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Cigarette smoking and male lung cancer in an area of very high incidence

II Report of a general population cohort study in the West of Scotland

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SUMMARY A general population cohort of 7055 men aged 45–64 and resident in Renfrew and Paisley, two urban burghs in the West of Scotland, has been followed for 10½ years. Analysis of the cigarette smoking and lung cancer (incidence and mortality) relation has been undertaken in order to establish whether unusual results found in a case-control study of cigarette smoking and lung cancer in the adjacent city of Glasgow could be confirmed. Lung cancer incidence and mortality rates increased markedly for exposure categories up to an average consumption of 15–24 cigarettes per day. Above this level the rates increased only marginally. Expressing these rates relative to that estimated for the never-smoked group and comparing them with the relative risks estimated in the case-control study revealed a similarity in terms of both the shape and the level of the dose-response relation. Comparison of the lung cancer rates found in this cohort with those observed in other cohort studies in the literature (UK doctors, US Veterans, and American Cancer Society volunteers) suggested that the West of Scotland rates were substantially higher at all levels of cigarette exposure.

A case-control study of smoking and lung cancer in men in the West of Scotland conducted between 1976 and 1981 showed that the risk of lung cancer did not increase significantly with increasing amounts of tobacco exposure above an average consumption of 20 cigarettes per day. An apparent paradox of low relative risk of lung cancer in an area of excessively high incidence was also observed. Data from a prospective cohort (1972–84) study examining the role of factors influencing cardiorespiratory health and disease in Renfrew and Paisley, two urban burghs representative of the West of Scotland,[2] were used to test whether these observations could be supported.

Materials and methods

Renfrew and Paisley are two adjacent urban burghs west of Glasgow with a population of 113 000, of whom 19 000 are aged between 45 and 64. Each individual was invited to attend a multiphasic screening clinic, and an 80% response rate was achieved during the period 1972–76.[2] Before attending, each respondent completed a standard questionnaire, which included a self-reported smoking history. These were carefully checked on attendance at the screening unit. Signed permission was obtained from those who attended to allow their future medical records to be examined by the authors. Information on subsequent cancer incidence was obtained through linkage with the Cancer Registry supplemented by mortality data obtained from the National Health Service Central Register and the General Register Office for Scotland. The data presented are complete to the end of December 1985, an average follow-up of 10½ years.

Exposure to tobacco products for individuals in the cohort has been expressed in terms of average numbers of cigarettes per day based on their smoking lifetime using exposure categories: never smoked, 1–14, 15–24, 25–34, and 35 or more cigarettes per day. The same exposure categories were used in the analysis of the case-control study. Ex-smokers and pipe/cigar only smokers were identified separately.

Self-reported smoking exposure was validated by examining the consistency of replies to the same questions in different studies of occupational groups

Table 1 *Age and social class distribution of men attending screening unit.*

	Age group				
	45–49	*50–54*	*55–59*	*60–64*	*Total*
Number	1816	1980	1683	1576	7055
%	25·7	28·1	23·9	22·3	100·0

	Social class						
	I	*II*	*IIIN*	*IIIM*	*IV*	*V*	*Total*
Number	352	981	833	2814	1566	436	6982*
%	5·0	14·1	11·9	40·3	22·4	6·3	100·0

*73 men could not be classified

examined in a similar time period in the West of Scotland with the same age and social class background as the cohort.

Lung cancer mortality and incidence rates for each exposure category were estimated using the life table approach which adjusts for competing causes of death. The rates were expressed as average annual rates per 10 000 based on 10 years of follow-up and age adjusted so that each five year age group was equally represented.

The question of whether the relation between increasing levels of cigarette consumption and increasing risk of lung cancer is linear has been examined by a statistical model[3] which determines whether it is necessary to include a quadratic term to describe the flattening observed.

One hundred and ninety-four male lung cancer deaths have been observed in the cohort in the first ten years of follow-up. This allowed the low relative risk/high lung cancer incidence paradox to be investigated by comparing the observed mortality in each of the exposure categories with that reported in three major cohort studies.[4–6]

Results

Table 1 shows the age and social class distribution of the men in the cohort; 69% of those attending were classified as social class III manual, IV or V.

Current smoking habits reported by men in the cohort are shown in table 2 together with those from the occupational cohorts. The percentage smoking 15

Table 2 *Distribution of self-reported smoking habits in West of Scotland cohorts (men aged 45–64).*

Smoking category (average number of cigarettes/day) present smokers	*Renfrew Paisley 1972–6*	*Industrial cohorts*	
		1970–2	*1965–8*
Never smoked	16·9	18·4	15·5
1–14	11·9	12·1	18·5
15–24	29·1	25·8	30·5
25–34	11·1	9·2	6·8
35+	4·4	2·6	1·6
Pipe/cigars only	2·0	1·2	2·3
Ex smokers	24·6	30·7	24·8
Total number	7055	3804	2300

Table 3 *Age standardised lung cancer incidence and mortality rate in men aged 45–64 by average number of cigarettes smoked daily.*

Average number of cigarettes smoked daily (present smokers)	*Number of respondents*	*Number of lung cancer cases*	*Average annual incidence rate per 10 000*	*Number of lung cancer deaths*	*Average annual death rate per 10 000*
Never smoked	1189	7	5·4	7	5·1
1–14	840	30	35·3	23	27·9
15–24	2056	98	51·4	87	45·4
25–34	782	40	56·5	38	54·8
35+	311	18	52·6	13	38·2
Pipe-cigar only	141	2	11·2	2	11·7
Ex smokers	1736	28	16·8	24	13·7
Total	7055	223		194	

or more cigarettes per day was slightly higher in the general population cohort (44·7%) than in the occupational cohorts (37·6%). The percentage who reported never having smoked was similar.

Table 3 presents male lung cancer incidence and mortality rates for each of the cigarette smoking categories. Incidence rates increase steeply for exposure categories up to an average consumption of 15–24 cigarettes per day. Above this level flattening is observed. Mortality rates show the same pattern. The quadratic term used to describe the flattening is statistically significant for both incidence ($p < 0.01$) and mortality ($p < 0.01$).

Table 4 compares the relative risks of lung cancer estimated in the cohort and the case-control studies using the never smoked group as the baseline category (ie, denominator) in the relative risk calculation. The relative risks in the case-control study were slightly lower at each level of cigarette consumption, but above an average consumption of 15–24 cigarettes per day no significant increase in relative risk in either the case-control or cohort study was observed.

The figure illustrates the lung cancer mortality rates in men at different levels of cigarette consumption, adjusted for age and length of follow-up, found in three major cohort studies in the literature (UK doctors,[4] US Veterans,[5] and the American Cancer Society volunteers[6]), together with the rates for the West of Scotland cohort.

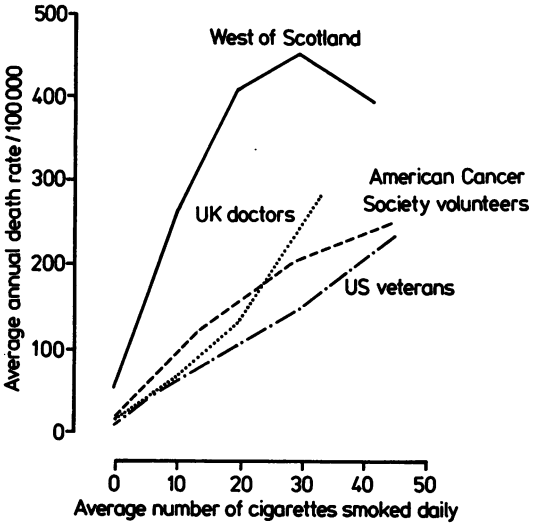
The three cohort studies show rates of lung cancer in relation to cigarette exposure which are remarkably similar. The West of Scotland cohort rates are substantially higher for each exposure level illustrated. The flattening of the dose-response relation observed in the West of Scotland cohort is different from the linear dose-response relation observed in the three other studies.

Discussion

The main reason for presenting the results derived from the cohort study is to establish whether the

Table 4 *Relative risks derived from the cohort and case-control studies for average number of cigarettes smoked daily.*

Average number of cigarettes smoked daily (present smokers)	*Relative risks*		
	Cohort study		*Case-control study*
	Incidence	*Mortality*	
0	1	1	1
1–14	6·5	5·5	4·5
15–24	9·5	8·9	7·6
25–34	10·5	10·7	8·6
35+	9·7	7·5	9·2



Lung cancer mortality in relation to average number of cigarettes smoked daily for the West of Scotland cohort and three other published cohort studies.

unusual finding of a flattening in the dose-response relation of cigarette smoking and lung cancer observed at the higher levels of cigarette consumption in the case-control study in the West of Scotland can be substantiated. The availability of results from both a case-control and cohort study conducted in the same geographical area during the same time period removes many of the biasses inherent in the former. This is particularly true in regard to the possible under-reporting of smoking habits by cases in case-control studies and the use of hospital controls to estimate smoking habits in the general population. Additionally, any possibility of interviewer bias is eliminated. The fact that both studies produce dose-response relations which flatten at the higher levels of cigarette consumption suggests that the observation is not an artefact.

The validity of self-reported cigarette smoking histories is always a criticism that can be levelled at epidemiological studies, and it is reassuring to find that the distributions of amount smoked in the cohort and case-control studies follow closely those reported in other surveys carried out in the West of Scotland.

One major advantage of cohort study is that it can provide an estimate of the lung cancer risk for each smoking category in absolute terms, whereas the case-control study can provide only relative risks. When the absolute estimates of risk found in the cohort study are expressed as relative risks and compared with those found from the case-control

study using the same definition of baseline group, the magnitude of these risks is low compared with those observed in other cigarette smoking and lung cancer studies in men in the literature. This is surprising in an area that 'boasts' one of the highest, if not the highest, incidence of lung cancer in the world. However, when the absolute rates for each of the smoking categories are compared with those found in other cohort studies in the literature (figure), it is clear that the West of Scotland rates are higher at all levels of cigarette consumption. The only explanation for the West of Scotland having high absolute levels of risk and low relative levels is that the rate of lung cancer in non-smokers must be higher than in other studies. One problem about estimating the lung cancer rates in men who have never smoked is that it is based on seven cases and seven deaths. By using data from the case-control study and assuming that the absolute rate for the 15–24 cigarettes per day smokers is the same as that found in the cohort study an alternative estimate can be derived. This approach produces an average rate of 6·8/10 000 per annum, higher than that observed for the cohort study and based on 13 lung cancer cases.

It thus appears that it is not just the West of Scotland smoker who is at an increased level of risk compared with his equal smoking counterpart elsewhere but also the West of Scotland non-smoker who may also experience a higher than expected lung cancer risk.

The flattening of the dose-response relation seen in the case-control study has not been explained by any of the smoking characteristics examined. The fact that both the size and shape of the relation can be reproduced in the cohort study leads us to believe that this is a genuine representation of the smoking and lung cancer relation in the West of Scotland.

What this might mean in terms of the aetiology of lung cancer in the West of Scotland is not known. However, the following possibilities would be consistent with the above observations:

1 The West of Scotland smoker may derive a larger dose per cigarette than smokers in the other studies reported, and the smoking characteristic which facilitated this has been either not measured at all or measured imprecisely. If this was the case, a separate explanation would be required to explain the high rate in non-smokers. With 83·1% of the male population aged 45–64 admitting to having smoked some form of tobacco regularly at some stage in their lifetime, the possibility of environmental tobacco exposure (passive smoking) has to be considered.[7]

2 The increased rate of lung cancer in non-smokers and smokers in the West of Scotland could be the result of a factor or factors unrelated to smoking or possibly a synergism between passive smoking and other factors. It has been suggested that dietary beta-carotene (the principal sources being dark-green leafy vegetables, carrots, and certain yellow and red fruits and vegetables) reduces the risk of cancer in man.[8] Data from the General Household Expenditure Survey consistently show a lower consumption of fresh fruit (25% less) and fresh green vegetables (50% less) in Scotland compared with England.[9]

Reasons that might explain the flattening of the dose-response relation are less obvious. One explanation could be that heavy smokers in the West of Scotland extract a smaller dose per cigarette than those smoking less than 20 cigarettes/day, and this fact has not been detected by the questionnaire. However, this appears unlikely as heavy smokers more often report that they were deep inhalers. Alternatively, some heavy smokers may have died before the age of 45 from lung cancer or other smoking-related diseases although the death rates in these age groups are low. There is the possibility that the heavier smokers may have extra protection as a result of abundant chronic mucus secretion.[10] Also, the existence of a dose-incidence threshold[11] might be considered as the rates of lung cancer in smokers generally in the West of Scotland appear to be extremely high.

Whichever proves to be the ultimate explanation, the only way in which the West of Scotland can currently reduce its high lung cancer incidence rate substantially is by persuading large numbers of present smokers to stop and dissuading young people from starting. Switching from higher tar to lower tar cigarettes will not produce major reductions in the lung cancer incidence rate.

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