12	0·00	0·13	0·13	0·12	0·10
Cirrhosis of liver and alcoholism	33	0·10	0·00	0·11	0·12	0·11	0·05
Pulmonary tuberculosis	42	0·13	0·06	0·14	0·15	0·11	0·11
Total ..	1,775	5·49	3·53	5·74	6·39	5·33	4·17
Unrelated causes :							
Other cancers	542	1·67	1·87	1·65	1·72	1·45	1·77
Other respiratory disease	181	0·54	0·63	0·53	0·55	0·49	0·47
Cerebrovascular accidents without hypertension ..	462	1·39	1·24	1·41	1·48	1·27	1·44
Myocardial degeneration	337	0·97	0·59	1·02	1·01	0·98	1·00
All hypertension	370	1·15	1·26	1·14	1·22	1·17	0·81
Other heart disease ..	135	0·41	0·41	0·41	0·42	0·43	0·33
Nephritis ..	43	0·13	0·09	0·14	0·14	0·13	0·12
Other cardiovascular disease ..	135	0·41	0·41	0·41	0·46	0·38	0·35
Other digestive disease ..	87	0·26	0·07	0·28	0·32	0·20	0·25
Violence ..	248	0·77	0·94	0·75	0·79	0·68	0·64
Remainder ..	282	0·85	1·00	0·85	0·89	0·81	0·87
Total ..	2,822	8·55	8·53	8·58	8·99	8·00	8·06
All causes ..	4,597	14.05	12·06	14·32	15·38	13·34	12·23

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that in non-smokers (*8.53*), but neither this difference ($0.3 < P < 0.4$) nor that between non-smokers and cigarette smokers ($P = 0.09$) is statistically significant.

TABLE 24.—*Standardized Death Rates from Causes Related to Smoking and from Causes Unrelated to Smoking in Relation to the Number of Cigarettes Smoked*

Cause of Death	Death Rate per 1,000				
	No. of Cigarettes Smoked Daily				Given Up Smoking Cigarettes
	1–14	15–24	25 or More	All Amounts	
Related causes :					
Cancer of lung ..	0·57	1·29	2·23	1·20	0·24
Other upper respiratory and digestive cancers ..	0·04	0·18	0·43	0·20	0·05
Chronic bronchitis	0·34	0·64	1·06	0·58	0·38
Coronary disease without hypertension ..	4·35	4·28	4·97	4·57	3·73
Peptic ulcer (including haematemesis)	0·02	0·18	0·19	0·13	0·12
Cirrhosis of liver and alcoholism	0·05	0·08	0·43	0·15	0·03
Pulmonary tuberculosis	0·10	0·16	0·26	0·17	0·12
Total ..	5·48	6·81	9·56	7·01	4·67
Unrelated causes :					
Other cancers ..	1·77	1·56	2·31	1·82	1·47
Other respiratory disease	0·41	0·69	0·40	0·51	0·61
Cerebrovascular accidents without hypertension ..	1·46	1·43	1·69	1·49	1·42
Myocardial degeneration	1·10	0·94	0·97	1·07	0·87
All hypertension ..	1·20	1·22	1·17	1·25	1·10
Other heart disease	0·32	0·59	0·21	0·41	0·41
Nephritis	0·16	0·14	0·29	0·17	0·08
Other cardiovascular disease	0·41	0·45	0·62	0·54	0·25
Other digestive disease	0·26	0·33	0·36	0·32	0·32
Violence	0·85	0·57	1·15	0·83	0·65
Remainder ..	1·02	0·75	0·94	0·90	0·84
Total ..	8·96	8·66	10·11	9·31	8·02
All causes ..	14·44	15·47	19·67	16·32	12·68

Mortality of Men who have Given Up Smoking

Cigarette Smokers

For detailed study of the mortality of the men who have given up smoking (ex-smokers) we have used the information given on both questionaries (see Method of Analysis, B) and have calculated man-years at risk at different ages for men who had given up for less than 5, 5–9, 10–19, and 20 years and over. For example, a man who stated on both questionaries that he gave up smoking in 1950 at 37 years of age is calculated to have been at risk for three-and-a-half years in the group that had stopped smoking for under five years (one-and-a-half years in the age group 35–39 years and two years in the age group 40–44 years), for five years in the group that had stopped smoking for 5–9 years (three years in the age group 40–44 years and two years in the age group 45–49 years), and for one-and-a-half years in the group that had stopped for 10–14 years (in the age-group 45–49 years). A man who was smoking in 1951 but who stated on the second questionary that he gave up in 1955 at age 52 years is recorded as an ex-smoker of three-and-a-half years' duration at the end of 1958, contributing one-and-a-half years at risk to the group that had given up for under five years and one-and-a-half years to the group that had given up for 5–9 years (all in the age-group 55 to 59 years).

Thus we have studied the mortality among ex-smokers from (*a*) cancer of the lung ; (*b*) chronic bronchitis ; (*c*) coronary disease without mention of hypertension ; (*d*) other cancers of the upper respiratory and upper digestive tract together with pulmonary tuberculosis, peptic ulcer, and cirrhosis of the liver and alcoholism—that is, all other causes of death related to smoking grouped together because of the small numbers of deaths attributed to each ; and (*e*) all causes unrelated to smoking (see Table 25). In Table 25 allowance has been made for the amount smoked by calculating separately for each age-group the deaths from each disease that would be expected among men smoking 1–14, 15–24, or 25 or more cigarettes daily, if death from the disease was unrelated to stopping smoking. The numbers of expected deaths were summed for each age and amount of smoking category and the standardized death rates calculated indirectly by multiplying the rate for all cigarette smokers (current and ex) by the ratio between the observed and expected numbers of deaths.

The results show three distinct patterns of behaviour. For cancer of the lung (Fig. 2) and the group of other diseases related to smoking, the mortality rates decline immediately and become progressively smaller as the length of time increases since smoking has been given up. Thus after 20 years the rates are only 15 and 34% respectively of the level for continuing

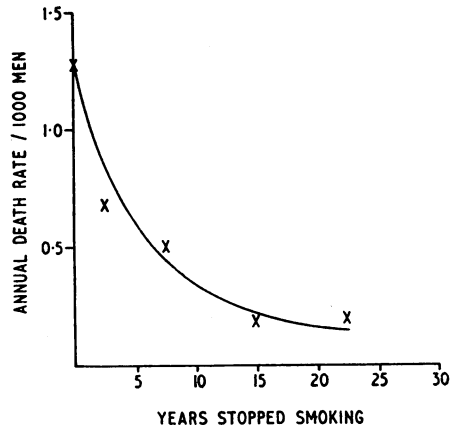

FIG. 2.—Death rate from lung cancer, standardized for age and amount smoked, among men continuing to smoke cigarettes and men who had given up smoking for different periods (men who had regularly smoked pipes or cigars as well as cigarettes excluded). The corresponding rate for non-smokers was 0.07 per 1,000.

smokers, although they are still two to three times the rates of non-smokers. On the other hand, for chronic bronchitis the mortality at first increases and then, after 10 years from giving up, falls well below the rate for men who continued to smoke. Lastly, for coronary disease without hypertension

TABLE 25.—*Mortality Among Cigarette Smokers at Different Times After Stopping Smoking (Numbers of Deaths in Parentheses)*

Cause of Death	Death Rate per 1,000					
	Continuing Cigarette Smokers*	Cigarette Smokers Stopped for (Years)				Non-smokers*
		<5	5–9	10–19	20 or More	
Lung cancer	1·28 (124)†	0·67 (5)	0·49 (7)‡	0·18 (3)	0·19 (2)	0·07 (3)
Chronic bronchitis	0·58 (48)	0·71 (5)	0·81 (11)	0·06 (1)	0·30 (4)	0·05 (2)
Coronary disease without hypertension ..	4·72 (464)	3·52 (28)	4·17 (61)	3·87 (59)	3·74 (40)	3·34 (113)
Other related causes	0·65 (69)‡	0·50 (4)	0·40 (6)	0·33 (5)	0·22 (2)	0·10 (3)
Unrelated causes	9·43 (865)	6·26 (49)	8·49 (120)	9·27 (136)	8·80 (105)	8·52 (315)
All causes	16·62 (1,566)	11·62 (91)	14·25 (204)	13·60 (204)	13·38 (153)	12·09 (436)

* Calculate by method B (see text) and therefore not in all cases exactly the same as the rates in previous Tables.
† Including three deaths, also included under their primary cause, in which the specified disease was a contributory cause.
‡ Including one death, also included under its primary cause, in which the specified disease was a contributory cause.

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and for the unrelated causes of death the pattern is complex. In both groups the mortality falls quite sharply in men who have recently stopped, but it then rises again to fall finally to a figure which, 20 or more years after stopping smoking, is only slightly above that for the non-smokers.

Clearly these different patterns cannot be due to a single cause, and we must postulate the interaction of several, probably competing, factors. For cancer of the lung and the group of other related diseases the results can be simply explained if cigarette smoking (or some factor commonly associated with it) is a direct aetiological agent. With chronic bronchitis, however, clinical experience suggests that the rates will be influenced by the tendency of patients to give up smoking because of the increasing severity of their symptoms. Thus the group of men who have given up smoking will include a disproportionate number of severe cases of chronic bronchitis, and, as a corollary, the mortality from this disease will remain higher in the ex-smokers compared with the smokers until, in the long run, the change in habits can exert a beneficial effect on the disease in the survivors.

For the unrelated diseases selective factors might operate in just the reverse way. A doctor who realizes that he may have a carcinoma of the large bowel or who has recently recovered from a stroke will hardly have the normal incentives to renounce smoking. There is little point in giving up if one is in danger of death and the act of smoking cannot influence it. It would not be surprising, therefore, if the doctors who chose to stop smoking were, so far as such diseases are concerned, the relatively healthy. From Table 25 it appears that this may well have happened and that the selective effect described has not fully worn off until smoking has been stopped for at least ten years. For coronary disease we believe the situation may lie between that for the related and that for the unrelated diseases: in other words, the mortality from the disease may be reduced by stopping smoking (directly or indirectly through some aetiological agent associated with smoking) but that effect will be complicated by a tendency for doctors not to modify their smoking habits after the disease is first suspected.

In short, the doctors who stop smoking are not a randomly selected cross-section, as one would ideally wish, but will include those whose actions have been influenced by the presence (or absence) of symptomatic disease. Assessment of the effects of stopping smoking must take this situation into account. The influence of such selective mechanisms will, clearly, be most marked during the first years after stopping smoking and are likely to wear off in time. We have therefore compared in Table 26 the mortality of men who have given up for more than five years with that of all other men who have either continued to smoke cigarettes or have given up for less than five years. In other words, those who recently selected themselves are put back in the smoking population, which is then compared with those who selected themselves as long as five years ago (and in many of them very much longer). For cancer of the lung, chronic bronchitis, and the group of other related causes the contrast between continuing and ex-smokers is increased. For coronary disease it is slightly lessened. For the unrelated diseases it is so appreciably diminished that there is only a 3% difference between the rates.

TABLE 26.—*Mortality Among Cigarette Smokers: Effect of Grouping Men Who Had Stopped Smoking for Less than Five Years with Continuing Smokers*

Cause of Death	Death Rate per 1,000		A as Percentage of B	Death Rate per 1,000		C as Percentage of D
	All Ex-smokers (A)	Continuing Smokers (B)		Ex-smokers of 5 Years or More (C)	All Other Smokers (D)	
Lung cancer ..	0·35‡	1·28†	**27**	0·29‡	1·24†	**23**
Chronic bronchitis	0·42	0·58	**72**	0·37	0·59	**63**
Coronary disease without hypertension ..	3·88	4·72	**82**	3·95	4·63	**85**
Other related causes ..	0·36	0·65‡	**55**	0·33	0·64‡	**52**
Unrelated causes	8·44	9·44	**89**	8·86	9·18	**97**
All causes ..	13·42	16·62	**81**	13·77	16·23	**85**

†‡ See footnotes to Table 25.

With such a fall in mortality—and the much smaller falls with other diseases—it might well be asked how far these changes are directly due to the stopping of smoking and how far to the "stoppers" being different in their previous smoking habits from the general run of smokers—for example, being late starters, non-inhalers, or smokers of lesser amounts. The answer is that such features are unlikely to account for the results. Differences in amount of smoking have already been allowed for in Tables 25 and 26 by the use of rates standardized for amount. Table 27 shows that the average age at which these men started to smoke grows a little less as the number of cigarettes smoked daily increases, but there are no appreciable nor progressive differences between men who continue to smoke cigarettes and those who have stopped.

TABLE 27.—*Average Age at Starting to Smoke Among Cigarette Smokers Divided by Continuity and Amount Smoked* (Standardized for Age at Inquiry)*

Group	Average Age at Starting when Daily Number of Cigarettes Last Smoked was:		
	1–14	15–24	25 or More
Smoking at 1/11/51	20·3	19·7	19·1
Stopped less than 10 years ..	20·7	19·9	19·8
„ 10 years or more ..	19·6	19·3	19·3

* The ages are somewhat higher than would be anticipated from present experience: they refer, however, to a section of the population composed of university graduates, some of whom completed their education before the first world war. The average is heavily weighted by the few doctors who began to smoke after 25 years of age; in each group the commonest age at starting was one to two years less than the average.

Ex-smokers do include a higher proportion of non-inhalers (Table 28). This difference, however, is found mainly among light smokers and therefore cannot have an important effect, since this particular group contributes only a small proportion of the excess mortality from the related diseases. We have too few data to measure the effect more quantitatively.

TABLE 28.—*Percentage of Inhalers Among Cigarette Smokers, Divided by Continuity and Amount Smoked (Standardized for Age at Inquiry)*

Group	Percentage of Inhalers when Daily Number of Cigarettes Last Smoked was:		
	1–14	15–24	25 or More
Smoking at 1/11/51	68	80	81
Stopped less than 10 years ..	59	77	80
„ 10 years or more ..	34	72	73

That factors of this nature are unlikely to be influential is also indicated by the results of the two halves of our study. The data, shown in Table 29, are classified according to the smoking habits recorded in the first questionary (and include the results for lung cancer already given in Table 11). For the three groups of diseases that are closely related to cigarette smoking the mortality among men who had stopped smoking was lower than that among men who continued to smoke and fell further with the passage of time. It is difficult to see how these results could have been produced if the fact of stopping smoking had not at the same time reduced the extent of exposure to some specific aetiological agent.

It is shown in Table 23 that pipe and cigar smokers had a mortality from all causes (*12.2*) negligibly higher than that of non-smokers (*12.1*). Although, at the same time, there was evidence that pipe or cigar smoking contributes to the development of cancers of the upper respiratory and digestive tracts

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and to chronic bronchitis, the effect on the total mortality was clearly small. It is not surprising, therefore, to find no reduction in total mortality when pipe or cigar smoking has been stopped. On the contrary, the death rate in ex-pipe or cigar smokers (*13.8*) is slightly higher than that among men who have continued to smoke (*11.9*). The information obtained from both questionaries shows that this excess mortality is entirely limited to men who have given up for under five years (*35.8*) and that men who have stopped for five years or more have a death rate that is even less than among non-smokers (*9.8* compared with *12.1* ; P=0.02).

TABLE 29.—*Mortality from Various Causes in First and Second Quinquennia of Observation : Continuing and Ex-cigarette Smokers*

Cause of Death	Death Rate per 1,000			
	Continuing Smokers		Ex-smokers	
	1st 5 Years	2nd 5 Years	1st 5 Years	2nd 5 Years
Lung cancer*	1·22	1·28	0·41	0·09
Chronic bronchitis	0·55	0·61	0·45	0·32
Coronary disease without hypertension	4·50	4·64	3·19	4·17
Other related causes	0·67	0·64	0·36	0·30
Unrelated causes	9·14	9·37	7·51	8·63
All causes	16·02	16·48	11·93	13·51

* Including 4 deaths among continuing cigarette smokers in which lung cancer was certified as a contributory cause (method A).

The numbers of deaths among ex-pipe or cigar smokers are too few to allow us to make any useful calculations for different causes of death. It may be noted, however, that for the first five years after stopping smoking there is an increased mortality from diseases that are unrelated to smoking as well as from related diseases. The most likely explanation for this increased mortality would seem to be that it was an artifact due to the effect of illness on smoking. If this is so, it follows that among doctors the effect varies with the method of smoking—pipe or cigar smokers tending to stop and cigarette smokers tending to continue (Table 25).

Mortality in Relation to Inhaling

Information about inhaling was obtained on our second (1957) questionary, and the deaths observed in the subsequent three years have been used to calculate mortality rates for men who said they inhaled and for those who said they did not. To these deaths we have added, to obtain more data, those that occurred in the eleventh year of the study. A few of these eleventh-year deaths—that is, occurring before 1 November, 1962—may not yet have been reported, and the death rates may therefore very slightly underestimate the true figures ; they may also be diminished by our failure to obtain replies from all the doctors in 1957, and some of them are known not to have replied because they were ill. The proportion not replying was, however, very small (2%), and this selective failure to reply cannot have appreciably affected the contrast between the rates.

TABLE 30.—*Inhaling Habits by Age, Method of Smoking, and Amount Smoked (Male Doctors Aged 25 Years and Over)*

Age (Years)	Percentage of Inhalers Among						
	Continuing Cigarette Smokers Smoking Daily			All Continuing Cigarette Smokers	Ex-cigarette Smokers	Continuing Smokers, Cigarette and Other	Continuing Pipe and/or Cigar* Smokers
	1–14	15–24	25 or More				
25–34	85	93	95	90	82	74	12
35–44	78	89	89	85	76	60	10
45–54	65	78	81	75	62	47	7
55–64	54	70	73	66	57	36	5
65–74	49	66	59	58	49	30	4
75 or more	38	47	46	41	41	26	4
All ages	67	81	81	76	63	47	7

* Figures for the few cigar smokers are almost identical with those for pipe smokers.

In several previous studies it has been shown that inhaling varies with age, with the method of smoking, and with the amount smoked. Similar trends were observed in this study and also for length of time stopped smoking (Tables 28 and 30). It is necessary, therefore, to allow for all these factors when comparing the incidence of deaths from different causes among inhalers and non-inhalers. The rates shown in Table 31 are therefore limited to pure cigarette smokers, and they have been standardized for amount smoked (using the three categories 1–14, 15–24, and 25 or more a day) as well as for age. Further, to avoid complications due to giving up smoking, the calculations have been confined to men who were still smoking only cigarettes at the time of the second inquiry.

TABLE 31.—*Mortality Among Continuing Cigarette Smokers According to Inhaling Habits, Compared with Non-smokers (Numbers of Deaths in Parentheses)*

Cause of Death	Death Rate per 1,000 Men per Year		
	Continuing Cigarette Smokers		Non-smokers
	Inhalers	Non-inhalers	
Lung cancer	1·88 (33)*	1·10 (11)	0·03 (1)
Chronic bronchitis	0·72 (12)	0·51 (7)	0·07 (1)
Coronary disease without hypertension	5·22 (113)	5·09 (60)	3·29 (50)
Other related causes	0·70 (17)	0·48 (4)	0·12 (2)
Unrelated causes	9·27 (171)	8·65 (99)	7·32 (112)
All causes	17·73 (345)	15·83 (181)	10·82 (166)

* Including one death, also included under its primary cause, in which lung cancer was certified as a contributory cause.

The results show that while the mortality from all causes was slightly higher in inhalers (*17.73*) than in non-inhalers (*15.83*) the difference varies very considerably with cause of death. The largest relative excess was observed with lung cancer (71%, P=0.10) and the next largest with chronic bronchitis (41%) and the group of other related causes[5] (46%). Only small and statistically insignificant differences were observed in coronary disease without hypertension (3% excess in inhalers) and in the large group of unrelated causes (7% excess in inhalers). With each cause the rate for non-inhalers was higher than that for non-smokers, but the excess is least for the unrelated diseases (only 18%).

With only 44 deaths from lung cancer, comparison of the rates among men who have smoked different numbers of cigarettes must be highly unreliable. Nevertheless, the figures shown in Table 32 may give an indication of the likely pattern —that is, that the importance of inhaling is most marked among light smokers (none of whom died of lung cancer if they did not inhale) and is least marked among heavy smokers. Among the light and moderate smokers the excess mortality of inhalers is significant (P=0.01). Among the heavy smokers the rate was actually higher among non-inhalers, but the difference could here have arisen by chance (0.4<P<0.5).

TABLE 32.—*Mortality from Lung Cancer According to Number of Cigarettes Smoked and Inhaling Habits (Numbers of Deaths in Parentheses)*

Number of Cigarettes Smoked Daily	Death Rate per 1,000 Continuing Cigarette Smokers per Year	
	Inhalers	Non-inhalers
1–14	1·59 (11)	0·00
15–24	1·95 (13)	0·86 (4)
25 or more	2·16 (9)*	2·98 (7)

* See footnote to Table 31.

Mortality Among Women

The women doctors available for study number less than a fifth of the male doctors (18%) and fewer of them are in the age-groups of high mortality rate (40% were under 35 years

[5] Other upper respiratory and upper digestive diseases, pulmonary tuberculosis, peptic ulcer, and cirrhosis of the liver and alcoholism.

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TABLE 33.—*Standardized Death Rates from Various Causes Among Women Doctors in Relation to Smoking Habits**

Cause of Death	No. of Deaths	Death Rate per 1,000 Women per Year							
		All Women	Non-smokers	Smokers	Ex-smokers	Continuing Smokers	No. of Cigarettes Daily (Continuing Smokers)		
							1–14	15–24	25 or More
Lung cancer	7	0·08	0·03	0·13	0·08	0·15	—	0·41	0·22
Other respiratory and upper digestive cancer	2	0·04	—	0·07	—	0·11	—	0·27	0·22
Chronic bronchitis	2	0·04	—	0·08	—	0·11	0·05	0·27	—
Pulmonary tuberculosis	1	0·03	0·04	—	—	—	—	—	—
Cirrhosis of liver and alcoholism	4	0·06	0·04	0·07	0·16	0·03	—	0·10	—
Coronary disease without hypertension	56	1·14	1·25	0·99	1·26	0·84	0·41	1·25	2·62
Other causes (unrelated)	342	6·72	6·60	6·60	5·94	6·93	6·30	8·60	5·70
All causes	414	8·10	7·95	7·94	7·44	8·17	6·76	10·89	8·76

* Only one woman said she smoked a pipe as well as cigarettes and no woman smoked only pipes or cigars. For the purpose of this analysis the small additional amount of pipe tobacco has been ignored.

of age against 29% of men, and 5% were 65 years or over against 12%). The observed deaths are therefore far fewer, and very little information can be obtained about the causes of death. To increase the numbers we have therefore included 48 deaths which occurred in the eleventh year of the study, and this brings the total number of deaths of women to 414.

Table 33 shows the mortality in each of the six groups of diseases which were shown to be related to smoking in men and for the remaining unrelated causes of death. The results agree with those for men in showing no relation with smoking in these "unrelated" causes—and with women they account for four-fifths of all deaths. The mortality among cigarette smokers (*6.60*) is identical with that among non-smokers (*6.60*). The 11 deaths attributed to cancer of the lung, cancer of the rest of the respiratory and upper digestive tracts, and chronic bronchitis were, as in men, concentrated among smokers; but cirrhosis of the liver and alcoholism (4 deaths) and coronary disease in the absence of hypertension (56 deaths) showed no such relation. (Only one death was attributed to pulmonary tuberculosis and none to peptic ulcer.) For coronary disease the mortality of male doctors who smoked cigarettes was only 10% greater than that of non-smokers, and the 56 deaths of women are really too few to be confident that the experience of the two sexes is different. It may, moreover, be noted that at ages under 65 years—at which the relation among men was most marked—the mortality rate of women was higher among cigarette smokers (*0.35*) than among non-smokers (*0.26*).

Examination of the few data for lung cancer shows that the mortality rate is highest among women who smoked 15 or more cigarettes a day (the rate was lower among the 244 women in the heaviest category of smokers—that is, those smoking 25 or more a day—but is based upon only one death). All the rates are lower (sometimes substantially) than those of men, and even with these minute numbers it seems that some factor other than the amount smoked is necessary to account for the difference.

Other features of the smoking history may indeed play a part, particularly: (1) the age at starting to smoke, and (2) the proportion of inhalers. Women doctors who were continuing to smoke cigarettes in 1951 began to smoke on average when aged 24.7 years—4½ years older than the corresponding male doctors (see Table 27). Among doctors aged 55 years and over in 1951—that is, those who have contributed most of the cases of lung cancer—the difference was greater; women of these ages began to smoke at an average age of 28.3 years compared with 20.2 years for men.

Differences in inhaling habits are shown in Tables 30 and 34. At each level of smoking and at each age the inhalers were fewer among women than among men—and the difference was most marked at 55 years and over, when the risk of cancer was highest. At these ages and at each level of smoking the proportion of inhalers was approximately twice as great in men as in women.

TABLE 34.—*Inhaling Habits by Age and Amount Smoked (Women Doctors Aged 25 Years and Over)*

Age (Years)	Percentage of Inhalers among Continuing Smokers		
	Number of Cigarettes Smoked Daily		
	1–14	15–24	25 or More
25–34	73	91	} 78*
35–44	63	71	
45–54	43	59	54
55–64	26	34	47
65–74	17	26	} 25*
75 or more	17	18	
All ages	44	55	58
†Women aged 55 years or more	22	29	36
†Men aged 55 years or more	50	65	64

* Age-groups combined because number of women in one age-group was less than 10.
† Standardized for age.

We have not sufficient data to take these differences into account, but it appears (from Table 32) that the difference in inhaling will lower the female mortality rate in relation to the male, and it is reasonable to suppose that the later average age at starting to smoke would have a similar effect. These differences, too, may affect not only the relative lung cancer mortality rate in the two sexes, but also, to a greater or less extent, the rates for all the other "related diseases."

[*The conclusion of this article, together with a list of references, will be published next week.*]

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