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Papers

Mortality in relation to smoking: 40 years' observations on male British doctors

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Abstract

Objective : To assess the hazards associated with long term use of tobacco.
Design : Prospective study of mortality in relation to smoking habits assessed in 1951 and again from20time to time thereafter, with causes sought of deaths20over 40 years (to 1991). Continuation of a study that was last reported after 20 years' follow up (1951-71).
Subjects : 34 439 British male doctors who replied20to a postal questionnaire in 1951, of whom 10 000 had died during the first 20 years and another 10 000 have died during the second 20 years.
Results - Excess mortality associated with20smoking was about twice as extreme during the second half of the study as it had been during the first half. The death rate ratios during 1971-91 (comparing continuing cigarette smokers with lifelong20non-smokers) were approximately threefold at ages 45-64 and twofold at ages 65-84. The excess mortality was chiefly from diseases that can be caused by smoking. Positive associations with smoking were confirmed for death from cancers of the mouth, oesophagus, pharynx, larynx, lung, pancreas, and bladder; from chronic obstructive pulmonary disease and other respiratory diseases; from vascular diseases; from peptic ulcer; and (perhaps because of confounding by personality and alcohol use) from cirrhosis, suicide, and poisoning. A negative association was confirmed with death20from Parkinson's disease. Those who stopped20smoking before middle age subsequently avoided almost all of the excess risk that they would otherwise have suffered, but even those who stopped smoking in middle age were subsequently at substantially less risk than those who continued to smoke.
Conclusion : Results from the first 20 years of this study, and of other studies at that time, substantially20underestimated the hazards of long term use of tobacco. It now seems that about half of all regular cigarette smokers will eventually be killed by their habit.

Clinical implications

- Clinical implications
- Observations on the mortality of British doctors with known smoking habits have

been reported over a 20 year period (1951-71); now the study period has been extended to 40 years (1951-91) and covers over 20 000 deaths

- Overall, the excess **mortality** of cigarette smokers was approximately twice as extreme **in** the second half as **in** the first half of this study
- Twenty five causes of death were significantly associated **with** cigarette **smoking** (24 positively and one negatively)
- Even **in** middle age stopp**in**g **smoking** substantially **in**creased the subsequent expectation of life - and those who stopped before 35 years of age had an expectation of life that was not significantly different from that of non-smokers

Introduction

After the two large case-control studies of 1950 that showed lung cancer to be closely related to **smoking**,[1,2] prospective studies were needed that could determ**in**e which other diseases were also related to the habit. **In** 1951 all the doctors **in** Brita**in** were asked what they smoked. Most of the 40 000 who replied were male, and a prospective study was started of the causes of death that subsequently occurred among them. The early results confirmed the strong **relation** between **smoking** and death from lung cancer,[3] and found that **smoking** was also related to **mortality** from many other diseases.*RF 4-6* Deaths have cont**in**ued to be recorded and, from time to time, further questionnaires have been sent to the survivors. The last report on these men was of the results after 20 years.[6] We now report the results of follow**in**g them for 40 years to 1991 and compare the apparent effects of cigarette **smoking** on **mortality** from all causes dur**in**g the first and dur**in**g the second halves of the study. We report also the **mortality** dur**in**g the entire 40 year period from 48 specific causes of death, or groups of causes, **in** men **with** different **smoking** habits, and the effects of stopp**in**g **smoking** at different ages, and we discuss the extent to which the effects of **smoking** on certa**in** causes of death are positively or negatively confounded by the effects of alcohol.

The hazards of tobacco have been documented by many other studies, which have been summarised by the Royal College of Physicians,[7,8] the United States Surgeon General,*RF 9-11* and the **In**ternational Agency for Research on Cancer.[12,13] Some prospective studies have been far larger than ours; ours, however, has been cont**in**ued for more than twice as long as any other, which gives it some special **in**terest, for long cont**in**ued cigarette use is particularly hazardous,*RF 14-16* and cigarette use by young men became widespread earlier **in** Brita**in** than **in** most other countries. Dur**in**g the first half (1951-71) of this study, therefore, the lung cancer rates **in** middle aged men were higher **in** Britian than anywhere else **in** the world, and dur**in**g the second half (1971-91), the lung cancer rates **in** men **in** old age **in** Brita**in** were among the highest. Hence, a study of **smoking** and death among British men dur**in**g these years may be particularly **in**formative about the hazards of long cont**in**ued cigarette use.

Methods

Questionnaires

At the end of October 1951, questionnaires were sent to all the men and women whose names were on the British medical register and who resided **in** the United K**in**gdom. Simple questions were asked about their **smoking** habits, and replies sufficiently complete to be used were received from

6194 women and 34 439 men. When last reported,[6] one woman had been mistakenly classified as male, until diagnosed as dying of uterine cancer. The relatively few female smokers had not, in general, smoked as long or as intensively as the male smokers, so that they do not provide direct information about the effects of long term smoking.[14] The present report is therefore restricted to the 40 year follow up of the men. Inquiries about changes in smoking habits and some further details about them were made of the men in 1957, 1966, 1972, 1978, and 1990; on the last two occasions, inquiries were also made about alcohol consumption and some other personal characteristics. Detailed accounts of the questions asked and of the response rates to the earlier questionnaires have been given previously.[3,5,6,17] Replies to our last questionnaire, which was sent out at the start of the 40th year of the study, were received from 10 807 (94% of those not known to have died), and information was obtained about changes in their smoking and drinking habits, their use of aspirin, and the previous occurrence of any vascular disease.

Follow up

In 1971, information was obtained about the vital status and place of residence of 99.7% of the men who had responded to the 1951 questionnaire; 10 074 were known to have died and 2459 to be living abroad. Those who lived abroad have not been followed since, nor have 218 others (1% of those not known to have died) if they then asked to be excluded from the study (102); if they had been struck off the medical register for unprofessional conduct (15); or if, before November 1971, contact with them had been lost (101). Of the remainder, 10 449 are known to have died before 1 November 1991; 118 have been censored at the date they were last known to be alive (71 known to have emigrated and 47 with whom contact has been lost); 10 615 replied to our questionnaire after 1 November 1990 and are thought to have been alive a year later; and 506 who did not reply to the questionnaire were traced alive after 1 November 1991.

Deaths have been monitored in several overlapping ways. The Office of Population Censuses and Surveys was to notify us automatically when members of the cohort died in Britain. In addition, we monitored the obituary columns of the BMJ and the Medical Directory, and we corresponded directly with the doctors themselves, with people who lived at their last known addresses, or with others who knew them. Our final round of correspondence began in November 1990, so some of the deaths that occurred in the 40th year of the study (November 1990 to October 1991) will have been missed. Judged by the number at risk at the start of this final year (11 652), the crude death rate in that year (489/11 652=4.20/1000), and the death rates in the previous four years when standardised to the age distribution of the 1990 survivors (4.61, 4.61, 4.65, 4.71; mean=1.1x4.20), the death rate in the final year should have been about 10% higher than we recorded (yielding about 543 deaths instead of 489). The deficiency has, therefore, been allowed for, when necessary, by multiplying the mortality recorded in the last year by 1.1.

Causes of death

For the vast majority of deaths, including many of those that occurred abroad, information about the underlying cause was obtained from official death certificates. In other instances, when no official information could be obtained, the cause was given in an obituary or described by a relative. In 217 instances (1% of all deaths) the cause remains unknown, commonly because the death occurred in a country in which information about the medical cause of death is not publicly available. Causes were classified according to the seventh revision of the International Classification of Diseases[18] if the death occurred during the first 27 years (1951-1978) and

according to the ninth revision of the international classification[19] if it occurred during the last 13 years (1 November 1978 to 1991). Special inquiry was made about the evidence for any deaths attributed to lung cancer in the first half of the study, but this rarely led to revision of the diagnosis,[6] and the certified causes are used for the present analysis. Exceptionally, deaths attributed to pleural mesothelioma were always separated from lung cancer and a special category was created for deaths that were thought likely to be due to pulmonary heart disease (see below).

Statistical methods

In calculating death rates for different categories of smokers we have assumed that questionnaires were returned soon after they were sent out (as the great majority were). Deaths that occurred in the year that a repeat questionnaire was sent out were related to the reply to the previous questionnaire. (This helps limit the effects of disease on smoking.) Otherwise non-smokers and continuing smokers were analysed in the category in which they last described themselves. The same is true for former smokers, except that they were classed as having stopped smoking for progressively longer periods as each year passed. The mortality attributed to continuing smokers has therefore been slightly attenuated by including with the deaths and the person years at risk some deaths and some years at risk when the individuals had recently become former smokers. Although in principle the mortality among non-smokers might likewise have been slightly increased by including with the non-smokers a few individuals who had recently become smokers, in practice the distortion will be negligible, as the proportion of non-smokers in 1951 who subsequently started smoking is small (see below), most of those who did start soon stopped, and the life threatening effects of smoking generally take many years to appear.

Mortality has been calculated separately for (i) lifelong non-smokers (that is, men who have never reported having smoked as much as one cigarette or 1 g of tobacco a day for as long as one year) and for men who, to the best of our knowledge, have habitually smoked (ii) only cigarettes, (iii) only pipes or cigars, or (iv) at times both cigarettes and tobacco in other forms. All analyses of non-smokers and of smokers refer to these categories, except where categories (iii) and (iv) have been combined as "other smokers." It is probable, however, that some of the men described as smoking only cigarettes in 1951, particularly those in the older age groups, may have smoked pipes or cigars at an earlier period, as inquiries about the way tobacco was smoked previously were not made until 1957 and were then made only of men smoking pipes or cigars in 1951. Consequently, men classified as smokers only of cigarettes during the second half of the study may have had more prolonged cigarette use (and hence greater hazard) than men of similar age who were similarly classified during the first year.

All mortality rates have been standardised for age and calendar period by calculating the number of deaths that would have been expected in each five year age group and each calendar year in each smoking category if the smoking habit had had no effect on mortality, summing the corresponding observed and expected numbers, and multiplying the ratio of the two numbers by the total death rate for the ages and period covered. Where differences are said to be "non-significant" this implies that the two sided P value is greater than 0.05, without any adjustment for the multiplicity of comparisons.

Results

Changes in smoking habits

The smoking habits of those who replied in 1951 and survived to the end of 1990 are contrasted, in table I, with the smoking habits of these subjects about 40 years later. Partly because of the disproportionate attrition of the smokers, but chiefly because most doctors who smoked in 1951 had ceased to do so, the overall proportion of smokers among these 40 year survivors was reduced from 62% to 18%, the proportion of cigarette smokers was reduced from 53% to 7%, and the proportion of smokers of cigarettes only (that is, who were not also smoking cigars or pipes) was reduced from 41% to 6%. These changes were not simply an accompaniment of aging, as they were much greater than the differences seen in 1951 between one age group and another (as is shown in table II), and occurred to much the same extent in each age group in 1951: for example, the proportion who smoked cigarettes only was reduced from 37% to 5% in men initially under 25 years of age and from 33% to 2% in men initially aged 45 years or more. Among the non-smokers in 1951 who replied in 1990, 11% had started smoking at some time during the intervening 40 years but most (65%) had subsequently stopped, and four fifths of those who had continued smoked only pipes or cigars in 1990. Similarly, very few of those who were former smokers in 1951 had started again and continued to smoke in 1990; again, of the 5% who did, almost all smoked only pipes or cigars. It cannot be assumed, however, that these changes are typical of all male doctors of the same ages, as only two thirds of the doctors in the United Kingdom responded to our 1951 questionnaire, those who did so smoked somewhat less than the non-respondents in 1951,[5] and the knowledge that they were the subjects of a study of the fatal effects of tobacco may itself have influenced their habits over the next 40 years. Those who did smoke cigarettes reported smoking much the same amount at each age at the beginning of both the first and second halves of the study (table II).

- Smoking habits of doctors who replied to 1951 and 1990-1
nnaires. Values are numbers (percentages)

habit	Non-smoker, 1990-1	Former smoker, 1990-1	Current smoker, 1990-1* Cigarette only	Cigarette and other	Pipe or cigar	All habits, 1951
ker, 1951	2361	198	17	4	86	2666 (25)
smoker, 1951	0	1374	10	3	66	1453 (13)
smoker, 1951*						
ttes only	0	3355	535	47	446	4383 (41)
ttes and other	0	897	74	31	308	1310 (12)
cigar	0	695	16	2	287	1000 (9)
lts	2361 (22)	6519 (60)	652 (6)	87 (1)	1193 (11)	10812(dagger) (100)

fined in response to respective questionnaires; apart from the
tion between non-smokers (who, by definition, had never smoked
ly) and former smokers, these do not take account of past habits.
r) Including 197 men who replied but died later in the 40th year of the

TABLE II - Change in amount smoked with age (cigarette smokers)

	Average No of cigarettes smoked daily: men who currently smoked only

	cigarettes in 1951 and 1971	
Age (years)	1951	1971
35-44	16.9	
45-54	19.3	18.2
55-64	19.7	19.1
65-74	18.2	18.6
75-84	14.7	16.6
>=85	10.6	14.4

Mortality by **smoking** habit and cause

Pipe and cigar smokers who had never regularly smoked cigarettes have been examined previously.[6] Their **mortality** from the causes that were classified as closely related to **smoking** (cancers of the lung, other respiratory sites, and oesophagus; chronic obstructive lung disease; pulmonary tuberculosis; pulmonary heart disease; non-syphilitic aortic aneurysm; hernia) was found to be less than **in** cigarette smokers, though greater than **in** non-smokers, while their **mortality** from other causes was similar to that **in** non-smokers. For simplicity, we now present **mortality** rates **in** detail only for cigarette smokers who had not also regularly smoked tobacco **in** other forms and have grouped the remaining smokers together as "other current smokers" or "other former smokers."

Mortality rates have been analysed separately for 54 specific causes of death, or groups of causes, and for a 55th group comprising those deaths for which we were unable to discover a cause. They are shown by **smoking** habit **in** tables III-V for all the 48 causes or groups of causes that were individually responsible for more than 50 deaths.

Table III shows the rates for 17 types of cancer. Because of the paucity of numbers for some individual types, we have grouped together cancers of the mouth (other than the salivary glands), pharynx (other then the nasopharynx), and larynx, all of which were regarded by the International Agency for Research on Cancer[12] as diseases that can be caused by **smoking**, into one group of "upper respiratory cancers." These, together **with** four of the five other types regarded by the agency as able to be caused by **smoking** (cancers of the lung, oesophagus, bladder, and pancreas) were **in** the present study all clearly related to **smoking**. Three types (cancers of the upper respiratory sites, lung, and oesophagus) were particularly closely related, **with** the **mortality in** heavy cigarette smokers at least 15 times that **in** non-smokers; two other types (cancer of the bladder and pancreas) were about three times more common **in** heavy cigarette smokers than **in** non-smokers. Too few deaths (nine) were specifically attributed to cancer of the renal pelvis (the remaining type regarded by the agency as able to be caused by **smoking**) for useful analysis. Several studies have suggested that four other types of cancer, which **in** our study each caused more than 50 deaths, might sometimes be caused by **smoking**. One (cancer of the stomach) showed a statistically significant **relation with smoking**, and another (myeloid leukaemia) showed a marginally significant **relation with** the amount smoked. The two others (cancer of the kidney, which includes here renal pelvis, and cancer of the liver) showed, **in** this study, a weak positive and non-significant **relation with smoking**. Six of the other seven specified types of cancer that we examined also showed no significant **relation** (cancers of the colon and prostate, lymphomas, multiple myeloma, other leukaemias, and a group of all other specified types of cancer), but the seventh (cancer of the

rectum) did, as it had done in our previous report.[6] A moderate but statistically significant relation was observed for cancers of unknown origin, as was to be expected, as a proportion of them is likely to have arisen in the lung.

from neoplastic diseases

Annual mortality per 100 000 men								
on-	Cigarette smokers					Other smokers		
kers ever ked larly)	Former	Current	Current No of cigarettes 1-14	15-24	>=25	Former	Current	N/X/S
1	3	24	12	18	48	8	15	6.6
14	58	209	105	208	355	59	112	17.4
4	19	30	17	33	45	14	23	5.5
16	23	35	30	29	49	11	24	3.4
13	21	30	29	29	37	13	21	3.0
26	25	43	40	46	44	23	30	2.7
7	9	11	17	3	15	9	6	0.7
9	11	13	13	14	12	11	16	1.8
4	8	7	3	9	10	8	8	1.2
36	50	46	49	39	52	55	47	0.8
10	15	23	13	19	44	17	24	3.5
68	58	67	54	73	84	54	64	-0.3
14	9	12	16	8	13	8	10	-0.3
16	15	16	15	22	7	16	17	0.3
11	8	9	5	12	10	9	5	-1.6
39	39	40	44	33	45	47	31	-0.8
15	15	30	18	42	30	10	21	3.3
05	384	656	482	645	936	369	474	14.2
14)	(885)	(1139)	(317)	(416)	(406)	(565)	(1081)	

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zero and a standard deviation of
3.29 correspond to P values (two

ers of any type of tobacco, current

nokers, smokers of 1-14, 15-24, and 25

Table IV shows mortality similarly divided for 18 diseases (or groups of diseases) of the respiratory and circulatory systems; respiratory tuberculosis is included here rather than with infections. Chronic obstructive lung disease (with which are classed all deaths attributed to "chronic bronchitis" or "emphysema") shows a relation almost as strong as that for cancer of the lung. Pulmonary tuberculosis continues to show a moderately close relation with smoking, but includes data for only nine more deaths than were recorded in the first 20 years of the study. A weak but statistically highly significant relation with smoking was observed for pneumonia, which was much the same at all ages, possibly because of an increased risk associated with the presence of chronic obstructive lung disease. Although this relation is weak it is of some importance because of the substantial number of deaths attributed to pneumonia (4% of the total). The lack of a clear relation of current tobacco use with death from asthma is not inconsistent with the belief that

smoking aggravates the disease. Asthma **mortality in** all who had ever been smokers (comb**inin**g current and former smokers) was more than double that **in** non-smokers (8.3 aga**in**st 3.7 per 100 000 per year), and the relatively high rate **in** former smokers suggests that the development of potentially life threaten**in**g asthma caused many smokers to stop **smoking**, but they still rema**in**ed at somewhat **in**creased risk of death from the disease.

habits from respiratory and vascular diseases

	Annual **mortality** per 100 000 men							Stan
	Non-smokers (never smoked regularly)	Cigarette smokers				Other smokers		
		Former	Current	Current No of cigarettes 1-14	15-24	>=25	Former	Current	N/X/S(dag
	4	8	11	7	9	20	8	4	1.1
(542)	10	57	127	86	112	225	40	51	9.9
	71	90	138	113	154	169	94	85	3.3
	4	11	7	6	8	6	9	7	0.4
	19	28	30	26	31	33	24	18	0.1
	107	192	313	237	310	471	176	164	8.2
	(131)	(455)	(490)	(161)	(170)	(159)	(290)	(392)	
	0	7	10	5	10	21	3	10	3.7
	572	678	892	802	892	1025	676	653	7.5
	61	88	125	122	109	173	96	85	3.5
	15	33	62	38	74	81	22	43	6.9
	22	18	40	31	38	72	28	23	1.9
	32	33	44	28	51	60	37	33	1.1
	93	95	122	93	150	143	100	106	2.4
	59	63	81	74	81	92	69	58	1.0
	7	10	15	10	12	24	4	6	1.4
025)	94	110	164	167	145	188	101	103	3.2
	9	11	14	17	11	14	13	9	0.5
	15	10	15	15	20	8	17	13	-0.1
5)	58	63	71	60	82	74	62	59	0.7
	1037	1221	1643	1447	1671	1938	1226	1201	10.5
	(1304)	(2761)	(2870)	(1026)	(1045)	(799)	(1878)	(2986)	

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ctation zero and a standard deviation of
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5=non-smokers, smokers of 1-14, 15-24, and 25

Pulmonary heart disease was the circulatory cause of death that was most closely related to **smoking**, which is hardly surpris**in**g. (We have **in**cluded **in** this category deaths attributed to myocardial degeneration and congestive heart failure that were associated **with** chronic obstructive lung disease as well as the few deaths specifically certified as due to pulmonary heart disease.) Next most closely related was aortic aneurysm, **with** the **mortality in** heavy cigarette smokers more than five times that **in** non-smokers. Peripheral vascular disease is another important vascular condition

that can be caused by **smoking**, but although it causes a great deal of disability, it rarely causes loss of life. **In** this study the number of deaths attributed to it (28) was under 50, and hence did not justify a separate table entry. (But, although based on small numbers, the **mortality** from this disease among cont**in**u**in**g cigarette smokers was four times that **in** non-smokers and three times that **in** former cigarette smokers.)

The relatively weak proportional **relation** observed for the common vascular diseases, ischaemic heart disease, myocardial degeneration (a condition that is be**in**g diagnosed much less often now than **in** the first 20 years of the study; the category **in**cludes all deaths classified as No 422 **in** ICD-7 or 429 **in** ICD-9), and for the various forms of cerebrovascular disease belie their absolute importance, particularly **in** middle age. Although the overall **mortality in** even the heaviest cigarette smokers (25 or more a day) was only about twice that **in** non-smokers, this ratio is more extreme **in** middle than **in** old age and the great number of deaths attributed to vascular causes (more than half of the total) means that the absolute excess **mortality** from vascular diseases **in** cigarette smokers was more than double that attributed to the cancers of the respiratory and upper digestive tracts that are so much more closely related to **smoking**. Of all the categories of vascular disease exam**in**ed, only two m**in**or categories (rheumatic heart disease and venous thrombosis) and the heterogeneous group of "other cardiovascular diseases" bore no significant **relation** to **smoking**.

Table V shows similar data for 13 other causes of death and for unknown causes. Two conditions stand out: cirrhosis of the liver, for which the **mortality** was five times as great **in** cont**in**u**in**g cigarette smokers as **in** non-smokers, and five times as great **in** heavy as **in** light cigarette smokers, and peptic ulcer, for which the correspond**in**g excesses were each about threefold. Both these conditions were highly significantly related to **smoking** ($P<0.001$). Seven of the other categories also showed higher **mortality** rates **in** cigarette smokers than **in** non- smokers and **in** heavy cigarette smokers than **in** light, but the **relation with smoking** was clearly significant only for a heterogeneous group of "all other diseases," suicide, and poison**in**g. Hernia, which we had classed previously as closely related to **smoking**,[6] is **in**cluded **in** "other digestive diseases" as only 25 deaths were attributed to it. The **mortality** from hernia was higher **in** current smokers than **in** non-smokers and **in** heavy than **in** light cigarette smokers, but the trends were not statistically significant and the **relation** was less close **in** the second than **in** the first half[6] of the study. Deaths attributed to "other violence" (but not deaths from traffic accidents or falls) were also related to **smoking**, but less clearly so than deaths from suicide and poison**in**g.

rom causes that are not neoplastic,
causes

	Annual **mortality** per 100 000 men							
Non-	Cigarette smokers					Other smokers		
okers (never	Current No of cigarettes							
moked egularly)	Former	Current	1-14	15-24	>=25	Former	Current	N/X/
8	12	24	11	33	34	12	15	3.4
6	15	32	13	22	68	14	16	5.0
25	32	43	38	47	47	28	32	2.2
16	13	24	21	27	25	15	14	1.1
23	19	32	32	31	36	29	17	-0.1

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  20          22          15          22           6          18          18           8          -3.1
   9          10          16          18          21           4          14           7           0.1
  64          79          98          89          90         124          81          72           2.0
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 170         202         286         242         277         382         212         182           3.9
(225)       (458)       (489)       (169)       (171)       (149)       (330)       (429)
-------------------------------------------------------------------------------------------------------
  23          29          37          26          33          57          25          34           2.8
   7           9          19          15          16          31          10          12           3.4
  17          12          16          21           7          22          18          12          -0.7
   8          12          13          17          10          11           7          12           1.5
  17          22          28          23          23          46          20          18           1.3
-------------------------------------------------------------------------------------------------------
  72          84         114         103          90         172          79          88           3.8
(114)       (165)       (254)        (81)        (80)        (93)        (95)       (196)
-------------------------------------------------------------------------------------------------------
  17          29          34          33          30          41          16          24           2.3
 (27)        (78)        (38)        (13)        (13)        (12)        (29)        (45)
-------------------------------------------------------------------------------------------------------
1706        2113        3038        2542        3004        3928        2078        2130          18.9
(2215)      (4802)      (5280)      (1767)      (1895)      (1618)      (3187)      (5039)
-------------------------------------------------------------------------------------------------------
from a particular disease the
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kers of any type of tobacco, current

smokers, smokers of 1-14, 15-24, and 25
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One disease showed a statistically significant negative **relation with smoking**: namely, parkinsonism. **Mortality** from this condition was higher **in** former smokers than **in** continuing smokers, presumably because the effects of the disease made **smoking** difficult, but it was almost the same **in** former smokers and non-smokers, so that the annual **mortality in** ever smokers (16 per 100 000) was lower than **in** lifelong non-smokers (20 per 100 000), supporting earlier evidence that **smoking in**hibits, the development (or the progress) of the disease.[20] No useful **in**formation was obtained to test the hypotheses that two other diseases might be negatively related to **smoking** - ulcerative colitis[21] and, more speculatively, Alzheimer's disease[22] - as only eight deaths were attributed to ulcerative colitis and 19 to Alzheimer's disease. It may be noted, however, that the annual **mortality** from dementia (regarded as **in**cluding all deaths classified under ICD 7th revision Nos 304-306 and 9th revision Nos 290 and 331), about half of which is probably attributable to Alzheimer's disease, was similar **in** non-smokers (nine per 100 000) and ever smokers (11 per 100 000).

Mortality by **smoking** habit, by age

No death was observed **in** men under 25 years of age and the total number observed at 25-34 years of age was so small (67) that **mortality** rates **in** different **smoking** categories were subject to large random variation. We can, therefore, usefully compare age specific **mortality in** detailed **smoking** categories only from about 35 years of age upwards, although it may be noted that under 35 years of age the **mortality** was higher **in** current smokers (1.5 per 100 000 per year, based on 35 deaths) than **in** non-smokers (1.1 per 100 000 per year, based on 17 deaths). No new members were recruited to the study after 1951, so the **mortality** at 35-44 years of age was observed almost entirely **in** the first

two decades (November 1951 to October 1971) and mortality during the fourth decade of the study (November 1981 to October 1991) will have contributed materially only to ages 55 and over.

The data in table VI show that, for the 40 year period of the study as a whole, the overall mortality was twice as great in continuing cigarette smokers as in lifelong non-smokers throughout middle and early old age. The proportional excess in cigarette smokers decreased, however, in later life, and the ratio was reduced to 1.6:1 at 75-84 years of age and 1.3:1 at ages 85 years and over. Some of the decrease can be attributed to a reduction with age in the average amounts smoked by continuing smokers (shown in table II), some to the reduction in the proportion of deaths from cancer (from 24% of all deaths at ages 65-74 years to 11% at ages 85 years and over), and some to the progressive reduction in the ratio of the mortality in cigarette smokers to that in non-smokers that is seen for deaths from cardiovascular disease (from 2.1 at ages under 65 through 1.7 and 1.4, to 1.2 at ages 85 years and over). How the ratios change with age for the diseases most closely related to smoking is unclear, as the numbers of deaths in non-smokers in each age group are too small to provide stable estimates.

VI - Total mortality by smoking habits and age at death

	Annual mortality per 1000 men*					
			Cigarette smokers only		Other smokers	
	Non-smokers		Current			
death (years)	(never smoked regularly)	Former	All	>=25/day	Former	Current
	(1.6)(dagger)	(2.0)	2.8	(5.1)	(2.8)	(1.6)
	4.0	4.9)	8.1	10.8	(4.8)	5.5
	9.5	13.4	20.3	26.0	11.2	12.5
	23.7	31.6	47.0	60.7	30.5	32.4
	67.4	77.3	106.4	117.0	77.6	79.4
	168.6	179.7	218.7	(284.7)	186.1	179.8
es, including under ars	17.1	21.1	30.4	39.3	20.8	21.3
f deaths)	(2115)	(4802)	(5280)	(1618)	(3187)	(5039)

dardised for age in five year age groups up to age>=95.
er)Parentheses indicate rates based on fewer than 100 deaths. The
cient of variation of each rate is approximately equal to the inverse of
uare root of the number of deaths on which that rate is based; hence,
based on fewer than 100 deaths have a coefficient of variation that
s 0.1 (10%).

Actuarial survival by smoking habit

As the observations have been made over such a long time, it has been possible to follow many men into their 10th - and a few even into their 11th - decade of life. It has, therefore, been possible to calculate "actuarial" survival curves for different categories of smoker not only throughout middle age but also into old age, with results that are reasonably reliable up to at least 85 years of age. The results from 35 years of age are shown for non-smokers and continuing cigarette smokers in figure 1, and for non-smokers and continuing light, moderate, and heavy cigarette smokers in figure 2. The most notable differences are in the proportions who die between 35 and 69 years of age, which

vary from 20% in non-smokers to 41% in cigarette smokers as a whole and to 50% in those who smoke 25 or more cigarettes a day. The absolute differences between the survival probabilities of smokers and of non-smokers become less in extreme old age, simply because almost nobody survives beyond 100. Even after middle age, however, the differences between smokers and non-smokers in their annual mortality rates are quite large: of those alive at 70, the probability of surviving to 85 is 41% in non-smokers against 21% in cigarette smokers. The loss of expectation of life shown by these figures is substantial. For cigarette smokers, the age by which half have died is eight years less than for non- smokers, while for heavy cigarette smokers it is 10 years less than for non-smokers.

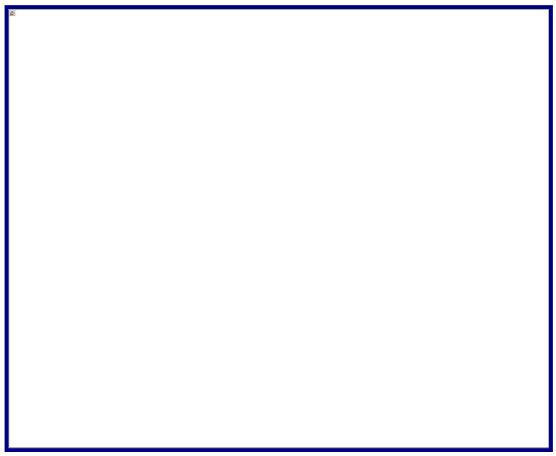

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FIG 1 - Overall survival after age 35 among cigarette smokers and non- smokers: life table estimates, based on age specific death rates for the entire 40 year period. (Note that, at 1990 British death rates, 97% of male infants would survive from birth to 35 years of age)

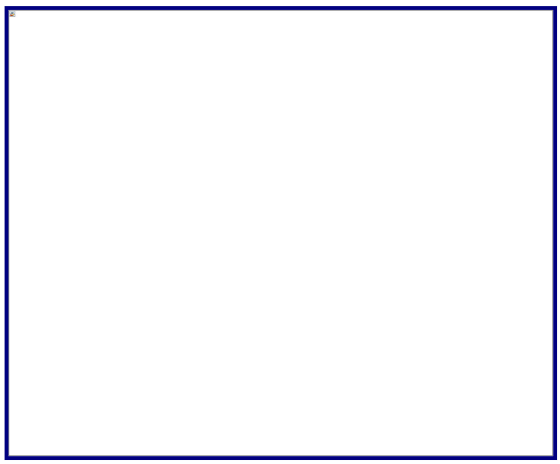

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FIG 2 - Overall survival (as fig 1), but with cigarette smokers subdivided by amount they were smoking at the time their last questionnaire was returned

Assessment of the effects of stopping smoking is complicated by the fact that people stop for different reasons, some stopping (particularly in old age or late middle age) because they are ill; coversely, some may, because they are ill, specifically choose not to stop, thinking that it is too late for any benefit from so doing.[6] Most of those who stopped in the doctors' cohort are likely to have

done so not because of an established illness but to avoid long term effects of smoking or to set an example,[23] and their state of health at the time they stopped (particularly if they stopped in early middle age or before) should not have distorted materially the pattern of their long term survival. The pattern will, however, be substantially distorted for a few causes of death that are preceded by long term irreversible morbidity, most notably, chronic obstructive lung disease.[6,24]

The survival of cigarette smokers who stopped at different ages is compared in figures 3 and 4 with that of non-smokers and with that of those who continued to smoke. Those who stopped before 35 years of age (at a mean of 29 years) had a pattern of survival that did not differ significantly from that of non-smokers (fig 3; two tailed P>0.05). For those who stopped later (fig 4) the survival was intermediate between that of non-smokers and that of continuing smokers; but even those who stopped at 65-74 years of age (mean 71 years) had age specific mortality rates beyond age 75 years appreciably lower than those who continued. The benefit of stopping in late middle age or old age is probably underestimated in these analyses because some of those who stopped in later life are likely to have done so specifically because of being ill.

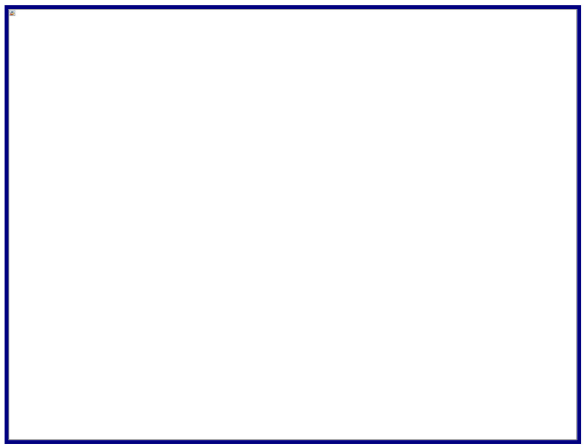

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FIG 3 - Effects on survival after age 35 of stopping smoking before age 35: life table estimates (as fig 1)

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FIG 4 - Effects on survival after ages 45, 55, 65, and 75 of stopping smoking in previous decade: life table estimates (as in fig 1)

Change in mortality and survival over time

In the course of 40 years many changes have occurred that could have modified the effect of smoking, including the efficacy of medical treatments (both therapeutic and preventive), the prevalence of other factors that interact with smoking, the type of tobacco smoked, and the amount of tobacco that had been smoked in the even more distant past. We have therefore calculated the excess risk (cigarette smokers versus non-smokers) separately during the first half (1951-71) and the second half (1971-91) of the study. These excesses are shown for five age groups in figure 5. No figure is given for men under 45 years of age in the second half of the study as the number of men in this age group in 1971 was too small to permit a reliable comparison. As a percentage of the mortality among those who had never smoked regularly, the excess among current cigarette smokers was consistently higher in the second half than in the first, particularly in late middle age. Examination of the separate survival curves for non-smokers and for cigarette smokers shows that the increase in relative risk was so extreme that it counterbalanced the substantial improvement that has taken place over the past few decades in the survival of the non-smokers (fig 6). Overall, therefore, there was practically no change between the first and second halves of the study in the age specific patterns of survival of the cigarette smokers (fig 6), even though this was a period when national mortality rates were improving rapidly.

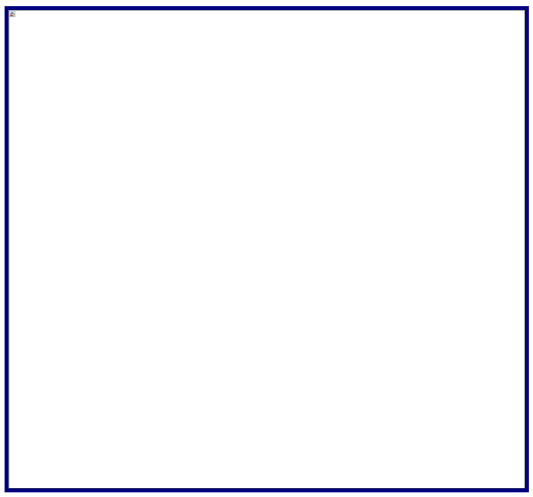

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FIG 5 - Excess age specific mortality in cigarette smokers in first half of study (lower line) contrasted with that in only second half (upper line). An excess of 100% represents doubled death rate. Bars indicate

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FIG 6 - Survival after age 35 among cigarette smokers and non-smokers in first half (left) and second half of study (right). For ages 35-44 rates for the whole study are used in both halves since little information on these is available from the second half

Changes in mortality between the two halves of the study are shown in table VII for some of the principal causes of death in non-smokers and in continuing cigarette smokers. (The detailed age specific rates are given in the appendix.) To allow for 2.0% of the causes of death in the second half of the study being unknown while only 0.05% were unknown in the first half, and for the possibility that some 50 deaths in the 40th year were missed, the cause specific mortality rates in the whole of the second half have been multiplied by 1.025. As few doctors were under 45 years of age in the second period, the rates are limited to men aged 45 years and over and are standardised to a population with the age distribution of the person years at risk over 45 years for the whole period. Most of these standardised rates, in consequence, are higher than those recorded in tables III-V.

- Mortality by cause in first and second 20 years among non-smokers
te smokers

	Annual death rate per 100 000 men	
	Never smoked regularly	Current cigarette smokers

eath	1951-71	1971-91	1951-71	1971-91
stic causes	382	394	743	993
er	17	17	264	314
cers substantially affected by smoking*	75	55	150	261
plastic(dagger)	290	322	329	418
atory causes	163	121	384	466
bstructive lung disease	7	15	151	208
piratory disease	156	106	233	258
ar causes	1626	1153	2416	2003
scular disease	401	278	516	501
cular disease	1225	857	1900	1502
ases	258	198	370	388
poisoning	94	74	119	156
	2523	1954	4077	4026

cancer of unknown site, plus remaining types recognised by the
nal Agency for Research on Cancer[12] as being able to be caused

For some of these sites (for example, stomach or liver) a small
of cases may be caused by smoking, and this category may include
agnosed cancers of sites substantially affected by tobacco.

Mortality in non-smokers for the most part decreased: from cerebrovascular diseases by 31%, from ischaemic and other cardiovascular diseases by 30%, and from respiratory disease other than chronic obstructive lung disease by 32%. The large reduction **in mortality** attributed to "other cardiovascular disease" is probably a nosological artefact due to the greater use of ischaemic heart disease as a diagnostic term **in** the second half of the study **in** place of vaguer terms like myocardial degeneration and arteriosclerosis. The true reduction **in mortality** from ischaemic heart disease is therefore likely to have been greater than the recorded figure. The proportions of the reduction that should be attributed respectively to the **in**troduction of preventive measures and improved treatment are not known but both must be appreciable. The reduction of 30% **in mortality** from the cancers other than lung cancer that are caused **in** part by **smoking** could be chiefly due to random variation, s**in**ce the numbers of deaths **in** non-smokers were small (18 and 25) but it could also reflect a reduction **in** the prevalence of carc**in**ogenic agents other than tobacco, as most of the deaths **in** this category were from cancers of the pancreas and bladder, both of which have other important causes. The **mortality in** non-smokers from lung cancer, **in** contrast, seems to have rema**in**ed constant, although the numbers are small. (The much larger prospective studies **in** the United States have also found no material change **in mortality** due to lung cancer **in** non-smokers between the 1960s and the 1980s.[11]

In smokers, the reductions **in** cause specific **mortality**, when they occurred, were smaller than **in** non-smokers (cerebrovascular disease was approximately constant, while ischaemic and other cardiovascular disease, taken together, decreased by only about a quarter). **In** several **in**stances, reductions **in** non-smokers were accompanied by **in**creases **in** smokers, most notably **in** the **mortality** from the cancers other than lung cancer that are caused by **smoking**, from respiratory disease other than chronic obstructive lung disease, and from "other diseases"; lung cancer, which was unchanged **in** non-smokers, **in**creased **in** smokers by 19%.

Two conditions showed **in**creased **mortality in** both non-smokers and smokers. For chronic obstructive lung disease the rates **in** non-smokers were based on such small numbers (two **in** the

first half and 10 in the second) that the increase may well have been due to chance. For the aggregate of all types of cancer that are "not associated" with smoking the increase in non-smokers was small (11%) but in smokers it was spread across a wide range of cancers and was somewhat larger (27%).

Discussion

Causation, confounding, and chance

In general, the results in this study for specific causes of death accord with those in many other studies. Reinforced by other evidence, they helped lead more than 30 years ago[7,9,25] to the conclusion that the associations observed between smoking habit and mortality are chiefly causal in character (see also the more recent reviews by the US Surgeon General[11] and the International Agency for Research on Cancer.[12]) In most of the causal associations, smoking seems to act synergistically with other aetiological agents such as consumption of alcohol[12,26]; various aspects of diet[27]; level of blood pressure, blood lipids, or other cardiovascular risk factors[28]; or exposure to asbestos,[12] radon,[29] or possibly some infective factors.[30] The quantitative effect of smoking will, therefore, vary with variation in the prevalence of these other agents.

In some instances smoking and other aetiological agents may also be confounded, as with the consumption of alcohol,[31] various aspects of personality,[32,33] and perhaps some aspects of diet.[34,35] Indeed, for a few causes of death the confounding between smoking and other factors may account for virtually all the observed association with smoking, in which case none of the excess mortality from those causes should be attributed to the habit. The only plausible examples of important associations that might be due to this, however, are those that involve cirrhosis, suicide, and other traumatic causes, for which the associations with smoking may be secondary to associations with alcohol and personality.

The close association between smoking and drinking habits was confirmed when, in 1978, the doctors in this study were invited to volunteer for a controlled trial of the value of aspirin as a prophylactic against the development of vascular disease in previously healthy men,[17] for the 1978 questionnaire also inquired about the consumption of alcoholic drinks. Among 12 322 doctors who replied, the proportion who drank 42 units or more per week (a half pint of beer, a glass of wine, or a single measure of spirits each constituting one unit) increased progressively from 2% in those who had never smoked regularly to 20% in men then smoking 25 or more cigarettes a day. If, therefore, death from cirrhosis was chiefly limited to men consuming 42 or more units per week, it would not be difficult to explain, as the result of confounding with the consumption of alcohol, most or all of the substantial excess of deaths from cirrhosis that is observed when heavy cigarette smokers are compared with non-smokers. Nor would it be difficult to explain at least a part of the excess mortality from suicide and poisoning in cigarette smokers in the same way, if these conditions were also associated with the consumption of alcohol (albeit less closely than is the case for cirrhosis of the liver).

The attribution of some of the excess mortality in cigarette smokers to confounding does not, however, necessarily mean that the overall effect of smoking on all cause mortality is less than that observed, as the factors with which tobacco is confounded may also have other effects which tend to reduce mortality. This is probably the case with alcohol, the consumption of which (at least in moderation) is associated with a reduced risk of ischaemic heart disease.[36,37] If, as now seems likely, the consumption of a few units of alcohol a day can reduce the age specific mortality from

ischaemic heart disease, then the confounding of cigarette consumption with the consumption of alcohol would mean that the total effect of cigarette smoking on ischaemic heart disease mortality is slightly more than that hitherto reported. The analysis of our own date on the effects of alcohol consumption is complex, because the doctors recorded as non-drinkers include some who gave up on health grounds; this is reported in detail elsewhere.[37] It may be noted, however, that preliminary estimates of the ratio of the mortality from ischaemic heart disease in cigarette smokers to that in non-smokers in the population with both smoking and drinking habits is 1.58:1 without standardisation for the consumption of alcohol and 1.76:1 after standardisation.

Whether the same is true of the confounding with personality, which could contribute to the excess mortality in cigarette smokers from suicide and poisoning, is another matter. It would seem unlikely, and in the absence of evidence to the contrary the contribution of these conditions to the excess mortality in cigarette smokers should perhaps be omitted, along with that of all other causes of violent death, when the contribution of smoking to the likelihood of premature death is estimated. Likewise, no deaths from these causes were attributed to smoking when estimates were being made of the worldwide mortality that is attributable to the habit in developed countries.[38]

There remain a few causes of death which, in our study, are related to smoking for reasons that are unclear. One is cancer of the rectum (table III) which was significantly related to smoking in our previous report[6] and continues to show much the same relation in these data with twice as many deaths. Colorectal cancer has not generally been related to smoking in other studies, though it has been in some.[39] Colorectal adenomas, however, have consistently been related to smoking and it has been suggested, on the basis of an American cohort study,[40] that cigarette smoke acts as an initiating agent and that a relation with cancer will be observed only after an induction period of several decades. (In that study a relation was recorded for small adenomas with smoking habits over the previous 20 years, and for larger adenomas with smoking habits more than 20 years previously.) If our data for colon and rectal cancer are combined, the association with smoking is still significant, but no longer particularly close, and a possible explanation of our results is that they reflect a real but weak association between colorectal cancer and smoking that has been inflated by the play of chance, particularly for rectal cancer. Whether such an association is causal[40] or reflects confounding with alcohol or with diet[26,41,42] remains to be seen.

The association (table V) with peptic ulcer is likely to be largely or wholly causal, that with cirrhosis is likely to be largely or wholly non- causal, and the associations with the heterogeneous group of other diseases in table V may reflect some causal effects on diseases that are not responsible for many deaths and whose relation with smoking has not been commonly studied, some confounding, some misdiagnosis, and some chance fluctuations.

Lastly, there was a weak relation with smoking for deaths from "other violence," after suicide, poisoning, traffic accidents, and falls were excluded. Some of these deaths - attributed, for example, to gunshot wounds - could have been unrecognised cases of suicide and due to confounding with alcohol and personality. At least two deaths were, however, directly attributable to smoking: namely, those due to conflagration from smoking in bed.

Temporal trend in excess mortality in smokers

A completely new feature of our results is the greater absolute and (particularly in middle age) relative excess of mortality associated with smoking in the second half of the study compared with the first. When current cigarette smokers were compared with lifelong non-smokers, the excess

mortality associated with smoking was already substantial during 1951-71, but it was considerably more extreme during 1971-91. During 1951-71, the death rates in cigarette smokers were about double those in non-smokers throughout middle age; during 1971-91, the corresponding difference was nearly treble. If, as is likely, most of the difference in mortality between smokers and non-smokers is actually caused by smoking then a threefold excess would imply that about two thirds of the deaths in middle age among the smokers were caused by tobacco. Even at older ages the excess mortality associated with tobacco was substantially greater in 1971-91 than it was during 1951-71. This difference between the apparent effects of tobacco in the two periods arose because age specific mortality decreased substantially only among non-smokers.

It may seem that if there is a difference of five years in median survival between smokers and non-smokers during 1951-71 and a difference of eight years during 1971-91 (both shown in fig 6) then a difference of about 6 1/2 years (the average of 5 and 8 years) might have been expected in the overall results, but in fact there was a difference of 7[elp] years (fig 1). This is because most of the deaths in non-smokers occurred in the second half of the study. So mortality in non-smokers for 1951-91 in figure 1 is closer to that in 1971-91 than to that in 1951-71, whereas the mortality in smokers was approximately constant in both halves of the study.

An improvement in the survival of non-smokers was to be expected, as there have been many major advances in preventive and therapeutic medicine. Diet has improved in several ways. The treatment of hypertension and ischaemic heart disease has improved (and national mortality from vascular diseases has been decreasing rapidly), the urban environment has become less heavily polluted with coal smoke, and the impact of AIDS has had little effect on men of the generations studied. In the United States, a comparison by the Surgeon General of two prospective surveys of a million people, one in the 1960s and one in the 1980s, found no evidence of a change in lung cancer rates in non-smokers over a 20 year period but a big decrease in the mortality from coronary heart disease.[11] Likewise, in the present much smaller study there has, over the same period, been no evidence of any change in the mortality of non-smokers from lung cancer, although there has been a substantial reduction in their mortality attributed to stroke and also to heart disease (if we combine ischaemic heart disease and other cardiovascular disease, as probably needs to be done to take account of nosological changes).

It is easy enough to understand why the mortality in non-smokers should have improved, but why has it not done so in cigarette smokers, who have generally experienced the same benefits of prevention and therapeutic medicine and have had the added advantage of the switch to cigarettes delivering low tar? The change in the type of cigarette would have had only a moderate effect on the overall hazards of smoking, for although it should have reduced the hazard of lung cancer [12,13] it may well have had little effect on mortality from the other main diseases caused by tobacco, particularly those that depend on deep inhalation, such as chronic obstructive lung disease[6] and ischaemic heart disease.[43]

What seems to have been more important[15,38] is the "maturing" of the epidemic of deaths of British men from smoking with those who reached later middle or old age in the 1970s and 1980s having had a longer history of regular consumption of cigarettes than men of the same ages would have had during the 1950s and 1960s. Another factor that may be important in the maturing of the epidemic (but which is impossible to quantify) is a change in the way cigarettes have been smoked in recent decades. The minority of doctors who continued to smoke cigarettes in the latter half of the study

may have tended to be those who smoked them in a different way from that of the greater number who had stopped smoking them earlier. The finding of a relatively increased risk from cigarette smoking in the second half of the study is not unique, for it parallels the findings in the two massive cohort studies carried out by the American Cancer Society, one in the 1960s and one in the 1980s, which show a similar increase over time in the excess mortality in cigarette smokers.[11]

If quantitative estimates of the current hazards of tobacco in developed countries are to be made,[38,44] they should be based on fairly recent epidemiological evidence, such as the second half of the present study or, better (because it involves much larger numbers), the second million person prospective study in the United States.[11,38,44] But, whatever its size, no single epidemiological study can provide an adequate basis for assessing the worldwide epidemic of death from tobacco, because the epidemic is at a different stage, and is evolving so differently, in different populations. In almost all developed countries lung cancer rates in women are now rising (which impedes prediction of the eventual hazard for women); in some the rates in men are still rising, in others they are falling, and in less developed countries where there has only in recent decades been a large increase in cigarette use among men, large increases in mortality from tobacco in men must be expected in the early decades of the next century as the future health effects of current smoking patterns.[44,45] The substantial differences between the effects of tobacco during the first and second halves of the present study underline the need for a worldwide network of prospective studies that can monitor the increases, and eventual decreases, in this great epidemic throughout the world.

The Imperial Cancer Research Fund and, previously, the Medical Research Council have supported this study for several decades. The British Medical Association, the Office of Population Censuses and Surveys, the General Register Office for Scotland, and the General Medical Council have consistently provided assistance, and we have had help from the General Register Office for Northern Ireland; corresponding offices in the Isle of Man, Jersey, Guernsey, and Alderney; the Department of Social Security; the Office of the Paymaster General; and many family health services authorities in England and Wales and area health boards in Scotland. We are grateful to them for their assistance and to the many individuals who have helped either scientifically or in tracing doctors and maintaining records, particularly: B Armstrong, G Bourke, A Clarke, R Collins, J Gilliland, N Gray, B Hafner, J Halliwell, R Harris, C Hennekens, M Hughes, K Jamrozik, K Jones, J Kaldor, J Kench, R MacLennan, J Mathews, S Milner, B Norman-Smith, S Norton, J Olsen, M Pike, A Radley, R Ripley, F Sitas, D Skegg, F Speizer, E Thompson and M Vessey. The chief acknowledgement, however, is to the many doctors who have replied to our questionnaires. The manuscript was typed by C Harwood. This 40 year report is dedicated to the achievements of Charles Fletcher[7] and the memory of its initiator, Sir Austin Bradford Hill (1897-1991).

lity per 100 000 men in
d second half (1 November
British doctors

ncer of upper piratory digestive racts	Other cancer		COPD		Other respiratory		Vascular disease		Cirrhosis		Other medical	
st	Second	First	Second	First	Second	First	Second	First	Second	First	Second	First	Secon

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0   NA      25     NA      0      NA      11    NA        63      NA       10   NA       29      NA
0   NA      41     NA      0      NA      13    NA        41      NA        3   NA        7      NA

6   NA      33     NA      0      NA      17    NA       147      NA        7   NA       39      NA
0   NA      42     NA      0      NA       0    NA        32      NA        0   NA       32      NA

4   62      58    184      7       0       9     0       295     477       10    0       52     128
0    0      44     29      0       0       0     0        92     240       13    0        7      27

4    0      82    112     17      42      48     0       569     501       24  115       87      99
8    0      92     40      0       0      26     0       292     178        0   13      111      24

0   13     121    267     18      26      75    68     1 018     997       39   96      101      66
0   10      77    124      0      10      47    47       627     279       12    0       34      58

8  140     354    360     84     141      85    11     1 549   1 356       25   46      174     153
7    8     212    210      0       9      63    32       989     511        8    7      102      77

2  128     615    582    193     179      79    85     2 455   1 757       42   67      332     365
0    0     344    344      0       0      92    19     1 250     981        0    0      135     137

8  261     884    925    270     333     365   379     3 731   2 703       32   58      382     314
7    0     671    597      0      25     215    63     2 865   1 553       35   12      419     333

4   91     934  1 441    471     627     597   517     5 430   4 452      142    0      822   1 002
0    0   1 204    833     58      58     232   314     5 068   2 996      113    0      693     402

9   59   1 964  1 755    534     867   1 262 1 643     8 388   7 549        0    0    1 270     923
0   73   1 243  1 332     86      76     799   692     5 187   4 909        0    0    1 282     947

7  280   1 215  2 009  1 014     949   2 261 3 334    14 998   9 738        0    0    3 180   2 939
0    0   1 688  2 185      0      74   2 064 1 259    12 808   9 233        0    0    2 308   1 783
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