PAPERS AND ORIGINALS

Mortality in relation to smoking: 20 years' observations on male British doctors

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Summary

In 1951 the British Medical Association forwarded to all British doctors a questionnaire about their smoking habits, and 34 440 men replied. With few exceptions, all men who replied in 1951 have been followed for 20 years. The certified causes of all 10 072 deaths and subsequent changes in smoking habits were recorded. The ratio of the death rate among cigarette smokers to that among lifelong non-smokers of comparable age was, for men under 70 years, about 2:1, while for men over 70 years it was about 1·5:1. These ratios suggest that between a half and a third of all cigarette smokers will die because of their smoking, if the excess death rates are actually caused by smoking.

To investigate whether this is the case, the relation of many different causes of death to age and tobacco consumption were examined, as were the effects of giving up smoking. Smoking caused death chiefly by heart disease among middle-aged men (and, with a less extreme relative risk, among old men), lung cancer, chronic obstructive lung disease, and various vascular diseases. The distinctive features of this study were the completeness of follow-up, the accuracy of death certification, and the fact that the study population as a whole reduced its cigarette consumption substantially during the period of observation. As a result lung cancer grew relatively less common as the study progressed, but other cancers did not, thus illustrating in an unusual way the causal nature of the association between smoking and lung cancer.

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Introduction

At the end of October 1951 Doll and Hill sent a questionnaire to all the men and women whose names were on the current British *Medical Register* and who were believed to be resident in the United Kingdom.[1] In addition to name, address, and age, they were asked a few simple questions about their smoking habits. Replies that were sufficiently complete to be used were received from 34 440 men*—that is, about 69% of the men who were alive when the questionnaire was sent. Observations of mortality began on 1 November 1951 and continued until 31 October 1971. Further inquiries about changes in habit and some additional characteristics of the men were made in November 1957, March 1966, and July 1972.

An account of this study and its earlier results have been reported.[1-5] We report now the mortality rates of male doctors over the 20 years from November 1951 to 31 October 1971, both in total and in relation to their smoking habits at different periods. Observations on the women doctors will be reported later.

Data

SMOKING HABITS

The numbers of men replying to the repeat questionnaires and the numbers not replying for different reasons are shown in table I. Further questionnaires were not sent to doctors who had been struck off the *Medical Register* nor to those who had refused to answer previously or had asked not to be written to again, although their mortality was still monitored. The proportions of survivors who did not supply us with further information in 1957, 1966, and 1972 were, respectively, 1·6%, 3·6%, and 2·1%.

On the first questionnaire doctors were asked whether they were (*a*) then smoking, (*b*) had smoked in the past, or (*c*) were lifelong non-smokers (defined as never having smoked as much as one cigarette† a day for as long as one year). The smokers and ex-smokers were asked the age at which they had begun and how much they were now smoking, or had smoked when they gave up (in cigarettes

*The total is different from that reported in 1964, as the sex of five women had been incorrectly recorded.

†Subsequently amplified to include an alternative of a quarter of an ounce of tobacco a week.

per day or ounces of tobacco a week as hand-made cigarettes or in a pipe). Questions about cigar consumption were not asked as cigar smoking was then uncommon. Those who had stopped smoking were also asked how old they were when they stopped.

On subsequent questionnaires respondents were told their previous answers and were asked if they were still smoking the same or, if not, what they were now smoking (including how many cigars) and, when relevant, their age at starting or last stopping. Extra questions were also asked, which varied on each questionnaire. On the second questionnaire men who were known to have been pipe or cigar smokers at any time were asked whether they had ever smoked as much as one cigarette a day for a year (unless this was already known); and all smokers, past or current, were asked "Do you (or did you) inhale—that is, take the smoke deeply into the lungs?" For ex-smokers this question referred to the time when they last smoked regularly. On the third questionnaire men who were then smoking but had changed the type of tobacco or amount smoked since their previous reply were asked separately whether now they usually, sometimes, or never inhaled when smoking cigarettes, pipes, and cigars; and men who had stopped smoking between the second and third questionnaires were asked whether they had done so because of ill-health. On the last questionnaire men who were smoking cigarettes were asked whether they usually smoked filter-tipped cigarettes or plain.

The proportion of non-smokers and the average numbers of cigarettes smoked each day by the doctors at different ages at the beginning of the study are shown in table II. The table also shows the average numbers smoked 5, 15, and 20 years later by the survivors of the same groups of doctors who replied to the subsequent questionnaires, and these numbers (both in 1951 and later) expressed as percentages of the numbers smoked by British men of the same age.[6] At each period middle-aged doctors smoked more cigarettes than either younger or older doctors. In 1951 the shortfall in cigarette consumption by the old was, however, greater among other British men, so that cigarette consumption by doctors, expressed as a percentage of that by British men, was actually greater among the old than among the middle-aged.

Between 1951 and 1971 the average number of cigarettes smoked each day by the doctors fell from 9·1 to 3·6 partly because of the relation between cigarette smoking and mortality. Those who replied to the last questionnaire, however, had in 1951 smoked an average of 8·7 cigarettes a day, so that the overall reduction must chiefly have been due to a change in habits. At each successive survey fewer cigarettes were smoked than at the previous survey by each cohort. Expressing these amounts as percentages of the amounts smoked by age-matched British men showed that these decreases were not paralleled in the general population, so that the average number of cigarettes smoked by doctors of all ages decreased from 88% of the number smoked by British men of the same ages to 37%.

DEATHS

Information about the death of doctors was obtained at first directly from the Registrars-General of the United Kingdom, who provided particulars of every death identified as referring to a medical practitioner. Later we obtained lists of deaths notified to the General Medical Council, and these were complemented by reference to the records of the British Medical Association and other sources at home and abroad. Some deaths came to light in response to the questionnaires. Others were discovered in the course of following up doctors who had not replied or who had not been sent repeat questionnaires. Of the 34 440 men studied, 10 072 are known to have died before 1 November 1971, 24 265 are known to have been alive at that date, and 103 (0·3%) have not yet been traced.

Many of the 103 untraced doctors were not British, and 67 (65%) are known to have gone abroad. Sixty are known to have been alive at the end of 1965. The age distribution of the untraced doctors in 1971 was similar to that of the doctors who are known to have survived (31% aged 65 to 84 years against 27%; 0% aged 85 years or more against 1%). Of the last 182 doctors successfully traced by personal follow-up, only 15 (8%) were found to have died before 1 November 1971. It is unlikely, therefore, that we can have missed more than about a dozen deaths relevant to the study.

Information on the underlying cause of death in the 10 072 doctors known to have died before 1 November 1971 was obtained for the vast majority from the official death certificates. Except for deaths where lung cancer was mentioned, we accepted without further inquiry the certified cause and (unless otherwise stated) classified the deaths according to the underlying cause. (In only four cases were we unable to obtain any evidence of the cause.) The underlying causes were classified according to the seventh revision of the *International List of Causes of Death*,[7] with the exception that we created a separate category of "pulmonary heart disease" (see below).

TABLE I—*Response to questionnaires*

	Second questionnaire	Third questionnaire	Fourth questionnaire
Survey period	November 1957–31 October 1958	March–31 October 1966	July–31 October 1972
Known to have died before end of survey period	3122	7301	10634
Presumably alive at end of survey period	31318	27139	23806
Replied by end of survey period (and % of men then alive)	30810 (98·4)	26163 (96·4)	23299 (97·9)
Reasons for non-response:			
Too ill	31	65	21
Refused	36	63*	102*
Address not found	72	403	22
Unknown and other reasons	369	445	362

*Includes all men who refused previously.

TABLE II—*Cigarette consumption of all male doctors, 1951-71, compared with national average*

Age		Respondents in 1951		Cigarettes smoked by all male doctors							
				Average No per day				Average as % of No smoked by UK men of same age†			
1951	1971	No of men	% Non-smokers	1951	1956*	1966	1971*	1951	1956	1966	1971
20-4	40-4	886	43	6·2	6·1	3·7	2·6	63	51	32	22
25-9	45-9	4375	30	7·9	7·2	4·6	3·5	69	61	40	28
30-4	50-4	4855	21	9·0	7·8	5·0	3·7	79	60	45	33
35-9	55-9	5086	17	10·1	8·4	5·5	3·9	84	64	51	41
40-4	60-4	3802	15	10·8	8·7	5·8	4·0	90	66	55	43
45-9	65-9	3538	13	10·9	9·0	5·6	3·9	91	71	64	53
50-4	70-4	3577	11	11·0	8·9	5·2	3·3	94	79	74	55
55-9	75-9	2177	10	9·6	7·6	4·1	2·3	92	78	77	53
60-4	80-4	1893	9	8·4	6·3	3·1	1·8	109	107	67	55
65-9		1477	8	7·3	5·1	2·8	1·3	157	115	113	
70-4		1211	9	5·9	3·8	1·3		169	112		
75-9		905	11	3·9	2·4			142	110		
80-4		481	13	3·2	2·3			193			
≥85		177	16	1·6							
All ages		34 440	17	9·1	7·7	5·0	3·6	88	68	51	37

*Data estimated from questionnaires administered the following year by ignoring changes reported to have taken place in previous year.
†Averaging the UK data for 1950-2, 1955-7, 1965-7, and 1970-2, and using 80 years and over for 80-84 years.

TABLE III—*Death rate by cause of death and smoking habits when last asked*

Cause of death	No of deaths	Annual death rate per 100 000 men, standardised for age							χ^2†	
		Non-smokers	Current or ex-smokers	Ex-smokers	Current smokers, any tobacco	Current smokers, any tobacco (g/day)			Non-smokers v others	Trend
						1-14	15-24	⩽25		
			Cancer							
Lung	441	10	83	43	104	52	106	224	41·98	197·04
Oesophagus	65	3	12	5	16	12	13	30	3·94	14·94
Other respiratory sites*	46	1	9	4	11	6	9	27	3·31	21·68
Stomach	163	23	28	21	32	28	38	32	—	—
Colon	195	27	34	34	34	35	33	31	—	—
Rectum	78	6	14	14	14	10	14	27	2·81	10·76
Pancreas	92	14	16	12	18	14	18	27	—	3·98
Prostrate	186	39	30	31	30	28	31	38	—	—
Kidney	46	3	8	9	8	8	9	9	—	—
Bladder	80	9	14	11	16	16	16	12	—	—
Marrow and reticuloendothelial system	152	33	24	26	24	27	22	19	—	(3·51)
Unknown site	64	12	11	9	12	10	13	14	—	—
Other site	151	25	26	29	24	19	24	35	—	—
			Respiratory disease							
Respiratory tuberculosis	57	3	11	11	10	8	7	21	3·83	10·51
Asthma	40	4	7	12	5	5	7	0	—	—
Pneumonia	345	54	59	62	57	47	62	91	—	6·94
Chronic bronchitis and emphysema	254	3	48	44	50	38	50	88	25·58	47·23
Other respiratory disease	121	16	21	24	19	20	14	26	—	—
			Pulmonary heart disease							
Pulmonary heart disease*	50	0	9	7	11	9	10	19	4·72	8·37
			Cardiac and vascular disease							
Rheumatic heart disease	77	14	13	12	13	14	16	5	—	—
Ischaemic heart disease	3191	413	554	533	565	501	598	677	22·59	53·56
Myocardial degeneration*	615	67	108	98	116	111	111	160	9·58	13·92
Hypertension	239	37	41	41	41	33	43	58	—	4·67
Arteriosclerosis	117	21	20	17	21	17	21	46	—	4·85
Aortic aneurysm (non-syphilitic)	121	5	22	16	26	18	28	45	8·40	25·60
Venous thromboembolism	48	9	8	8	8	8	5	14	—	—
Cerebral thrombosis	616	86	106	105	107	92	123	131	—	9·54
Other cerebrovascular disease	692	107	118	122	115	112	114	128	—	—
Other cardiovascular disease	267	53	44	49	41	37	42	52	—	—
			Other diseases							
Parkinsonism	51	14	8	13	5	8	1	4	—	(9.10)
Peptic ulcer	79	8	14	12	15	10	20	23	—	8·26
Cirrhosis of liver, alcoholism	80	7	14	10	16	10	10	40	—	22·53
Hernia	16	0	3	2	4	3	4	7	—	4·16
Other digestive disease	144	20	25	27	24	18	33	26	—	3·25
Nephritis	79	10	14	10	16	15	14	21	—	—
Other genitourinary disease	136	19	23	24	23	22	24	26	—	—
Other disease	391	59	67	73	64	65	58	73	—	—
			Violence							
Suicide	173	21	31	27	32	30	28	46	—	6·26
Poisoning	74	9	13	6	16	12	14	26	—	6·86
Trauma	240	46	39	36	41	47	25	56	—	—
All causes	10 072	1317	1748	1652	1802	1581	1829	2452	68·47	244·16
(No of deaths)		(940)	(9132)	(3114)	(6018)	(2707)	(1986)	(1325)		

*See text for definition.
†Figures are given whenever the value was greater than 2·71 ($P < 0·1$); figures in parentheses indicate a decreasing trend from non-smokers to heavy smokers; others indicate an increasing trend.

Cancer of the lung, including trachea or pleura, was given as the underlying cause of 467 deaths and as a contributory cause in a further 20. For each of these 487 deaths we sought confirmation of the diagnosis from the doctor who had certified the death and, when necessary, from the consultant to whom the patient had been referred. We thus obtained information about the nature of the evidence in all but two cases. When there seemed any doubt about the interpretation of the report we sought the advice of J R Bignall (professor of medicine, Brompton Hospital for Diseases of the Chest), who was kept in ignorance of the patient's smoking history. As a result, we accepted carcinoma of the lung as the underlying cause of 441 deaths and as a contributory cause of 17. Twenty-six deaths were considered to be due to other underlying causes* and three to other contributory causes.†

Statistical analysis

Almost all the doctors who replied to the first questionnaire did so within a few weeks and those who did not reply to a single mailing were not pursued. Most of the survivors responded equally quickly to the later questionnaires, but we had to send reminders on two or more occasions to obtain the high response rates shown in table I. As we continued to accept replies to the second questionnaire up to 31 October 1958 and to the third up to 31 October 1966, we related deaths to the information received in reply to these two questionnaires only if death occurred on or after 1 November 1958 or 1 November 1966, respectively. Therefore, apart from the deaths recorded in 1951-2, the mortality usually relates to smoking habits more than a year before death. We have no useful information about the possible effect on mortality of changes of habit within a year of their being made.

We always asked about the method of smoking, the amount smoked, and, if relevant, the date of stopping. Thus we could examine mortality in relation to these aspects of the smoking history by relating deaths that occurred in the first seven years of the study to information obtained in the first questionnaire, deaths that occurred in the next eight years to information obtained in the second questionnaire, and deaths that occurred in the last five years to information obtained in the third questionnaire. The few doctors who did not reply to the second or third questionnaires were retained in the study, and we related the deaths that occurred among them to the information provided in the last questionnaire to which they had replied. Information about inhalation and the previous use of cigarettes by pipe and cigar smokers was not obtained until the second questionnaire, so that we could use this information only in relation to deaths in the last 13 years of the study.

For each of the subgroups defined by smoking habits and age, we calculated the person-years at risk of death between 1951 and 1971 in five-year age groups from 20 to 84 years of age and 85 years and

*Cancers of the trachea (2); pleura; stomach; colon; rectum (2); kidney; bladder; and prostate (2); melanoma of skin; leukaemia; carcinomatosis, primary not known (5); peripheral neuritis; aortic valve disease; non-syphilitic aortic aneurysm; heart failure; pulmonary embolus; bronchopneumonia; collapsed lung; and coma.

†Carcinomatosis, primary not known; coronary thrombosis (2).

over.* (Further division at older ages was not justified despite the fact that the oldest attained age was 101 years, as four-fifths of the man-years in the last group were accumulated under 90 years of age.) Taking all men in the study together, we then calculated the total number of deaths from a particular cause per person-year in each age group. These age- and cause-specific rates were applied to the number of person-years at risk in each age and smoking subgroup to estimate the number of deaths that would have been expected from this cause if mortality were unrelated to smoking. The observed and expected numbers for a particular smoking category were then summed over all ages. The observed and expected numbers in each smoking category form the chief basis of our analysis. For some purposes their ratio (observed:expected) was multiplied by the total annual death rate for that disease among all men of all ages together, giving for each smoking category death rates indirectly standardised for age that could be used for comparison with each other.

Values of χ_1^2 with correction for continuity were calculated for the difference between the rates for life-long non-smokers and all other men, and for the trend in the rates for non-smokers and current smokers of 1-14, 15-24, and 25 or more grams of tobacco a day, for each of the causes of death examined. In each case, χ^2 values were based on the expected numbers rather than on the exact variance/covariance matrix.

Results and comment

MORTALITY BY CAUSE AND PRINCIPAL SMOKING HABITS

The numbers of deaths attributed to 40 different causes (or groups of causes) and the corresponding mortality rates, standardised for age, are shown in table III for all men who had ever smoked, ex-smokers, and current smokers, and for men smoking 1-14, 15-24, and 25 or more grams of tobacco a day (the last group smoking on average slightly more than 30 g a day).† For this purpose we regarded any cigarette as equivalent to 1 g of tobacco, and cigars as equivalent to 3 g of tobacco (if small) or 5 g of tobacco (if large). Causes of death were examined separately if there were 40 or more such deaths, since at least five deaths would then have been expected among non-smokers if smoking were not associated with the disease. All such causes of death are included in table III if we had any reason to suppose that they might be related to smoking habits, either positively or negatively, or if they constituted a clearly defined group of interest for comparison. Cancers of the lip, tongue, mouth, pharynx (excluding nasopharynx), larynx, and trachea were classed together as "other respiratory cancers" because the numbers of deaths attributed to the individual types were too few. Deaths attributed (*a*) to myocardial degeneration or functional and other diseases of the heart (ICD Nos 422 and 430-434) with mention of chronic bronchitis or emphysema on the death certificate or (*b*) to cor pulmonale were classed together as "pulmonary heart disease."‡ Other deaths attributed to myocardial degeneration and other conditions classified under ICD No 422 were described simply as "myocardial degeneration." The 16 deaths attributed to hernia were included as a separate group because of the interest of the observations.

Half the conditions in table III were positively related to smoking, some very strongly so, and one disease, Parkinsonism, was negatively related. To say that these conditions were related to smoking does not necessarily imply that smoking caused (or prevented) them. The relation may have been secondary in that smoking was associated with some other factor, such as alcohol consumption or a feature of the personality, that caused the disease. Alternatively, smoking habits may have been modified by the disease or the relation may have been an artefact due to misdiagnosis, so that deaths that were really due to diseases associated with smoking may have been miscertified as due to diseases that are not. We postpone discussion of the interpretation of the relation for individual diseases until later, when our other results can also be taken into account.

*A man aged 38 years at entry, for example, was taken to be 38·5 years old and death during any particular study year, numbered from 1 to 20 from 1 November 1951 to 31 October 1971, was assumed to have occurred at mid-year for calculating man-years (but for no other purpose).

†Tables showing the numbers of deaths observed and expected for each group of causes and each smoking category from which the rates shown in tables III-IX have been calculated are held in the Radcliffe Science Library, Oxford, and in the library of the National Institute of Medical Research, Mill Hill.

‡The underlying causes of death were described as myocardial degeneration (20), myocarditis (5), congestive heart failure (8), cor pulmonale (6), and 11 other terms each once.

Meanwhile, we classified the diseases positively related to smoking in three main groups.

Firstly, ischaemic heart disease was kept in a class by itself because many more deaths were attributed to it (3191) than to any other cause. The trend in mortality from non-smokers through men smoking 1-14 and 15-24 grams of tobacco a day to smokers of 25 or more grams a day and the difference in mortality between ever-smokers and non-smokers were both statistically highly significant ($P<0·001$).

Secondly, eight conditions were closely associated with smoking (cancer of the lung, cancer of the oesophagus, cancers of other respiratory sites, respiratory tuberculosis, chronic bronchitis and emphysema, pulmonary heart disease, non-syphilitic aortic aneurysm, and hernia). For each of these conditions the mortality was at least three times as high in men who had ever smoked as in lifelong non-smokers and at least twice as high in continuing smokers who smoked heavily ($\geqslant$25 g/day) as in light smokers (<15 g/day). The trends in mortality from non-smokers to heavy smokers were all statistically significant ($P<0·05$), many of them highly so. For all but three of the conditions, which caused only a few deaths (cancers of other respiratory sites (46 deaths), respiratory tuberculosis (57), and hernia (16)), the difference between the mortality rates in ever-smokers and non-smokers was also statistically significant ($P<0·05$).

Thirdly, there were other conditions positively associated with smoking for which the χ^2 for trend in table III exceeded 3·84 ($P<0·05$). This was an extremely heterogeneous group of conditions, comprising cancers of the rectum and pancreas; pneumonia; myocardial degeneration, hypertension, arteriosclerosis, and cerebral thrombosis; cirrhosis of the liver and alcoholism; peptic ulcer; and suicide and poisoning. To it we also added cancer of the bladder (see below).

Parkinsonism was negatively related to smoking in that the mortality rate was higher in non-smokers than in men who had ever smoked, and the trend in mortality from non-smokers through light and moderate to heavy smokers was statistically significant ($P<0·01$). Parkinsonism is a chronic disease and it was a contributory cause in 26 other deaths. These also showed a similar type of relation, and when the two groups were combined, making 77 deaths in all, the differences were more distinct (χ^2 comparing non-smokers with men who had ever smoked $=2·73$; $P<0·1$; for the trend from non-smokers through light and moderate to heavy smokers $=13·70$; $P<0·001$).

The remaining 18 conditions* did not, in our data, show any significant association with smoking. Neither did cancer of the bladder, although it has consistently been related to smoking in other studies.[8-10] Only 80 deaths were attributed to this disease in our study. Possibly chance operated to prevent the appearance of a positive relation, as our data were easily compatible with the existence of the twofold relative risk that has commonly been reported. In eight other deaths cancer of the bladder was referred to as a contributory cause but their inclusion did not materially affect the results. For our present purpose we classed cancer of the bladder with the conditions associated with smoking and described the other 18 groups together as unrelated to smoking. Altogether, these unrelated conditions accounted for 3192 deaths (32% of the total). The annual death rates from them were, in non-smokers and in men who had ever smoked, respectively, 518 and 540 per 100 000; in ex-smokers and current smokers 556 and 532; and in light, moderate, and heavy current smokers 518, 522, and 601. Neither the difference between non-smokers and men who had ever smoked, nor the increase with amount smoked, was statistically significant (χ_1^2 for trend $=3·12$). But the highest rate was in men who smoked the most. Some small excess in smokers must be expected, however, as a result of misdiagnosis of other conditions, and the death of at least one man, who smoked 30 cigarettes a day and died of burns caused by setting fire to his bedclothes while smoking in bed, was directly attributable to the habit.

TYPE OF SMOKING

Table IV shows mortality rates similar to those in table III for men who, at the time of the last questionnaire before their death smoked cigarettes only, pipes or cigars (or both) only, or a combination including cigarettes (mixed smokers). The rates also differ from those in table III in that men are subdivided by numbers of cigarettes smoked instead of total tobacco consumption. Rates are given for

*Cancers of the stomach, colon, prostate, and kidney; cancers of the blood and reticuloendothelial systems; other cancers; cancers of unknown primary site; asthma; rheumatic heart disease; venous thromboembolism; nephritis; trauma; and residual groups of other cerebrovascular, cardiovascular, respiratory, digestive, and genitourinary diseases, and all other diseases not separately considered.

TABLE IV—*Death rate by cause of death, method of smoking, and number of cigarettes smoked per day when last asked*

Cause of death	No of deaths (excluding ex-smokers)	Annual death rate per 100 000 men, standardised for age						
		Non-smokers	Current smokers					
			Cigarettes only	Pipe and/ or cigars only†	Mixed (cigarettes and others)	Cigarettes only, No/day:		
						1-14	15-24	≥25
		Closely associated causes						
Cancer of lung	362	10	140	58	82	78	127	251
Cancer of oesophagus	56	3	14	11	27‡	11	12	21
Cancer of other respiratory sites*	38	1	13	9	10	5	7	33
Respiratory tuberculosis	38	3	15	3	8	9	10	30
Chronic bronchitis and emphysema	167	3	74	28	34	51	78	114
Pulmonary heart disease*	35	0	10	9	14‡	6	9	25
Aortic aneurysm (non-syphilitic)	91	5	33	18	23	17	38	52
Hernia	12	0	5	4	0	3	4	11
		Ischaemic heart disease						
Ischaemic heart disease	2205	413	669	425	528	608	652	792
		Other associated causes						
Cancer of rectum	51	6	16	10	17‡	11	11	33
Cancer of pancreas	70	14	22	12	16	19	20	29
Cancer of bladder	58	9	19	14	13	20	20	13
Pneumonia	218	54	73	38	59	56	84	105
Myocardial degeneration*	408	67	139	101	103	136	116	202
Hypertension	162	37	50	34	30	33	59	65
Arteriosclerosis	82	21	29	17	17	21	25	68
Cerebral thrombosis	402	86	115	99	104	94	134	137
Cirrhosis of liver, alcoholism	63	7	21	9	13	11	14	44
Peptic ulcer	57	8	20	10	13	9	30	27
Suicide	135	21	33	32	28	22	30	53
Poisoning	66	9	19	11	11	14	17	28
		Parkinsonism						
Parkinsonism	25	14	6	4	4	9	2	6
		Unrelated causes						
All other causes	2157	518	616	473	434	615	573	697
All causes (No of deaths)	6958	1317 (940)	2154 (3343)	1434 (1527)	1591 (1148)	1857 (1209)	2066 (1137)	2843 (997)

*See text for definition.
†About half these men had once smoked cigarettes (see table VI).
‡Mortality rates for mixed smokers, smoking 1-14, 15-24, or ≥25 g/day respectively were: 22, 20, and 49 per 100 000 for cancer of the oesophagus; 12, 17, and 15 per 100 000 for pulmonary heart diseaase; and 10, 24, and 15 per 100 000 for cancer of the rectum.

ischaemic heart disease, the conditions closely associated with smoking, the other associated conditions, the one negatively associated cause of death, and all the unrelated causes grouped together. In every case the rate was higher in cigarette smokers than in those who smoked pipes or cigars or both. For three conditions, however, the rate was higher in mixed smokers than in men who smoked only cigarettes, owing partly perhaps to chance variation of small numbers. For these conditions (cancer of the oesophagus, cancer of the rectum, and pulmonary heart disease) mortality rates for mixed smokers by total tobacco consumption are given in the footnote to table IV. Only for cancer of the oesophagus were the rates consistently higher than among cigarette smokers.

CIGARETTE SMOKING

Table IV also shows the mortality rates for continuing smokers who smoked only cigarettes and smoked different amounts a day. For all but four of the positively associated conditions the mortality increased progressively from light, to moderate, to heavy cigarette smokers. For cancer of the rectum it was equal in light and moderate smokers, for myocardial degeneration it was higher in light smokers than in moderate ones, and for cancer of the bladder and peptic ulcer it was higher in moderate smokers than in heavy ones. Some such irregularities must be expected when the numbers of deaths are small (as with cancers of the bladder and rectum and peptic ulcer) and particularly when the relation with smoking is weak. Even for other conditions, little attention can be paid to the exact shape of the dose-response relation as many men changed the amount smoked during the course of the study, especially after the age of 65. Heavy cigarette smokers, particularly, tended to reduce the number smoked a day, so that the group of light smokers contained an appreciable proportion of men who had smoked heavily in the past. Such changes will have a particularly strong effect on the dose-response relation for diseases that may manifest themselves many years before death (for example, anginal symptoms can occur years before a fatal infarct, or chronic dyspnoea long before death from bronchitis), since these manifestations may cause heavy smokers to smoke less and to have reported their reduced consumption to us in the last questionnaire before they died. The effect of such changes on the dose-response relation for lung cancer will be discussed elsewhere.[11]

Table V shows the mortality rates at different ages in non-smokers and in cigarette smokers from ischaemic heart disease, myocardial degeneration, and cerebral thrombosis. For ischaemic heart disease the mortality rate increased progressively from non-smokers through light and moderate smokers to heavy cigarette smokers at all ages under 65 years. The relative risk in heavy cigarette smokers compared with non-smokers was 15:1 at ages under 45 years, 3:1 at 45-54 years, and 2:1 at 55-64 years of age. Over 65 years of age the progression was irregular and the risk in heavy cigarette smokers was increased by less than 50%.

Myocardial degeneration is an ill-defined diagnosis that is rarely cited as the cause of death under 65 years of age. At older ages the relation with smoking was more definite than for ischaemic heart disease, the relative risk in heavy smokers compared with non-smokers being 5:1 at ages 65-74 and 2:1 at 75 years and over.

TABLE V—*Mortality in non-smokers and current cigarette smokers, by age: selected causes. Numbers of deaths are given in parentheses*

Age (in years)	Annual death rate per 100 000 men*			
	Non-smokers	Current smokers, smoking only cigarettes: No/day		
		1-14	15-24	≥ 25
	Ischaemic heart disease			
<45	7 (3)	46 (12)	61 (22)	104 (18)
45-54	118 (32)	220 (38)	368 (90)	393 (69)
55-64	531 (79)	742 (91)	819 (123)	1025 (125)
<65	166 (114)	278 (141)	358 (235)	427 (212)
65-74	1190 (83)	1866 (134)	1511 (101)	1731 (81)
≥75	2432 (92)	2719 (113)	2466 (50)	3247 (27)
	Myocardial degeneration			
<65	6 (4)	6 (3)	9 (6)	23 (11)
65-74	44 (3)	124 (9)	186 (12)	204 (9)
≥75	945 (40)	1932 (79)	1307 (21)	2114 (11)
	Cerebral thrombosis			
<65	10 (6)	18 (9)	14 (9)	22 (11)
65-74	131 (9)	166 (12)	353 (23)	290 (13)
≥75	1039 (41)	985 (41)	1397 (26)	1448 (10)

*Indirectly standardised for age to make the four entries in any one line comparable

TABLE VI—*Mortality in non-smokers and pipe or cigar smokers by additional cigarette smoking: selected causes (last 13 years of study only)*

Cause of death	No of deaths (excluding ex-smokers)	Annual death rate per 100 000 men, standardised for age: Non-smokers	Current pipe or cigar smokers: Never cigarettes	Current pipe or cigar smokers: Cigarettes previously	Current pipe or cigar smokers: Cigarettes now	Current smokers of cigarettes only
Cancer of lung	232 } 519	11 } 28	54 } 138	77 } 182	113 } 257	156 } 350
Cancers of oesophagus and other respiratory sites	65	4	23	21	46	35
Chronic bronchitis and emphysema and pulmonary heart disease	138	3	31	60	64	101
Other conditions closely associated with smoking	84	9	30	24	35	58
Ischaemic heart disease under 65 years	607	189	124	240	285	413
Ischaemic heart disease age 65 years and over	836	1655	1586	1536	1945	2259
Myocardial degeneration	236	75	114	82	108	142
Other conditions associated with smoking	843	275	324	312	371	465
All other conditions	1353	560	493	524	498	701
All causes	4394	1418	1540	1000	1855	2456
(No of deaths)		(628)	(388)	(595)	(737)	(2046)

Examination of the mortality rates for cerebral thrombosis shows that the relation with smoking was somewhat similar, at each age, to that for ischaemic heart disease. Deaths under 75 years of age were, however, much less common, so that the overall relation was less close, being dominated by the weak relation in old age.

PIPE AND CIGAR SMOKING

It is evident from table IV that the excess overall mortality among smokers was due principally to an excess among men who had smoked cigarettes. Those who smoked only pipes or cigars experienced mortality rates which, with few exceptions, were similar to, or only slightly above, those of men who did not smoke at all. Substantial differences between pipe and cigar smokers and non-smokers were observed only for the eight conditions closely associated with smoking and for myocardial degeneration, which, it has already been noted was more closely related to smoking among men aged 65 years and over than was ischaemic heart disease. The numbers of deaths attributed to these conditions in pipe and cigar smokers were small, and significant excesses over the rates for non-smokers were observed only for lung cancer, chronic bronchitis and emphysema, pulmonary heart disease, non-syphilitic aortic aneurysm, and myocardial degeneration.

The first questionnaire in this study did not inquire whether pipe or cigar smokers had ever smoked cigarettes. Some had undoubtedly done so, and the excess mortality among them might therefore have been attributable to cigarette smoking in the past. The second questionnaire asked specifically about cigar consumption as well as other forms of smoking and about any history of cigarette consumption so that, during the last 13 years of the study, we could describe the death rates of pipe and cigar smokers who had never smoked cigarettes. The results are shown in table VI.

Because the numbers of deaths in several of the smoking categories were small, we have presented only the major causes of death related to smoking and have grouped allied conditions together. The results show an excess mortality among those pipe and cigar smokers who had never smoked cigarettes for the eight conditions closely related to smoking and for myocardial degeneration, but not for ischaemic heart disease. For lung cancer, chronic bronchitis and emphysema, and pulmonary heart disease, there was a progressive increase in mortality from non-smokers through pipe and cigar smokers who had never smoked cigarettes and those who had smoked cigarettes only in the past to those who were also smoking cigarettes at the time of observation. The trends for cancers of the oesophagus and other respiratory sites and for other conditions closely associated with smoking were irregular, perhaps because of the small numbers. There seemed, however, to be a distinction between cancer of the lung and cancers of the oesophagus and other respiratory sites, in that the risk of cigarette smoking was much greater than the risk of pipe or cigar smoking for the former, but not for the latter—an observation that is relevant to the interpretation of secular trends in mortality (see Discussion).

INHALING

Not all smokers smoke in the same way. In our second and third questionnaires we asked whether they thought they inhaled the smoke, and the great majority who replied to both questionnaires answered similarly both times, despite an interval of nearly nine years. Of those cigarette smokers who had said they inhaled in response to the second questionnaire, 83% said in the third questionnaire that they usually inhaled and 16% that they sometimes inhaled. Of those who had said they did not inhale in response to the second questionnaire, 68% later said that they never inhaled and 28% that they sometimes inhaled. Even the few who gave indefinite answers to the second questionnaire (that could not be understood as either a clear yes or a clear no) were consistent, only 18% saying that they usually inhaled and 10% that they never inhaled when questioned again.

TABLE VII—*Death rate by cause of death and inhaling in continuing cigarette smokers: standardised for age and amount smoked*

Cause of death	No of deaths	Annual death rate per 100 000 men responding to question: "Do you inhale?"*: Yes	No	Risk in inhalers compared with unity in non-inhalers
Cancer of lung	123	124	147	0·84
Cancers of oesophagus and other respiratory sites	28	31	27	1·13
Chronic bronchitis and emphysema and pulmonary heart disease	71	89	58	1·53
Other conditions closely associated with smoking	49	63	31	2·01
Ischaemic heart disease under 65 years	305	418	266	1·57
Ischaemic heart disease at 65 years and over	320	2444	2164	1·13
Myocardial degeneration	76	88	80	1·09
Other conditions associated with smoking	331	356	359	0·99
All other conditions	509	559	529	1·06
All causes	1812	2034	1810	1·12
(No of deaths)		(1177)	(635)	

*Excluding the 6% of men who gave an indefinite answer, as the deaths among them were few (117) and the rates were subject to large random errors.

The proportions of men who responded in different ways varied with the method of smoking and the amount smoked. We therefore limited our comparison to cigarette smokers only and standardised the mortality rates for age and for amount smoked.*

As we could use only those observations made after the completion of the second questionnaire, the number of deaths available for analysis was substantially reduced. We have therefore presented only the broad groupings of selected causes of death which we examined in relation to pipe and cigar smoking. The results (table VII) show a notably higher mortality among men who said they inhaled than among men who said they did not for chronic bronchitis and emphysema and pulmonary heart disease, for ischaemic heart disease at young ages, and for "other conditions closely associated with smoking," but not for cancer of the lung, cancers of the oesophagus and other respiratory sites, or for any other group of diseases. Indeed, the mortality rate for lung cancer was lower among inhalers than among non-inhalers. This last result corresponds to that in a restropective study,[12] when Doll and Hill found that the relation with inhaling varied with the amount smoked. We have, therefore, presented the figures for lung cancer separately for three levels of smoking. The results support the findings in the earlier study (table VIII). For light and moderate smokers the mortality rates were higher in men

*In nine groups, from 1-4 cigarettes a day up to 40 or more a day.

TABLE VIII—*Death rates from lung cancer in continuing cigarette smokers by amount smoked and inhaling habits. Numbers of deaths are given in parentheses*

No of cigarettes smoked per day	Annual death rate per 100 000 men* responding to question "Do you inhale?"		
	Yes	Indefinite	No
1-14	98 (16)	188 (4)	54 (8)
15-24	113 (29)	196 (6)	75 (9)
≥25	185 (32)	420 (5)	417 (29)

*Standardised for age in quinquennia and for amount smoked in categories of five cigarettes a day up to 35-39 a day and then 40 or more a day. Entries in any line should therefore be comparable with each other though not with entries in other lines.

who said they inhaled than in men who said they did not. For men who smoked 25 or more cigarettes a day, however, the reverse was found. A few men were unable to classify themselves definitely in either category, and they consistently recorded the highest mortality rates, irrespective of the amount smoked.

STOPPING SMOKING

Many doctors had stopped smoking, so we were able to observe mortality rates in ex-smokers who had stopped for different lengths of time. To facilitate comparisons we confined the analysis to men who at the time of our first questionnaire smoked only cigarettes, were ex-smokers who had smoked only cigarettes at the time they last stopped, or were lifelong non-smokers. Non-smokers were reclassified as smokers if they started smoking cigarettes and nothing else. Smokers were reclassified as ex-smokers if they subsequently reported that they had stopped smoking. Ex-smokers who started again and cigarette smokers and non-smokers who started smoking pipes or cigars were excluded from the time we learnt of the change. Cigarette smokers who had not started before 25 years of age and ex-smokers who had given up before 30 years of age were also excluded. All ex-smokers studied had therefore smoked for at least five years, and most had smoked for much longer. Examination of the ages at which men started to smoke showed that continuing smokers and ex-smokers had started to smoke at about the same age (about 19 years), irrespective of the length of time that smoking had been stopped. Those who stopped smoking, however, had smoked about 10% fewer cigarettes per day than men of the same age who continued.

The results (tables IX and X) show the numbers of deaths from selected causes of death in men who had given up smoking for different periods, compared with the numbers that would have been expected from the experience of men of the same age who were (*a*) continuing cigarette smokers (ignoring the fact that those who gave up smoked on average 10% less than smokers of the same age who did not give up) (table IX), and (*b*) life-long non-smokers (table X).

TABLE IX—*Mortality in ex-cigarette smokers by number of years they had stopped smoking compared with mortality in continuing cigarette smokers*

Cause of death	No of deaths as % of No expected in continuing cigarette smokers (actual No in parentheses) Years since smoking stopped:			
	<5	5-9	10-14	≥15
Cancer of lung	102*(15)	35 (12)	28†(9)	11 (7)
Cancer of oesophagus and other respiratory sites	45 (4)		17 (3)	
Chronic bronchitis and emphysema and pulmonary heart disease	112 (9)	158 (30)	22 (4)	28 (12)
Other conditions closely associated with smoking	145 (7)	44 (5)	49 (5)	49 (10)
Ischaemic heart disease in men 30-54 years	54 (7)	35 (10)	45 (10)	47 (7)
Ischaemic heart disease in men 55-64 years	111 (19)	83 (34)	102 (38)	74 (45)
Ischaemic heart disease in men 65 years and over	76 (24)	102 (76)	87 (62)	83 (148)
Myocardial degeneration	31 (3)	87 (21)	76 (19)	47 (31)
Other conditions associated with smoking	72 (26)	79 (67)	84 (65)	71 (118)
All other conditions	102 (55)	100 (125)	84 (97)	86 (210)
All causes at 30-64 years	86 (67)	80 (141)	69 (104)	56 (106)
All causes at 65 and over	87 (99)	89 (242)	78 (206)	71 (484)
All causes	87 (166)	85 (383)	75 (310)	68 (590)
Mean No of years stopped	3·3	7·5	12·4	21·6

*When five men who stopped smoking after they developed lung cancer were excluded the percentage reduced to 68%.
†When one man who stopped smoking after he developed lung cancer was excluded the percentage reduced to 25%.

TABLE X—*Mortality in ex-cigarette smokers by number of years stopped smoking compared with mortality in lifelong non-smokers. Current smokers are described as having stopped 0 years ago*

Cause of death	No of deaths divided by number expected in lifelong non-smokers Years since smoking stopped:					No of deaths in lifelong non-smokers
	0	<5	5-9	10-14	≥15	
Cancer of lung	15·8	16·0*	5·9	5·3†	2·0	7
Cancer of oesophagus and other respiratory sites	6·1	2·9		1·2		3
Chronic bronchitis and emphysema and pulmonary heart disease	35·6	34·2	47·7	7·3	8·1	2
Other conditions closely associated with smoking	7·7	10·2	3·2	3·4	3·2	5
Ischaemic heart disease in men 30-54 years	3·5	1·9	1·3	1·4	1·3	32
Ischaemic heart disease in men 55-64 years	1·7	1·9	1·4	1·7	1·3	75
Ischaemic heart disease in men 65 years and over	1·3	1·0	1·3	1·2	1·1	182
Myocardial degeneration	2·4	0·7	2·1	1·8	1·0	47
Other conditions associated with smoking	1·8	1·2	1·3	1·4	1·1	194
All other conditions	1·2	1·2	1·2	1·0	1·0	390
All causes at 30-64 years	2·0	1·7	1·6	1·4	1·1	326
All causes at 65 and over	1·6	1·4	1·4	1·2	1·1	611
All causes	1·8	1·5	1·5	1·3	1·1	937

*When five men who stopped smoking after they developed the disease were excluded the ratio reduced to 10·7.
†When one man who stopped smoking after he developed the disease was excluded the ratio reduced to 4·7.

For lung cancer the relative (though not the absolute) mortality decreased steadily with duration of stopping until more than 15 years after stopping (table IX)*; but at this time the mortality was still double the rate in life-long non-smokers of similar ages (table X). The few deaths from cancers of the oesophagus or other respiratory sites and from other conditions closely associated with smoking (excluding chronic bronchitis and pulmonary heart disease) also showed a decline in relative mortality. For chronic bronchitis and pulmonary heart disease, however, the pattern was materially different, a peak mortality being recorded five to nine years after stopping followed by a rapid decline to a death rate only a quarter of that in continuing cigarette smokers after a longer interval. Other conditions associated with smoking showed variable patterns, but in general the mortality tended to resemble that for lifelong non-smokers after smoking had been stopped for 15 years or more. For the group of other conditions the rate remained much the same throughout.

In interpreting these results, it must be remembered that men do not stop smoking at random. Some give up because of ill health, particularly if they have a condition like chronic bronchitis that is likely to be improved symptomatically by stopping. For such a condition, in which the progression of the disease itself strongly affects smoking habits during the decade preceding death, mortality should be related to the smoking habits at least 10 years before death. Better still, the effect of smoking can be determined directly by measuring the rate of loss of lung function and relating it to contemporaneous smoking habits, as has been done by Fletcher *et al.*[14]

Another form of bias may be introduced if men who know they are seriously ill see no point in stopping and become less likely to give up than men who are well or do not reply to our questionnaires at all. Such biases could well account for the relatively low mortality from a variety of chronic diseases during the first five years after stopping. Lung cancer, in contrast, is usually fatal within two years, and such selective factors are less likely to influence its pattern of mortality. Our inquiries about individual case histories identified six men who gave up smoking only after they had developed lung cancer and who were recorded as having been ex-smokers when they died (five living for less than five years after stopping and one for 12 years). These men should properly be excluded from the ex-smokers (see footnote to tables IX and X). The more pertinent relation between the incidence of (as opposed to the death rate from) lung cancer and the length of time that smoking has been stopped will be reported elsewhere.[11]

Comparisons with the mortality of non-smokers (table X) are crucially dependent on the numbers of deaths in non-smokers and, for several of the diseases of greatest interest, these were so small that

*The extra death rate from lung cancer among smokers seems to have remained constant after smoking stopped, so the effect of giving up was to avoid the increase in the death rate that would have occurred had smoking continued.[11 13]

the confidence limits of the estimated relative risks were large. In the case of lung cancer we can check the reliability of the esimates by using the mortality rates of non-smokers in two American studies,[15 16] in which 127 deaths from lung cancer occurred in male non-smokers. On the basis of these rates, we should have expected nine deaths among our non-smoking doctors whereas we observed seven; there was, therefore, no reason to suppose that the incidence of the disease in non-smokers differed materially between the two countries. Had the relative risks in the first line of table X been derived from the American rates, they would have been within 30% of the tabulated values.

Another comparison of interest was made possible by the separate examination of the ex-smokers who had stopped smoking cigarettes before they had reached 30 years of age. Such men had smoked for an average of seven years. Only 57 deaths occurred among them, which was too few to permit the calculation of disease-specific mortality rates. Nevertheless, their mortality was 53% of that in men of the same age who continued to smoke ($P<0.001$) and 93% of that in non-smokers. This statistically non-significant difference suggested that these men suffered few, or no, deaths due to the seven years for which they smoked.

TRENDS IN MORTALITY WITH TIME IN DOCTORS COMPARED WITH TRENDS IN GENERAL POPULATION

During 1951-71 each cohort of British men smoked fairly steadily throughout their working lives from 25 to 64 years of age. From retirement, however, average tobacco consumption decreased steadily throughout old age,[6] partly because older men really did reduce their smoking and partly because death removed disproportionately many of the heavier smokers. In 1951 the consumption among doctors aged 25 to 64 years was similar to the national average in that age group, although the lower consumption among older men was less pronounced than in the general population, possibly because of better financial resources. The pattern among doctors of decrease on retirement was similar at each subsequent survey, but the mean amount smoked at each age decreased progressively, until by 1971 doctors in each age group were smoking between about a quarter and a half as much as men of the same ages in the general population (table II).

To compare the trends in smoking habits, we calculated the average daily number of cigarettes smoked per man in each five-year age group in 1951, 1956, 1966, and 1971. Our own data were numerous enough to allow us to do this for doctors with confidence; but the national data, which had been collected by the Tobacco Research Council[6] for commercial purposes, had been derived from quota samples and were relatively few. We therefore averaged the national data over three-year periods to diminish inaccuracy due to random variation. The results are shown in fig 1.

If smoking is a cause of disease it might be supposed that the ratio of the mortality rates of doctors to those of other men would also have

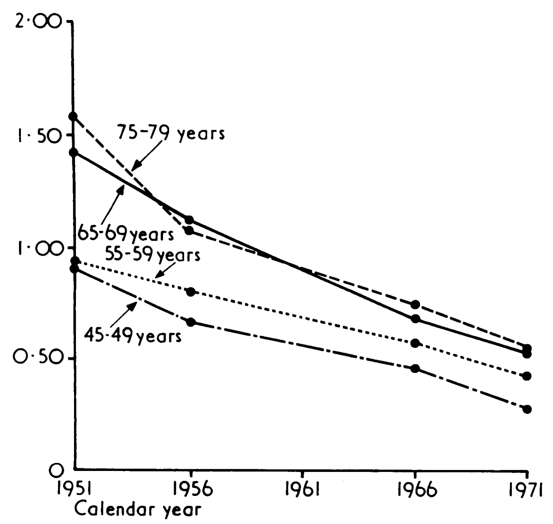

FIG 1—Trend in numbers of cigarettes smoked by male doctors as fraction of numbers smoked by all British men of same ages 1951-71—four age groups: 45-49 years, 55-59 years, 65-69 years, and 75-79 years (from table II).

TABLE XI—*Deaths of doctors as percentage of deaths expected at national rates and trend of percentage with time: study years 4-20: ages under 85 years*

Cause of death	Age at death (years)	No of deaths observed	Observed deaths as % of No expected	Slope of regression of percentage on time ± SE
Cancer of lung, trachea, pleura, or mediastinum ..	20-64	159	35	-1.5 ± 0.6*
	65-84	242	60	-2.1 ± 0.8**
Cancers of oesophagus and other respiratory sites ..	20-84	93	78	-0.8 ± 1.6
Chronic bronchitis, emphysema, and bronchiectasis	20-84	220	27	-0.5 ± 0.4
Ischaemic heart disease and myocardial degeneration..	20-54	356	90	-4.6 ± 1.0***
	55-64	746	106	-3.3 ± 0.8***
	65-74	986	102	-1.8 ± 0.7**
	75-84	875	93	$+1.2\pm0.7$
Other vascular causes associated with smoking†	20-64	166	84	-3.0 ± 1.5*
	65-84	615	77	$+1.1\pm0.6$
Other non-vascular causes associated with smoking‡	20-64	367	87	$+1.1\pm0.9$
	65-84	436	61	$+1.3\pm0.6$*
All other causes	20-64	900	74	-0.1 ± 0.5
	65-74	723	77	$+0.4\pm0.6$
	75-84	785	81	$+1.5\pm0.6$*
All causes	20-64	2788	76	-1.2 ± 0.3***
	65-74	2423	75	-0.4 ± 0.3
	75-84	2458	78	$+0.9\pm0.3$**

*$P<0.05$, **$P<0.01$, ***$P<0.001$. (Negative slopes indicate relative improvement among doctors.)
†Aortic aneurysm, hypertension, cerebral thrombosis, and arteriosclerosis.
‡Respiratory tuberculosis; cancers of rectum, pancreas, and bladder; pneumonia; hernia; hepatic cirrhosis and alcoholism; peptic ulcer; suicide; and poisoning.

decreased. This would be so, however, only if smoking were sufficiently important as a cause of disease for changes in smoking habits to outweigh the differential effects of other environmental changes, the efficacy of treatment, and accuracy of certification, and if the effect of reduced consumption showed itself within 10 years.

In examining trends in mortality among doctors, we were further handicapped by the fact that those doctors who replied to our first questionnaire were a self-selected sample of all those to whom it was sent. The seriously ill would have been unable to respond, so that the mortality rate of those who replied would have been, at least for a time, abnormally low. This bias would presumably have affected different diseases to a different extent and would have worn off more quickly for diseases that are rapidly fatal than for those that usually cause death only after a long period of ill health. We preferred, however, to ignore differences between diseases that would have been difficult to allow for objectively and studied the experience of the total mortality in a random sample of the non-responders. The figures indicate that by the fourth year of the study the effect of self-selection on grounds of health had effectively disappeared.[2 3]

For each of the 20 years of the study, we compared the numbers of deaths certified from different causes in each five-year age group among the doctors with the numbers certified as due to those causes in such men in England and Wales. To make the two sets of data as comparable as possible, we attributed deaths of doctors to lung cancer (including trachea, pleura, or mediastinum) if that was the stated cause on the death certificate, even if our subsequent inquiries showed that the certified cause was wrong, and we excluded observations on men aged 85 years and over because we could not take account of the difference in age distribution between doctors and the general population at these ages. We also had to combine ischaemic heart disease with myocardial degeneration and pulmonary heart disease to overcome the difficulty introduced by the eighth revision of the ICD in 1968 and to combine the few cases of bronchiectasis with chronic bronchitis and emphysema because of possible differences in the accuracy of diagnosis in doctors and the general population.

In each of the last 17 years of our study, we calculated for each cause or group of causes of death the number of deaths observed among the doctors as a percentage of the number expected from the national death rates. Finally, we calculated the regression line* of these percentages on time from the fourth year of the study to the 20th. Because of paucity of numbers in single years, almost all individual

*Fitted by maximum likelihood.

percentages were unstable and even the slopes of many of the regression lines for individual conditions were unreliable. We therefore combined many diseases into broad groups. The results are summarised in table XI, which shows the overall percentage and the slope of the regression line for various conditions in various age groups. If any slope is negative, then mortality among doctors is progressively improving compared with that in the general population.

For lung cancer the trends were significantly downwards both under and over 65 years of age. For chronic bronchitis and emphysema there were far fewer deaths than expected, reflecting the social class gradient of the disease, so that the downward trend, although substantial, was not statistically significant. Likewise, the downward trend for cancers of the oesophagus and other respiratory sites was not statistically significant, although it too may have been real and due partly to changes in smoking. The trends for heart diseases and other vascular diseases associated with smoking were hard to interpret. These diseases were strongly related to smoking only in younger adults (table V), and so we would expect changes in smoking to affect trends only in these age groups. This is what we observed. The magnitude of the change was, however, surprisingly large, and we were probably chiefly observing the secular tendency for decline in the standardised mortality ratio (SMR) for coronary heart disease in social class I, some of which may have been due to factors other than smoking habits. It will, therefore, be of interest to compare the trends in the SMR for doctors with those for other professional groups and for social class I as a whole when the occupational mortality tables for 1971 are published. Despite these reservations, we note that the trend was downwards for all of the major diseases that are believed to be caused by smoking.

Detailed figures for all ages (25-84 years) for each year of the study from the second to the 20th are shown for cancer of the lung and for all other cancers in fig 2. The regression lines are those calculated from the data for the fourth to the 20th years. The contrast was great: the slopes of the regression lines were, respectively, $-1\cdot4$ (SE $\pm0\cdot47$) and $0\cdot0$ (SE $\pm0\cdot50$). Had data for the second and third years been included, the difference between the slopes would have been greater and statistically more significant ($P < 0\cdot01$). On this evidence it seems unlikely that the relative reduction in the certified death rate for lung cancer in doctors could have been an artefact of diagnosis or certification.

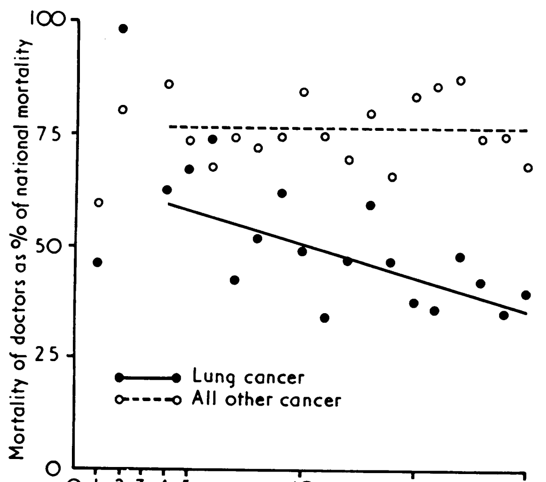

FIG 2—Trend in number of deaths certified in male doctors as percentage of number expected from experience of all men in England and Wales of same ages. Results are given from second to 20th years of study for (*a*) lung cancer (459 deaths observed *v* 931·9 expected) and (*b*) all other cancers (1238 deaths observed *v* 1630·7 expected). Regression lines on time were calculated from data for fourth to 20th years of study (regression coefficients: —1·4 for lung cancer and 0·0 for all other cancers).

Discussion

Cancers of the lung, oesophagus, and other respiratory sites, chronic bronchitis and emphysema, and pulmonary heart disease have been known to be associated with smoking for many years, and there is a mass of evidence to indicate that the association is mostly causal, without, of course, implying that smoking is the only cause (see [8–10 17–23] and, for chronic bronchitis and emphysema[14]). Only for cancers of the oesophagus and other respiratory sites does it seem likely that some of the excess in smokers can be attributed to a secondary association with other factors, particularly alcohol consumption. Our present data reinforce earlier conclusions and are qualitatively new only in so far as they provide detailed comparisons between mortality rates in the general population and a subgroup that reduced its consumption of cigarettes more than average. The results of this comparison confirm that death rates were reduced correspondingly, in the way that would be expected if smoking were a cause of disease. The extent of the reduction did not correlate exactly with the extent of the reduction in smoking, but neither could it be expected to do so. The reduction in smoking was achieved partly by doctors not starting to smoke, but mostly by smokers giving up or reducing the number of cigarettes smoked, and the effects of these changes in habit are likely to manifest themselves to different extents and after different periods for different diseases. The most we can expect, therefore, is that trends should be compatible in direction and then only if there have not been other changes that outweigh the beneficial effect of decreased smoking in one or other group.

LUNG CANCER

We note that the results of the Swedish twin study do not support Fisher's genetic explanation for the association between smoking and lung cancer.[24 25] The only material objection to the inference that smoking causes lung cancer is the difference in the trends in mortality between cancer of the lung and cancers of the oesophagus and other respiratory sites,[26–29] despite the fact that smoking is associated with the development of cancer of all three types. In England and Wales, for example, men began to smoke cigarettes at about the turn of the century and the annual standardised mortality rate for cancer of the lung in men increased fiftyfold from 2 per 100 000 in 1911-15 to 102 per 100 000 in 1966-70. The mortality from cancer of the oesophagus, however, decreased from 12 to 7 per 100 000, and the mortality from other respiratory cancers (lip, tongue, mouth and tonsil, pharynx,* and larynx) actually decreased from 22 per 100 000 to 7 per 100 000.[30]† These differences are likely to be due to a combination of factors, including the failure to diagnose a large proportion of lung cancers before about 1950, different trends in the efficacy of treatment, and differential relationships to pipe, cigar, and cigarette smoking. The last of these is confirmed by our data in table VI, which show that changes from pipe to cigarette smoking would have had a far greater effect on the incidence of lung cancer than on the incidence of other types of cancer. More important still may be the fact that smoking interacts with other environmental factors to produce its effect.[13 31] One of these is the consumption of alcoholic drinks, which is closely related to the incidence of oesophageal and other respiratory cancers, but not of lung cancer[32–36]; another is exposure to asbestos, which might be related to the incidence of lung cancer but not of oesophageal cancer.[37 38]

Whether our observations on inhaling support the belief that cigarette smoking is a cause of lung cancer is uncertain. To produce the disease cigarette smoke must, we presume, reach the bronchi, principally the primary divisions but also to some extent the smaller bronchi, and it has usually been assumed that cancer would be most likely to occur in men who said they inhaled. Several investigators have reported a higher mortality in inhalers than in non-inhalers,[15 16] but they have not standardised for amount smoked. In Doll and Hill's retrospective study[12] there was a slight excess of inhalers among patients with lung

*Including the nasopharynx, which is excluded from our group of cancers of "other respiratory sites."

†The comparable figures for women were 2 and 20 per 100 000 for cancer of the lung, 4 and 5 per 100 000 for cancer of the oesophagus, and 3 and 3 per 100 000 for other respiratory cancers.

cancer who smoked less than 15 cigarettes a day, but a greater excess of non-inhalers among men who smoked more heavily, and similar results were obtained by Spicer[39] in England and by Schwartz *et al*[40] in France. In the only other prospective study that separated inhaling by amount smoked, Cederlöf *et al*[41] found that an excess mortality in inhalers disappeared when the comparison was limited to cigarette smokers who smoked 16 or more cigarettes a day (relative risk in comparison to non-smokers: deep inhalers 15·7:1; light or non-inhalers 16·2:1). In our study the relative risk comparing inhalers with non-inhalers changed from about 2:1 for light smokers to 1:2 for heavy smokers (table VIII). These relative risks are, of course, subject to considerable statistical error, as the numbers in each category are small. (The greater risk in men who were unable to classify themselves was based on very small numbers indeed, but it was consistent at all levels of smoking and should perhaps be noted.)

The distinction between inhaling and not inhaling is not absolute and smokers who say they do not inhale nearly always take enough smoke into their lungs to raise their carboxyhaemoglobin level well above that in non-smokers. Preliminary results of a large-scale survey being undertaken by Wald[42] show, for example, a greater difference between non-inhalers (including slight inhalers*) and non-smokers (4·6% and 0·6% carboxyhaemoglobin) than between deep inhalers and non-inhalers who have smoked the same number of cigarettes on the day of the test (5·2% and 4·6%). The fact remains, however, that we still do not know where the smoke droplets are most likely to deposit when people describe their method of smoking in different ways, and it is impossible to interpret the results until we do. Meanwhile we note that smoke droplets that contain polycyclic hydrocarbons are initially so small when drawn into the mouth (less than 1 μm in diameter) that they could be carried down into the alveoli in the main stream without touching the walls of the bronchi. In a warm moist atmosphere they swell rapidly and if held in the respiratory tract for more than a second may deposit; but whether this will be on the bronchial epithelium or in the alveoli, whence they will be speedily removed by the lymph stream and the blood, will depend on the level they have reached in the lungs.[43]

CHRONIC OBSTRUCTIVE LUNG DISEASE

The deaths certified as due to chronic bronchitis, emphysema, or pulmonary heart disease, which may be grouped together as "chronic obstructive lung disease," were somewhat fewer than those attributed to lung cancer (304 against 441; table III); but the number was probably underestimated, since some of the deaths attributed to pneumonia or myocardial degeneration (or even, perhaps, other forms of heart disease) may have been due to complications of obstructive disease. Death rates from chronic obstructive lung disease are, moreover, much lower in social class I men than in the general population, so our data also underestimate the real death rates due to the condition in a general population of smokers. In our study the relative risk for cigarette smokers compared with non-smokers was actually greater for chronic obstructive lung disease than for lung cancer, although in other prospective studies the relative risks have been about the same. It seems, therefore, that chronic obstructive lung disease is as important a fatal effect of smoking as lung cancer. The interactive effect of atmospheric pollution may, however, be greater for chronic obstructive lung disease than for lung cancer, and the relative importance of chronic obstructive lung disease as an effect of smoking may be less great in countries with less pollution than the UK.[44]

A recent monograph[14] described the development of chronic obstructive lung disease in smokers as an irreversible process (except among asthmatics), in which lung function deteriorates slowly over decades. This deterioration is much more rapid in some smokers than in others and is least rapid among non-smokers. When a smoker suffering excessively rapid progressive deterioration gives up smoking, lost lung function is not restored, but the subsequent rate of loss reverts to the normal rate of loss typical of non-smokers. This offers hope for the smoker who is prepared to stop smoking as soon as simple spirometry shows his lung function to have fallen well below the normal range for non-smokers. Those who wait until they are really disabled before they stop may prolong life a little, but their lung function does not recover and death probably ensues within five or 10 years. This description of the disease explains the initially surprising finding in table IX that the greatest death rate among ex-smokers (156% of that expected among continuing smokers) occurred five to nine years after stopping. The men who died in this period were presumably the men who stopped because they were becoming disabled but who had already lost so much lung function that a further few years of normal decline sufficed to kill them. The fact that the death rate in the first five years after stopping was less than that five to nine years after stopping suggests that it usually takes more than five years to progress from respiratory disability severe enough to cause the doctors we studied to stop smoking to death from the disease.

*Wald found that 34% of smokers said that they did not inhale or inhaled slightly, which is similar to the proportion of "non-inhalers" in our study, and we have therefore used this combined group for the purpose of comparison.

OTHER CONDITIONS CLOSELY ASSOCIATED WITH SMOKING

Of the three other conditions that were found to be closely associated with smoking, one (non-syphilitic aortic aneurysm) has been similarly associated with smoking in several other major studies.[9 42] In this study the death rate in heavy cigarette smokers was 10 times the rate in non-smokers, but the number of deaths was small and this estimate of the relative risk is about double that in other studies.

Respiratory tuberculosis has also been associated with smoking in retrospective studies[9] and in Dorn's prospective study,[15] and it is easy to understand how smoking could facilitate the spread of the disease by decreasing the ciliary activity of the bronchial mucosa. There is, however, also some evidence to suggest that the association might, in part, be secondary to the consumption of alcohol,[45] though perhaps not in members of the upper socioeconomic classes, who maintain a reasonable standard of nutrition.

The third condition, hernia, was responsible for only 16 deaths and has not been examined separately before. That deaths from the complications of hernia should be more likely in smokers seems reasonable when one considers the extent to which a hernia can be aggravated by a chronic cough.

ISCHAEMIC HEART DISEASE AND MYOCARDIAL DEGENERATION

Our data for ischaemic heart disease are similar to those that have been reported in many other studies throughout the world.[8 9 17–19 41] As in other studies, the relation with smoking is strong in young people and weakens as age increases. Seventy-one deaths were attributed to ischaemic heart disease in men under 45 years of age. At these ages the risk among heavy cigarette smokers was 15 times that in non-smokers. This relative risk is subject to large random error, but is similar to that recorded by Hammond[16] and slightly less than that estimated from a retrospective study of women who were aged under 45 and who were discharged from hospital with a diagnosis of myocardial infarction.[46] In that study of women information had been obtained about four other risk factors which, it was found, interacted with one another so that when three or more risk factors were present the relative risk was estimated to be more than 100:1. This implies a considerable absolute risk and suggests that the fall in the relative risk in smokers with age might be due in part to the progressive elimination of people who are particularly susceptible to its effects. The mortality for younger smokers was so much greater than that for non-smokers that it seems reasonable to suppose that most of the excess was caused by smoking. Among older men, however, the relative risk was much less pronounced. It is possible that much of the excess mortality from ischaemic heart disease in this group of men arises not because of an effect of smoking, but because smoking correlates with some other factor which contributes directly to the disease. If, however, smoking is a major cause of ischaemic heart disease in young men, it would seem likely that it also contributes to causing the disease in the old.

Associations between smoking and myocardial degeneration or cerebral thrombosis have not been reported before, but similar findings for cerebrovascular diseases as a whole have been reported by Hammond[16] and Kahn[15] in the USA. The fact that the relation with cigarette smoking was closer for myocardial degernation than for ischaemic heart disease at ages 65 years and over (table V) makes it difficult to believe that the deaths attributed to myocardial degeneration should properly have been attributed to ischaemic heart disease. Myocardial degeneration was also more closely related than ischaemic heart disease to pipe and cigar smoking (table VI). The term includes a hotch-potch of diagnoses like myocarditis and cardiovascular degeneration that were classified under Code No 422 of the 7th revision of the ICD. The close relation with smoking would readily be explained if about half of these 615 deaths were actually due to pulmonary heart disease or to the aggravation of other heart disease by respiratory insufficiency even though we have already subtracted and classified separately those 27 deaths from ICD 422 for which chronic bronchitis or emphysema was mentioned on the certificate as a contributory cause.

OTHER CONDITIONS ASSOCIATED WITH SMOKING

There remain the nine other conditions that were positively associated with smoking in our study, and cancer of the bladder. There is independent evidence to suggest that both peptic ulcer and cancer of the bladder can be produced or aggravated by smoking[8-10] and there is nothing in our data to throw doubt on this conclusion. Cancer of the bladder was not found unusually often in heavy smokers, but the deaths were few and the deficiency might have been due to chance. For three of the conditions—cirrhosis of the liver and alcoholism, suicide, and poisoning—the association was presumably secondary to an association with psychological factors.

Non-causal associations could also be produced by the misdiagnosis of other conditions and may, perhaps, have contributed to the slightly increased death rates recorded among cigarette smokers from cancer of the pancreas, hypertension, arteriosclerosis, and pneumonia. Pneumonia, however, may result from lung cancer or be caused or aggravated by chronic obstructive lung disease without either of these underlying conditions being referred to on the death certificate, and there is substantial evidence that smoking may contribute to the production of arteriosclerosis in general,[9 10 20] apart from the evidence relating it to ischaemic heart disease, cerebral thrombosis, and aortic aneurysm. Nothing is known about the causes of cancer of the pancreas, apart from its association with diabetes and the repeated finding in both retrospective and prospective studies that it is particularly common in heavy cigarette smokers.[17 21 41 47] The increasing death rate due to cancer of the pancreas may be an artefact due to improved diagnosis but it may also be partly due to the increased prevalence of an external carcinogen. It is, of course, immaterial from the point of view of estimating the mortality attributable to smoking whether these four conditions can be caused by smoking or whether the excess in smokers is due to diagnostic confusion with other conditions that are.

An association between cancer of the rectum and smoking has not generally been found in other studies and may be due to chance or to a secondary association with some other factor, though what that factor might be is difficult to envisage. The recent observations that rectal cancer may also be associated with the consumption of beer do not provide any obvious clue.[36]

A negative relation between Parkinsonism and smoking was found originally by Dorn.[15] It was confirmed by Hammond[16] and by an earlier analysis of our own data, and similar results have been obtained in large-scale retrospective studies.[48 49] The deficiency of deaths in heavy smokers must partly be because the disease makes smoking more difficult, but this cannot be the whole explanation. If it were one would expect compensatory increases in light smokers and ex-smokers, and these were not found. The negative relation is, therefore, unlikely to be entirely the result of the disease, unless the disease makes itself apparent so early in life as to affect the start of the habit. No ready explanation exists, however, by which cigarette smoke could exert a beneficial effect on the central nervous system.

Conclusion

From this review, we conclude that much of the excess mortality in cigarette smokers can be attributed with certainty to the habit, but whether the greater part is attributable depends on the interpretation of the evidence regarding ischaemic heart disease. In table XII we list the 23 causes and groups of causes of death that we used to summarise our results in four categories according to whether the excess mortality in cigarette smokers: (*a*) could be directly attributed to smoking, (*b*) could probably be attributed to smoking, (*c*) was of uncertain origin, or (*d*) could be attributed to other causes. Because so many deaths were attributed to ischaemic heart disease and there was some doubt about its categorisation, particularly for the older age groups, we placed ischaemic heart disease in a separate subdivision of the second category. On this basis table XIII shows the quantitative distribution of the excess mortality in the five categories by age. The results suggest that at ages 35-84 years the excess mortality in cigarette smokers that was actually caused by smoking was at least 22% of the total mortality in non-smokers (the excess in category 1) and may have been over 52% (the excess in categories 1, 2A, and 2B). In the older age groups the excess in cigarette smokers, and particularly the excess in categories 1 and 2, must have been underestimated because (*a*) men with chronic heart and pulmonary disease tend to stop smoking some years before these diseases kill them, and so do not appear as cigarette smokers when they die, and (*b*)

TABLE XII—*Reason for excess mortality in cigarette smokers by cause of death*

Excess mortality in cigarette smokers	Category	Cause of death
Caused by cigarette smoking	1	Cancer of lung Cancer of oesophagus* Cancer of other respiratory sites* Chronic bronchitis and emphysema Pulmonary heart disease
Probably wholly or partly attributable to smoking	2A	Ischaemic heart disease
	2B	Non-syphilitic aortic aneurysm Myocardial degeneration Cerebral thrombosis Arteriosclerosis Respiratory tuberculosis Pneumonia Peptic ulcer Hernia Cancer of bladder Parkinsonism†
Reason unknown	3	Hypertension Cancer of pancreas All other causes
Attributed to causes other than smoking (including chance)	4	Cancer of oesophagus* Cancer of other respiratory sites* Cancer of rectum Cirrhosis of liver and alcoholism Suicide Poisoning

*Half number of deaths arbitrarily attributed to each of categories 1 and 4.
†Deficiency of deaths in cigarette smokers.

TABLE XIII—*Excess death rate in cigarette smokers by age and attribution category*

Age (years)	Annual death rate per 100 000 men						
	Non-smokers (No of deaths)	Excess in cigarette smokers due to diseases in category:					Cigarette smokers‡ (No of deaths)
		1	2A	2B	3	4	
35-9	132 (20)	*−7*†	*33*	*−1*	*−3*	*41*	196 (47)
40-4	151 (27)	*11*	120	*16*	*−5*	*33*	326 (91)
45-9	221 (35)	45	175	23	84	26	574 (152)
50-4	540 (66)	105	267	63	43	72	1090 (261)
55-9	844 (75)	146	342	110	162	75	1679 (324)
60-4	1431 (89)	406	366	209	238	116	2767 (384)
65-9	2081 (90)	741	650	282	684	136	4573 (426)
70-4	4236 (114)	1011	*349*	*303*	*593*	*150*	6642 (355)
75-9	7529 (131)	1495	*208*	*398*	*−109*	*114*	9636 (286)
80-4	9071 (105)	1056	*558*	*1232*	*2171*	*173*	14 261 (206)
All ages* 35-84	1245	270	255	126	184	73	2153

*Directly standardised to male population of England and Wales 1961.
†Rates in italics are unreliable because the standard errors of the rates of the corresponding diseases in non-smokers and in cigarette smokers were both large.
‡Started smoking before 25 years of age and continuing to smoke and no history of ever smoking anything but cigarettes.

social class I men get far less chronic obstructive lung disease than average. At ages 35-39 years, the observed excess (from alcohol-related diseases, suicide, and poisoning) was largely attributed to other factors with which smoking is associated.

After 1951 many doctors gave up smoking or reduced the number of cigarettes smoked, and the mortality rate* among the doctors in our study fell from the fourth to the 20th years of the study by 28% in those under 65 years of age (from 564 to 404 per 100 000) and by 5% in those aged 65-84 years (from 5703 to 5405 per 100 000). Men in England and Wales as a whole reduced their consumption much less and their mortality rates* fell in the same age groups by 9% (from 700 to 634 per 100 000) and 5% (from 7563 to 7192 per 100 000) respectively. Total mortality must be affected by many factors other than smoking and it seems probable that the progressive improvement in social conditions in the postwar period had a relatively greater beneficial effect on the population as a whole than on doctors, particularly after the age of retirement, thus obscuring (especially at old ages) the greater benefit that doctors obtained from their greater reduction in cigarette smoking.

For 25 years this work has been based on the records and cooperation of the British Medical Association and was made possible by thousands of doctors who completed the questionnaires and gave details of the evidence on which their diagnoses were based. We are most grateful to them for their help. The study was conceived by Sir Austin Bradford Hill and guided by him for 10 years, and our debt to him is immense. We also thank Professor J R Bignall, who advised on the diagnosis of difficult cases; the Registrars-General of the United Kingdom and the Registrars of the General Medical Council and its councils in Ireland and Scotland, who provided information about doctors' deaths; Mr Richard Gray, Ms Susannah Howard, and Dr Malcolm Pike, who helped with some of the analyses; Mrs Jean Gilliland and Miss Barbara Hafner, who collected and maintained the mass of individual records; Mrs Sutherland, who traced many missing doctors; Mrs Norton and Mrs Thompson, who prepared the data for computer analysis and, with Mrs Sutherland, helped with much of the clerical work; Ms Gale Mead, who typed innumerable manuscripts; Dr J Howlett, Dr G Manning, and the staff of the SRC Atlas Computing Laboratory, who provided excellent computing facilities, without which our analyses would have been impossible; and the Medical Research Council for financial support.

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