

PAPERS AND SHORT REPORTS

Modifying risk of developing lung cancer by changing habits of cigarette smoking

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Abstract

Data from a hospital based case-control study of lung cancer in Western Europe were used to examine changes in the risk of developing lung cancer after changes in habits of cigarette smoking. Only data for subjects who had smoked regularly at some time in their lives were included. The large size of the study population (7181 patients and 11 006 controls) permitted precise estimates of the effect of giving up smoking.

Risks of developing lung cancer for people who had given up smoking 10 or more years before interview were less than half of those for people who continued to

smoke. The reduction in risk was seen in men and women and in former smokers of both filter and non-filter cigarettes but varied by duration of smoking habit before giving up. The protective effect of giving up became progressively greater with shorter duration of smoking habit. The risks after not smoking for 10 years for both men and women who had previously smoked for less than 20 years were roughly the same as those for lifelong non-smokers.

Reducing the number of cigarettes smoked a day or switching from non-filter to filter cigarettes also lowered the risk of developing lung cancer but not to the extent associated with giving up smoking.

Introduction

In most populations the prevalence of lung cancer among people who smoke cigarettes is lower in those with a low cigarette consumption and in ex-smokers.¹⁻⁵ Using data from a large international case-control study, we considered two issues related to prevention of lung cancer—namely, how the reduction in risk of developing lung cancer after giving up smoking is influenced by previous patterns of cigarette smoking and how the change in risk of developing lung cancer after a reduction in the number of cigarettes smoked a day or a switch from non-filter to filter brands compares with the change after giving up.

Subjects and methods

A description of the methods of collecting data has been given previously.⁶ In brief, a case-control interview study of lung cancer was carried out in seven study areas in five Western European countries. Patients admitted to hospital in 1976-80 for suspected lung cancer were interviewed while in hospital. Only patients with histologically confirmed lung cancer were entered into the study population. Interviews were carried out soon after admission; patients discharged before being interviewed were excluded. Nearly all patients contacted agreed to participate. For each patient two controls, matched for age at diagnosis (within five years), sex, centre, and, if possible, category of hospital accommodation, were selected from other hospital patients in whom diseases not related to tobacco had been

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TABLE I—Relative risk of developing lung cancer by years after stopping smoking. All risks adjusted for duration of smoking

Years after stopping smoking	Men			Women		
	No (%) of patients (n=6631)	No (%) of controls (n=10 439)	Relative risk	No (%) of patients (n=551)	No (%) of controls (n=567)	Relative risk
0	4684 (70.6)	6211 (59.5)	1.00*	440 (79.9)	410 (72.3)	1.00*
1-4	866 (13.1)	1047 (10.0)	1.07	60 (10.9)	55 (9.7)	0.94
5-9	466 (7.0)	822 (8.5)	0.71	30 (5.4)	40 (7.1)	0.68
10-14	270 (4.1)	693 (6.6)	0.56	10 (1.8)	26 (4.6)	0.36
15-19	130 (2.0)	478 (4.6)	0.43	3 (0.5)	7 (1.2)	0.49
20-24	106 (1.6)	413 (4.0)	0.43	4 (0.7)	9 (1.6)	0.47
≥25	109 (1.6)	715 (6.9)	0.29	4 (0.7)	20 (3.5)	0.27

*Test for linear trend, $p < 0.001$.

TABLE II—Relative risk of developing lung cancer by time since stopping smoking and total duration of smoking habit

Years after stopping smoking (years)	Duration of smoking habit (years)			
	1-19	20-39	40-49	≥50
	<i>Men</i>			
0	1.0*	2.2	2.8	3.0
1-4	1.1	2.1	3.3	3.8
5-9	0.4	1.5	2.2	2.8
≥10	0.3	1.0	1.6	2.7
	<i>Women</i>			
0	1.0†	2.1	2.7	5.2
1-4	1.0	2.3	2.1	7.1
5-9	0.4	2.0	1.1	1.7
≥10	0.4	0.8	2.3	

*Baseline category. Risk for current smokers who had smoked for one to 19 years relative to that for people who had never smoked was 0.3.
†Baseline category. Risk for current smokers who had smoked for one to 19 years relative to that for people who had never smoked was 0.6.

TABLE III—Relative risk of developing lung cancer by number of years since stopping smoking, controlling for several other factors. All risks adjusted for duration of use in years

	Time since stopping smoking (years)							
	Men				Women			
	0	1-4	5-9	≥10	0	1-4	5-9	≥10
No of cigarettes a day:								
1-9	1.00*	1.47	0.90	0.67	1.00	1.55	1.16	0.66
10-19	1.00	1.31	0.88	0.61	1.00	1.04	0.62	0.20
20-29	1.00	1.08	0.75	0.51	1.00	0.95	0.64	0.33
≥30	1.00	0.86	0.80	0.40	1.00		0.24	0.42
Type of cigarette:								
Filter	1.00	1.11	0.91	0.34	1.00	0.88	0.83	0.25
Mixed	1.00	0.98	0.69	0.53	1.00	0.73	0.61	0.27
Non-filter	1.00	1.12	0.64	0.33	1.00	2.16	0.65	0.30
Frequency of inhalation:								
All the time	1.00	1.01	0.71	0.50	1.00	0.95	0.93	0.35
Most of the time	1.00	1.81	0.66	0.43	1.00	1.53	0.52	0.57
Part of the time	1.00	0.97	0.81	0.60	1.00	0.94	0.19	0.35
Rarely or never	1.00	1.13	0.69	0.39	1.00	1.49	1.02	0.29
Depth of inhalation:								
Deeply	1.00	0.94	0.67	0.47	1.00	0.90	1.09	0.58
Moderately	1.00	1.22	0.73	0.43	1.00	1.01	1.68	0.47
Slightly or never	1.00	1.19	0.67	0.37	1.00	1.31	0.16	0.32

*Tests for differences in linear trends, $p < 0.05$.

diagnosed. A list of the tobacco related diseases diagnosed and the initial variations we made in the above procedure have been described elsewhere.⁶

We interviewed 7804 patients (6920 men and 884 women) and 15 207 controls (13 460 men and 1747 women). In the present study we analysed data only for those subjects who had smoked cigarettes regularly at some time in their lives. Of the patients, 6631 men (95.8%) and 551 women (62.3%) satisfied this criterion; of the controls, 10 439 men (77.6%) and 567 women (32.5%) did so.

We noted the duration of smoking habit, the number of cigarettes smoked each day, and the names of four brands previously smoked. Most subjects (15 834 (87.1%)) had smoked three or fewer brands. When more than four brands were reported during the interview coding procedures varied slightly among study centres. At most centres consecutive brands were combined, filter or non-filter type being coded as missing if the consecutive brands differed in this respect. Less often the four brands used for the longest duration were coded. Using information about brands we created a smoking profile for each subject, detailing changes in the number of cigarettes smoked each day and from non-

filter to filter brands. Profiles could be computed only for those with a complete smoking history; others were coded as missing.

Summary relative risks of developing lung cancer associated with several smoking variables were computed over strata defined by centre and, when appropriate, other factors, using the method of Gart.⁷ The Mantel extension procedure⁸ was used to test for linear trend across multiple exposure categories, with weights defined by consecutive integers. In addition, a multivariate regression analysis for matched case-control data was carried out,^{9 10} the results of which closely paralleled those from analysis of unmatched, stratified data. Because duration of smoking habit was an important risk and confounding factor in analyses of patterns of giving up smoking all relative risks were adjusted by categories of duration—namely, one to 19, 20-39, 40-49, and 50 or more years of use.

Results

Table I shows that most of the subjects included in the present study were smoking at the time of interview and that a higher proportion of women than men were still smoking. The risk of developing lung cancer dropped sharply after giving up smoking with the gradient of decrease similar in both men and women. The patterns of decrease were similar after further adjustment for number of cigarettes smoked a day.

In each category of duration of smoking habit the risk of developing lung cancer decreased as the number of years since stopping smoking increased (table II); in men, however, the rate of decline was greater in those who had smoked for a shorter time ($p < 0.001$). For men who had smoked for one to 19 years the risk of developing lung cancer after 10 years of not smoking dropped to less than one third of that for current smokers, but even for men who had smoked for 50 years or more the risk was still 90% of that for men who continued to smoke.

(The risks for lifelong non-smokers relative to current smokers who had been smoking for one to 19 years were 0.25 for men and 0.59 for women. Thus, after 10 years of not smoking, the risk of developing lung cancer for men who had smoked for one to 19 years approached that for lifelong non-smokers; but risks remained substantially raised for subjects who had smoked for more than 19 years, even after 10 years of not smoking. For women the level of risk found in non-smokers was attained after five years of not smoking in those who had smoked for one to 19 years, but in longer term smokers risks remained raised even after 10 years of not smoking.)

Table III shows relative risks for years since stopping smoking according to various other variables. In men the rate of decline in relative risks with stopping smoking varied significantly ($p < 0.05$) between categories of number smoked each day, with an increasingly greater proportional reduction in risk in those who had not smoked for 10 years or more and had previously smoked a greater number each day. In women no such significant differences were seen. No significant differences in trend were seen according to type of cigarette smoked (only filter, only non-filter, or both), but there was some indica-

tion of a greater reduction in risk for those who inhaled less often or deeply.

We also expressed relative risks, adjusted for duration of cigarette use in years, by changes in habit during the course of smoking life. Small numbers prevented us giving the results for women. Table IV shows risks by the percentage change in the number of cigarettes smoked a day (the number a day of the most recent brand compared with the highest daily consumption among the earlier brands) relative to no change in the number smoked a day. Of the patients, 1874 (29%) had stopped smoking altogether, 745 (11%) had reduced their cigarette consumption but were smoking at the time of interview, 2599 (40%) had not changed, and 1266 (20%) reported an increase. Of the controls, 3983 (39%) had stopped smoking altogether, 1083 (11%) had reduced their cigarette consumption, 3628 (36%) had not changed, and 1401 (14%) reported an increase. A slightly lower risk occurred for those who had stopped smoking (relative risk = 0.76; as noted in table I, however, the relative risk for those who had given up for a long time was less than 0.50), while among current smokers those who had reduced their cigarette consumption to less than one half their original number a day were not at lower risk (relative risk = 1.01) than those with a smaller reduction in intake (relative risk = 0.84). As expected, the relative risk was greater for those who had increased their daily cigarette consumption compared with those who had not altered their habit (relative risk = 1.26). Table V shows risks (relative to no change) for those who had reduced their daily consumption, by years since the reduction. In former smokers lower risks were found by years since the decrease occurred (test for trend, $p < 0.001$), and in current smokers there were only moderate trends (for $\geq 50\%$ reduction) or no trend (for $< 50\%$ reduction) according to the time since the reduction took place (tests for trend: 50% or more decrease, $p < 0.05$; less the 50% decrease, $p = 0.23$).

TABLE IV—Relative risks for men of developing lung cancer by the percentage change in daily consumption (the most recent brand compared with the maximum daily consumption of earlier brands). Risk adjusted for duration of use in years

Change in daily consumption	No (%) of patients (n = 6486)	No (%) of controls (n = 10 095)	Relative risk	95% confidence limit
None	2599 (40.1)	3628 (35.9)	1.00*	
Increased	1266 (19.5)	1401 (13.9)	1.26	1.1-1.4
Decreased:				
Stopped (100%)	1874 (28.9)	3983 (39.5)	0.76	0.7-0.8
Reduced ($\geq 50\%$)	387 (6.0)	522 (5.2)	1.01	0.9-1.2
Reduced ($< 50\%$)	358 (5.5)	561 (5.6)	0.84	0.7-1.0
Total	2619 (40.5)	5066 (50.3)	0.79	0.7-0.9

*Baseline exposure. For men the risk of never having smoked relative to not changing number smoked per day was 0.13.

TABLE V—Relative risk* of developing lung cancer for subjects who decreased their daily consumption, by years since decrease

Years since decrease	Extent of decrease		
	100%	$\geq 50\%$	$< 50\%$
1-4	1.1	1.5	0.8
5-9	0.7	1.0	0.6
10-14	0.6	1.0	1.0
15-19	0.5	0.6	0.6
20-24	0.5	0.9	0.8
≥ 25	0.5	0.9	1.0

*All risks relative to those who did not change.

TABLE VI—Relative risks of developing lung cancer by most recent change in type of cigarette smoked. (All risks adjusted for duration of use in years)

Type of cigarette	No (%) of patients (n = 6512)	No (%) of controls (n = 10 250)	Relative* risk	Relative† risk
No change:				
Filter only	326 (5.0)	777 (7.6)	1.00‡	1.00‡
Non-filter only	1140 (17.5)	1271 (12.4)	1.78	1.53
Filter to non-filter	644 (9.9)	863 (8.4)	1.49	1.61
Non-filter to filter	4402 (67.6)	7339 (71.7)	1.60	1.48

*Current smokers only.

†Ex-smokers only. Risks adjusted for time since stopping smoking.

‡Baseline exposure. Risks of never smoked relative to filter only were 0.26 (current smoker) and 0.22 (former smoker).

Table VI shows that in current smokers (from table I 4684 (71%) of the patients and 6211 (60%) of the controls) and among former smokers (adjusted for year since giving up) the risks were greater for lifelong smokers of non-filter cigarettes (current smokers: relative risk = 1.78, 95% confidence limits 1.5, 2.1; former smokers: relative risk = 1.53, 95% confidence limits 1.1, 2.1) and those who had switched from filter to non-filter brands (current smokers: relative risk = 1.49, 95% confidence limits 1.2, 1.9; former smokers: relative risk = 1.61, 95% confidence limits 1.1, 2.4) than for those who had smoked only filter cigarettes. Risks for smokers who had switched from non-filter to filter brands were raised compared with those for subjects who had smoked only filter cigarettes (current smokers: relative risk = 1.60, 95% confidence limits 1.4, 1.9; former smokers: relative risk = 1.48, 95% confidence limits 1.1, 2.0). For smokers switching from non-filter to filter brands, table VII shows that the risks by years since the change (relative to smokers of filter cigarettes alone) remained 30-40% above those for subjects who smoked filter cigarettes exclusively, even after 20 years of filter use.

TABLE VII—Relative risk* of developing lung cancer by years since changing from non-filter brands of cigarettes

Time since change (years)	Current smokers	Former smokers
1-4	1.6	2.2
5-9	1.6	1.6
10-14	1.6	1.5
15-19	1.4	1.6
20-24	1.4	1.3
≥ 25	1.6	1.5

*Risks relative to smokers of filter cigarettes only. Adjusted for years since stopping smoking.

The analyses in tables IV and VI were repeated, adjusting for number of cigarettes smoked each day and age at diagnosis; the results were not materially affected. We also found that the patterns of risk were similar when subjects who had changed brands only once in their smoking experience were studied.

Discussion

Smokers who smoke filter or lower tar brands, who smoke fewer cigarettes a day, or who give up smoking are known to be at lower risk of developing lung cancer.¹⁻⁶ Our analyses help to measure the effect of such modifications in smoking habits. The results show that changes in patterns of cigarette smoking that lower exposure were associated with lower risks of developing lung cancer but, when compared with completely stopping smoking, the reductions in risk were small.

This study also shows that the decline in relative risk after stopping smoking was greater in those who had smoked for shorter periods. The subjects who had smoked for one to 19 years returned to the risk level of lifetime non-smokers within five to 10 years after stopping smoking. This finding suggests that the carcinogenic effects of smoking can be minimised by stopping smoking if the habit is not continued for too long. This should induce people starting to smoke regularly and short term smokers to stop before changes become irreversible. Those subjects who gave up smoking after 40 years of cigarette use were still at a substantially increased relative risk 10 years after stopping compared with those who had never smoked and, indeed, were unlikely ever to approach the level of risk found in those who had never smoked. The finding of a smaller relative decline in long term smokers who give up is consistent with that reported for British doctors,¹¹ among whom the arithmetic excess in death due to lung cancer in smokers who give up compared with lifetime non-smokers was almost constant.

Several potential biases in this hospital based study (resulting from the method of case acquisition, choice of control diseases, and differences in the referral patterns of the patients and controls) have been discussed previously⁶ and were thought to be minimal. Recall bias was also thought to be small as general knowledge of the association between smoking and lung cancer

was high in all groups, respondents were told only that the survey was to gather health information, and many patients were unaware of their specific diagnosis at the time of interview. Furthermore, all the subjects in this analysis acknowledged themselves to be smokers. There may have been some gaps in the smoking histories as we do not know how often patients stopped smoking between changes in brand or while smoking a single brand. By comparing age at interview with age at start of smoking habit plus time since giving up plus years of use we estimated that 17 690 (97%) of the subjects who had smoked had done so continuously or with a total smoking free interval of two years or less. Another limitation was that the questionnaire recorded no more than four different brands of cigarettes. The procedures that were used for those smoking five or more brands would have tended to underestimate exposure, particularly the duration of use. The rarity of this occurrence, however, argued against any appreciable impact on patterns of risk.

In summary, our results suggest that reducing the risk of developing lung cancer induced by cigarette smoking in middle aged and older smokers requires primary emphasis on stopping the smoking habit or lowering the amount smoked each day. Smoking only filter brands was also associated with a lowered risk (although changing from a non-filter to a filter cigarette had only a relatively small impact on risk of developing lung cancer) but was not as effective a preventive measure as giving up completely.

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The difficult choice of treatment for poorly controlled maturity onset diabetes: tablets or insulin?

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Abstract

Patients with maturity onset diabetes that is poorly controlled on maximal doses of oral hypoglycaemic agents are difficult to treat. A prospective randomised crossover study was performed in 58 predominantly non-obese patients on maximal doses of glibenclamide or metformin, or both, to find out if insulin would improve control or well being. The patients were given daily injections of up to 48 units of highly purified porcine lente insulin. Glycaemic control was improved by 15% or more in only 18 patients; 14 others felt better but their diabetes was no better controlled. Those whose control was improved by insulin could not be distinguished by age, duration of diabetes, body mass index, or their own treatment preference. C peptide concentrations, however, did help predict the response to insulin, the fasting C peptide to glucose ratio being considerably lower in those patients whose control was better on insulin.

These findings suggest that a simple insulin regimen

does not necessarily lead to better glycaemic control in maturity onset diabetes. Nevertheless, a trial of insulin is often justified since it poses few practical difficulties and makes some patients feel better even if their control is not improved. A more complex regimen might improve control in more cases, but it might also be less acceptable to older patients.

Introduction

At first sight treatment of maturity onset diabetes seems simple. The basis is diet, especially for overweight patients. When this fails a sulphonylurea or a biguanide is added, or a combination of the two if either alone does not achieve good control. Finally, "when oral agents are used and found to be ineffective, either initially or secondarily, insulin should be substituted"¹—the implication being that all will then be well.

In practice treatment of maturity onset diabetes is less straightforward. It is hard to change eating habits, and dietary advice is often ignored. Many patients progress to oral hypoglycaemic agents (subsequently referred to as "tablets") but still remain poorly controlled. Both doctor and patient may be reluctant to accept that tablet treatment has failed and move on to insulin. This reluctance may be justified since there is no evidence that insulin treatment necessarily produces better control of maturity onset diabetes. Indeed, there are many patients whose control appears to be worse on insulin, perhaps not surprisingly because maturity onset diabetes is a complex and heterogenous disorder resulting from insulin resistance as well as insulin deficiency.²⁻⁴

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