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Lung cancer, smoking, and environment: a cohort study of the Danish population

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Abstract

Objective—The almost twofold difference in lung cancer incidence between people living in Copenhagen and in the rural areas of Denmark in the 1980s led to public concern; this study was undertaken to assess the effects of air pollution and occupation on lung cancer in Denmark, with control for smoking habits.

Design—Cohort study of national population.

Subjects—People aged 30–64 and economically active in 1970 (927 470 men and 486 130 women).

Main outcome measures—Relative risks for lung cancer estimated with multiplicative Poisson modelling of incidence rates.

Results—Differences in smoking habit explained about 60% of the excess lung cancer risk in Copenhagen for men and 90% for women. After control for smoking, workers had double the lung cancer risk of teachers and academics. There was only a small independent effect of region.

Conclusion—Smoking is the main factor behind the regional differences in lung cancer incidence in Denmark, and occupational risk factors also seem to have an important role. The outdoor air in

Copenhagen around 1970 contained on average 50–80 µg/m³ of sulphur dioxide, 80–100 µg/m³ total suspended particulate matter, and up to 10 ng/m³ benzo(a)pyrene and had peak values of daily smoke of 120 µg/m³. Region had only a small effect on incidence of lung cancer in the present study, which suggests that an influence of outdoor air pollution on lung cancer is identifiable only above this pollution level.

Introduction

The incidence of lung cancer incidence in Denmark varied in the 1980s from a world standardised rate of 47/100 000 for men in rural areas to 80/100 000 in Copenhagen.¹ Air pollution is higher in Copenhagen than in rural areas, and the possible link between lung cancer and air pollution has been an issue of public concern. Using register based data we measured the impact of smoking and occupational and environmental exposures on the risk of lung cancer in Denmark.

Methods

The study included people aged 30–64 years, living and economically active in Denmark on the census date

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Table 1—Distribution of study populations by sex and risk factors. Values are percentages (numbers)

	Census data (1970)		Tobacco data (1970-2)	
	Men (n=927 470)	Women (n=486 130)	Men (n=17 739)	Women (n=7993)
Age (years):				
30-34	16.1 (149 081)	16.6 (80 733)	25.8 (4 569)	28.7 (2290)
35-39	14.6 (135 518)	16.0 (77 748)		
40-44	14.7 (136 223)	16.4 (79 925)	31.9 (5 653)	36.0 (2875)
45-49	15.4 (142 808)	17.1 (83 221)		
50-54	14.6 (135 304)	15.0 (72 821)		
55-59	13.6 (126 134)	11.9 (57 624)	42.4 (7 517)	35.4 (2828)
60-64	11.0 (102 402)	7.0 (34 058)		
Marital status:				
Married	83.9 (778 467)	72.5 (352 415)	89.3 (15 834)	70.0 (5599)
Unmarried	9.3 (86 519)	10.6 (51 502)	6.9 (1 231)	10.6 (849)
Previously married	6.7 (62 484)	16.9 (82 213)	3.8 (674)	19.3 (1545)
Dwelling:				
One family house	68.3 (633 697)	58.2 (282 710)	66.8 (11 846)	51.7 (4134)
Apartment house	31.7 (293 773)	41.8 (203 420)	33.2 (5 893)	48.3 (3859)
Region*:				
Capital	15.6 (144 446)	21.7 (105 697)	16.6 (2 952)	25.2 (2015)
Suburbs	12.6 (117 047)	14.4 (70 164)	11.0 (1 950)	14.8 (1183)
Towns	36.7 (340 746)	34.9 (169 754)	32.8 (5 817)	35.9 (2872)
Rural areas	35.1 (325 231)	28.9 (140 515)	39.6 (7 020)	24.1 (1923)
Occupation†:				
Farmer	11.6 (107 553)	8.7 (42 478)	15.6 (2 769)	2.1 (170)
Other self employed	15.6 (144 850)	13.3 (64 096)	15.8 (2 798)	7.8 (623)
Highly educated employee	10.2 (95 001)	7.2 (34 912)	13.1 (2 315)	7.7 (615)
Other employee	18.8 (174 781)	35.2 (171 195)	15.1 (2 684)	33.8 (2701)
Skilled worker	14.5 (134 099)		18.0 (3 193)	
Unskilled worker	29.2 (271 186)	35.7 (173 449)	22.4 (3 980)	48.6 (3884)

*Capital: Copenhagen, Frederiksberg, and Gentofte municipalities. Suburbs: Copenhagen county except Gentofte. Towns: towns with more than 10 000 inhabitants.

†Farmer: self employed in agriculture. Highly educated employee: salaried employee with university and college education (for example, teacher). Other employee: other salaried employee (for example, policeman, nurse, secretary). Skilled worker: worker who has served an apprenticeship (for example, blacksmith, carpenter, bricklayer, printer, painter).

Table 2—Variations in tobacco smoking* and heavy tobacco smoking† for economically active men and women in Denmark 1970-2. Odds ratio (95% confidence intervals) are shown

	Men		Women	
	Smoker*	Heavy smoker†	Smoker*	Heavy smoker†
Age (years):				
30-39	1.00	1.00	1.00	1.00
40-49	1.4 (1.3 to 1.5)	1.2 (1.1 to 1.4)	1.0 (0.9 to 1.1)	1.2 (1.1 to 1.4)
50-64	1.1 (1.0 to 1.2)	1.1 (1.0 to 1.2)	0.8 (0.7 to 0.8)	0.9 (0.8 to 1.0)
Marital status:				
Married	1.00	1.00	1.00	1.00
Unmarried	0.7 (0.6 to 0.8)	0.9 (0.8 to 1.1)	0.9 (0.8 to 1.0)	1.0 (0.8 to 1.2)
Previously married	1.2 (1.0 to 1.5)	1.5 (1.3 to 1.8)	1.5 (1.3 to 1.7)	1.4 (1.2 to 1.6)
Dwelling:				
One family house	1.00	1.00	1.00	1.00
Apartment house	1.5 (1.3 to 1.6)	1.3 (1.2 to 1.4)	1.4 (1.2 to 1.6)	1.4 (1.2 to 1.6)
Region:				
Capital	1.0 (0.8 to 1.1)	1.5 (1.4 to 1.8)	1.4 (1.2 to 1.6)	3.0 (2.4 to 3.7)
Suburbs	0.9 (0.8 to 1.1)	1.4 (1.3 to 1.6)	1.2 (1.0 to 1.4)	2.6 (2.1 to 3.2)
Towns	0.9 (0.8 to 1.0)	1.0 (0.9 to 1.2)	1.2 (1.1 to 1.4)	1.9 (1.6 to 2.3)
Rural areas	1.00	1.00	1.00	1.00
Occupation:				
Farmer	0.6 (0.5 to 0.7)	0.5 (0.4 to 0.6)	0.4 (0.3 to 0.5)	0.4 (0.2 to 0.6)
Other self employed	0.9 (0.8 to 1.0)	1.2 (1.1 to 1.4)	0.8 (0.7 to 0.9)	1.2 (1.0 to 1.5)
Highly educated employee	0.8 (0.7 to 0.9)	1.0 (0.9 to 1.2)	1.0 (0.8 to 1.1)	1.3 (1.0 to 1.6)
Other employee	1.00	1.00	1.00	1.00
Skilled worker	1.0 (0.9 to 1.1)	0.9 (0.8 to 1.0)		
Unskilled worker	1.2 (1.0 to 1.3)	1.0 (0.9 to 1.2)	1.1 (1.0 to 1.2)	1.0 (0.9 to 1.2)

Gallup data; models without interaction.

*72% of men (12 699/17 739) and 56% of women (4641/7993) were smokers; 44% of men (7952/18 176) and 46% of women (4140/8972) were cigarette smokers.

†27% of men (4877/17 739) and 17% of women (1555/7993) were heavy smokers.

by the municipalities and coded by the bureau. Information on sex, age, marital status, dwelling, region, and occupation were used as risk factors in the present analysis (see table 1).

The cohort was followed up until 8 November 1987. Deaths and emigrations were identified by linkage with the Danish central population register, and incident lung cancer cases by linkage with the Danish cancer register.²

Each person contributed to the person years at risk from 9 November 1970 until the date of diagnosis of lung cancer, death, emigration, or 8 November 1987, whichever came first. Person years at risk were divided into five year age groups defined by age on 9 November 1970, and into four periods of follow up: 1970-5, 1975-80, 1980-5, and 1985-7.

The smoking information stems from surveys from 1970 to 1972 made by the private marketing company Gallup for Scandinavian Tobacco Company. Each year, up to 20 000 people, chosen to be representative of the population above age 15, were interviewed about type and amount of tobacco smoked the previous day. Questions on sex, age, marital status, dwelling, region, and occupation were included (table 1). In the data processing, Gallup had compensated for people unwilling to participate or not contacted (18%) by duplicating data for people with the same demographic characteristics. As the data were stored anonymously, description of smoking habit was possible only on a group basis.

Each person was classified as non-smoker, moderate smoker, or heavy smoker. Heavy smokers were defined as 15 or more cigarettes the previous day; three or more packages of pipe tobacco bought last week, or nine or more fills the previous day; or four or more cigars, cheroots, or cigarillos the previous day. Mixed smokers were classified according to most frequent use.

For a given combination of risk factors, the observed proportion of smokers was often based on small numbers. We therefore modelled the smoking proportion by using logistic regression dependent on the risk factors. The variation in smoking proportions was then measured as odds ratios—for example, for men in Copenhagen compared with men in the rural areas. Table 2 shows the variation measured in tobacco consumption models with main effects of age, marital status, dwelling, region, and occupation. Models with interactions between risk factors were used where needed (see appendix A). When analysing lung cancer we used a smoking risk score, with relative risks for lung cancer of 1 for non-smokers, 5 for moderate smokers, and 15 for heavy smokers (see appendix B).³

The analysis was based on multiplicative Poisson models, with risk time multiplied with the smoking risk score (in models including smoking) as the offset variable. Separate analyses were made for men and women and for each of the four periods. Models were fitted using Epicure (Hirosoft, Seattle, WA) and Genstat version 5 (NAG, Oxford).

Results

Figure 1 shows the relative risk of lung cancer for men by region in Denmark 1980-5. In the first analysis, which controlled only for age, an almost twofold difference was seen between the incidence in rural areas and the incidence in the capital (relative risk 1.78, 95% confidence interval 1.68 to 1.89). The second analysis, controlling for both age and marital status, only marginally changed the relative risk for the capital (1.72). Adding occupation reduced the relative risk for the capital to 1.51, and adding smoking reduced it to 1.23. Adding dwelling had some effect, mostly for the capital (1.11, 1.03 to 1.20); relative risk was 1.00 (0.92 to 1.08) for the suburbs and 1.11 (1.05 to 1.18) for the towns.

The pattern for women was similar. With control for age only, the relative risk was nearly double for the

of 9 November 1970 (927 470 men and 486 130 women). The central bureau of statistics collected data by means of self administered questionnaires, checked

Table 3—Variation in lung cancer incidence in Denmark 1970–87 among economically active men. Relative risks (95% confidence intervals)—controlled for age, tobacco smoking, and the other risk factors listed in the table—for risk factors in four calendar periods are shown

	1970–5 (n=4080)	1975–80 (n=6308)	1980–5 (n=8530)	1985–7 (n=3616)
No of cases of lung cancer	4080	6308	8530	3616
Marital status:				
Married	1.00	1.00	1.00	1.00
Unmarried	0.95 (0.84–1.08)	0.84 (0.76 to 0.94)	0.95 (0.88 to 1.04)	0.95 (0.84 to 1.09)
Previously married	1.14 (1.04 to 1.26)	1.04 (0.96 to 1.13)	1.10 (1.02 to 1.18)	1.09 (0.97 to 1.22)
Dwelling:				
One family house	1.00	1.00	1.00	1.00
Apartment house	1.16 (1.07 to 1.25)	1.16 (1.09 to 1.23)	1.14 (1.08 to 1.20)	1.26 (1.16 to 1.36)
Region:				
Capital	1.23 (1.10 to 1.37)	1.18 (1.08 to 1.24)	1.11 (1.03 to 1.20)	1.02 (0.91 to 1.14)
Suburbs	1.22 (1.09 to 1.37)	1.07 (0.97 to 1.17)	1.00 (0.92 to 1.08)	0.99 (0.88 to 1.12)
Towns	1.15 (1.06 to 1.26)	1.16 (1.08 to 1.24)	1.11 (1.05 to 1.18)	1.05 (0.96 to 1.15)
Rural areas	1.00	1.00	1.00	1.00
Occupation:				
Farmer	0.77 (0.67 to 0.90)	0.76 (0.67 to 0.86)	0.81 (0.73 to 0.90)	0.84 (0.72 to 0.98)
Other self employed	1.05 (0.95 to 1.17)	1.14 (1.05 to 1.24)	1.13 (1.05 to 1.22)	1.06 (0.95 to 1.19)
Highly educated employee	0.60 (0.51 to 0.70)	0.67 (0.61 to 0.78)	0.61 (0.54 to 0.68)	0.78 (0.67 to 0.91)
Other employee	1.00	1.00	1.00	1.00
Skilled worker	1.25 (1.13 to 1.39)	1.32 (1.22 to 1.44)	1.42 (1.32 to 1.53)	1.31 (1.17 to 1.46)
Unskilled worker	1.15 (1.05 to 1.26)	1.22 (1.14 to 1.32)	1.30 (1.22 to 1.38)	1.29 (1.17 to 1.42)

Fig 1—Analysis by region of relative risk of lung cancer in Denmark 1980–5 in economically active men. Bars indicate 95% confidence intervals

Fig 2—Analysis by occupation of relative risk of lung cancer in Denmark 1980–5 in economically active men. Bars indicate 95% confidence intervals

capital (1.95, 1.71 to 2.22) than for rural areas. Adding marital status and occupation changed the relative risk to 1.71. When smoking was added, relative risk was not increased for women in the capital. Adding dwelling had hardly any effect.

Figure 1 shows that control for occupation had a considerable impact on the difference in lung cancer risks between regions. Figure 2 illustrates this point further by showing the relative risk of lung cancer in 1980–5 for men by occupation. With control for age only, there was a threefold increase in risk for skilled workers compared with farmers. Adding marital status

and dwelling only had minor effects. Adding smoking reduced the relative risk to 1.8, and adding region reduced it to 1.74. Highly educated employees had the lowest risk, with skilled workers having more than twice their risk (2.33, 1.67 to 2.08). The pattern for women was similar (data not shown).

Table 3 shows the relative risks of lung cancer by time since the 1970 census. Men in rural areas had a lower risk than men in other regions in 1970–5; this difference diminished with time. Relative to other employees, farmers and highly educated employees had a lower risk in 1970–5 (0.77 and 0.60, respectively) while skilled workers had a higher risk (1.25). With time, the risk for farmers rose, but risk remained low for highly educated employees. For skilled workers the raised risk increased with time. The estimates for 1980–5 for region and occupation are the same as for the last model in figures 1 and 2. For women, relative risk increased for workers and was constantly low for highly educated employees (data not shown).

Discussion

This study showed that exposure to outdoor air pollutants was not the main explanation for the almost twofold difference in the incidence of lung cancer for people living in the capital of Copenhagen compared with those living in the rural areas. The excess lung cancer risks in the capital were reduced from 80% to 10% for men and from 90% to 0 for women when differences between the capital and the rural populations in smoking habit, occupation, dwelling, and marital status were controlled for. Given the aggregated data used in the present analysis, it is not possible to assess whether the 10% excess risk of lung cancer among men in Copenhagen is a true effect of air pollution or an effect of residual confounding for which we have not been able to control.

A recent review on air pollution and lung cancer based on data from the United States, the United Kingdom, Sweden, and Finland concluded that, after adjustment for smoking, urban residents seem to have an increase in lung cancer up to 1.5 times that of rural residents.⁴ In line with this, another recent review found that the relative risks for urban compared with rural populations were 1.1–1.4 for non-smokers but went up to 1.8 for smokers.⁵

AIR POLLUTION

Association with air pollution have been reported in three lung cancer studies. In Cracow, Poland, exposure was measured by the level of sulphur dioxide and total suspended particulate matter.⁶ Men in the highest exposure group (sulphur dioxide $>104 \mu\text{g}/\text{m}^3$ at the 50th centile and total suspended particulate matter $>150 \mu\text{g}/\text{m}^3$) had a significantly raised relative risk of lung cancer of 1.48 when smoking and occupational exposures were controlled for. In Shenyang, China, the average outdoor concentration of benzo(a)pyrene was $60 \text{ ng}/\text{m}^3$.⁷ People from this city reporting a smoky outdoor environment had significantly raised relative risks for lung cancer—2.3 for men and 2.5 for women—when age, education, and indoor pollution were controlled for. In Athens, Greece, smoke often exceeds $400 \mu\text{g}/\text{m}^3$; women who were long term smokers had a relative risk of lung cancer of 2.23, whereas no effect of outdoor air pollution was seen among non-smokers.⁸

Outdoor air pollution in Denmark stems from traffic, domestic heating and industries, and long range pollution from central Europe. Before 1982, the air quality measurements included mainly sulphur dioxide and black smoke. In 1982 a national air quality monitoring programme was established, with systematic measurements including nitrogen monoxide, nitrogen dioxide and lead.⁹

In comparison with the outdoor air pollution levels reported in epidemiologic studies, Copenhagen around

1970 had an average of sulphur dioxide of 50-80 $\mu\text{g}/\text{m}^3$, total suspended particulate matter probably about 80-100 $\mu\text{g}/\text{m}^3$, benzo(a)pyrene probably about 1-10 ng/m^3 , and peak values of daily smoke 120 $\mu\text{g}/\text{m}^3$. In Copenhagen today, the levels are sulphur dioxide 10-20 $\mu\text{g}/\text{m}^3$, total suspended particulate matter 60-80 $\mu\text{g}/\text{m}^3$, benzo(a)pyrene 0.5-3 ng/m^3 , and peak values of daily smoke 80 $\mu\text{g}/\text{m}^3$.¹⁰

The results from Cracow, Shenyang, and Athens and compared with the results from Copenhagen suggest that an association between outdoor air pollution and lung cancer is identifiable only above a certain pollution level. Compared with Copenhagen in 1970, the level of total suspended particulate matter in Cracow was 1.5-fold to twofold higher, and the level of sulfur dioxide was 1.3-fold to twofold higher. The level of benzo(a)pyrene was 6-60 times higher in Shenyang, and the peak values of daily smoke were more than three times higher in Athens than in Copenhagen.

SMOKING HABIT

Differences in smoking habit explained a large part of the variation in lung cancer. When the analysis controlled for smoking the 78% excess risk of lung cancer for men in Copenhagen fell to 32%.

Standardisation for smoking habit was based on interview data on type and amount of tobacco smoked on a given day. This means that additional characteristics of importance for risk of lung cancer, such as age at start of smoking, inhalation pattern, tar content, and smoking cessation, could not be taken into account. However, further analyses (not reported) showed the results to be rather insensitive to the choice of relative risks used in the calculation of the smoking risk score (see appendix B).

The four follow up periods can be regarded as different lag periods. Data from 1980-5 are presented as the main results with 10-15 years lag. As Gallup data from the 1980s show that smoking cessation was no more frequent in the capital than in the rural areas,¹¹ differences in smoking cessation over time are not likely to have distorted the results. Furthermore, smoking seemed to explain the same proportion of the regional variation in lung cancer in 1970-5 as it did in 1980-5.

Interactions between smoking and pollution have mostly been described as multiplicative, but an additive effect is also seen.⁴ Interaction cannot be examined here since individual smoking data are not available. The models used assume multiplicative effects.

OCCUPATIONAL FACTORS

As previously found in Sweden¹² and the Netherlands,¹³ the relative risk of lung cancer remained low among farmers and highly educated employees even after control for smoking. When other factors were controlled for, skilled workers had twice the risk of teachers and academics. Skilled workers in Denmark served an apprenticeship in their trade after they left school, usually at the age of 14, and they stayed on in their trade. However, one third of the unskilled workers in 1970 had worked in farming in their youth.¹⁴ It is therefore not surprising that skilled workers had the highest lung cancer risk due to spending a longer period of their working life in the same (and probably more hazardous) environment than unskilled workers, employees, and farmers.

Unemployment and the risk of lung cancer may be associated.¹⁵ Unemployment was negligible in 1970 but increased, especially among workers, in the 1970s and '80s. Therefore the higher lung cancer risk for workers could be associated, besides direct exposure at work, with experience of unemployment in the follow up period. It seems prudent to conclude that, besides smoking, occupational risk factors have played an

important role in determining the risk of lung cancer in the Danish population in the 1980s.

HOUSING

The type of dwelling showed an independent influence on the risk of lung cancer, with higher risk for people living in apartments than for people in one family houses. Dwelling may include an element of socioeconomic level, but more specific exposures could also have a role. The average radon level in houses in Denmark is 50 Bq/m^3 ,¹⁶ which is about half the average level in Sweden.¹⁷ Furthermore, the Danish radon exposure stems mostly from the subsoil and is therefore highest in one family houses. If radon was important it would thus result in a higher lung cancer risk to people living in one family houses.

In 1970, 22% of apartments in the capital but only 6% of one family houses were heated with a kerosene heater in each room. In the capital 76% of apartments but only 44% of one family houses had cooking facilities with gas that develops nitrogen dioxide.¹⁸ Data from the Netherlands showed high concentrations of nitrogen dioxide with non-ventilated gas appliances.¹⁹ The indoor exposure from gas appliances may thus have been much higher than the outdoor air pollution in Denmark, and this may explain the higher risk for people living in apartments.

CONCLUSIONS

This multivariate analysis of national data showed that smoking habit explained about 60% of the twofold difference in lung cancer incidence between men living in the Danish capital and men living in rural areas in the 1980s, and about 90% of the difference for women. However, even after control for smoking, workers assumed to have had long term occupational exposures had double the risk of lung cancer than did teachers and academics. After smoking, occupation, and demographic factors were controlled for, only a small effect of region on the risk of lung cancer remained. This indicates that the influence of outdoor air pollution on lung cancer was not identifiable in Denmark, as levels of pollutants were below those at which an association between air pollution and lung cancer had been found elsewhere.

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Key messages

- An almost twofold difference in lung cancer incidence between people living in Copenhagen and in rural areas of Denmark was seen in the 1980s
- This cohort study of the national population shows that smoking explained about 60% of the excess lung cancer risk in Copenhagen for men and 90% for women
- After control for smoking, however, workers had double the cancer risk of teachers or academics, whereas there was only a small independent effect of region
- The outdoor air in Copenhagen around 1970 contained on average 50-80 $\mu\text{g}/\text{m}^3$ of sulphur dioxide, 80-100 $\mu\text{g}/\text{m}^3$ total suspended particulate matter, and up to 10 ng/m^3 benzo(a)pyrene and had peak values of daily smoke of 120 $\mu\text{g}/\text{m}^3$
- The fact that only a small effect of region on lung cancer incidence was seen in the present study indicates that an influence of outdoor air pollution on lung cancer is identifiable only above this pollution level

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Appendix A

Interactions in tobacco consumption models

Some interactions were included in the models when the smoking percentages were estimated. The main dif-

ferences for men were that fewer men aged 30-39 in one family houses or working as other employees smoked than would be expected from the main effects model described in table 2. More young unskilled workers smoked, as did the oldest (50-64) other employees, highly educated employees, and other self employed men. More than expected of the young unskilled workers and highly educated employees in the oldest age group were heavy smokers. Married unskilled workers, unmarried skilled workers, and previously married highly educated employees were heavy smokers more often than expected, while fewer unmarried highly educated employees were heavy smokers. For economically active women, more middle aged (40-49) women in the capital, young women in rural areas, and unmarried highly educated employees smoked than expected. Fewer unmarried female farmers and other self employed women and more unmarried highly educated employees were heavy smokers.

Appendix B

Calculation of smoking risk score

The likelihood curve found when trying to estimate the values for the relative risk for moderate and heavy smoking had a flat top with estimates clearly above 1 and with a proportion of 1 to 3 between moderate and heavy smoker. This flatness is probably due to a systematic variation between cells in the risk factors of smoking on which we have no information, such as type of tobacco, inhalation pattern, and age at start smoking. Therefore we calculated a smoking risk score for each cell using the following formula:

$$\text{smoking risk score} = 1 \times \% \text{ non-smokers} + 5 \times \% \text{ moderate smokers} + 15 \times \% \text{ heavy smokers}$$

The relative risk values of 1, 5, and 15 for non-smokers, moderate smokers, and heavy smokers, respectively, were chosen after consulting the literature.³ The score was calculated for each cell of the study population formed by combinations of risk factors for lung cancer and based on the estimated tobacco consumption in each cell. Values of 3 and 10 could also have been chosen with only minor effects on the estimates for the other risk factors of lung cancer presented in table 3.

Case-control study of evening melatonin concentration in primary insomnia

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See editorial by Arendt

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The function of melatonin is not fully established, but recent studies suggest that it plays a role in the regulation of sleep. Thus, physiological doses of melatonin given to healthy volunteers decreased the time taken to fall asleep,¹ and the incidence of insomnia in the population rises during middle and old age,² when serum concentrations of melatonin decline.³ Haimov *et al* found that elderly patients with insomnia had lower than normal peak urinary concentrations of the melatonin metabolite 6-sulphatoxy melatonin and a delayed onset to peak secretion.⁴ We investigated evening plasma melatonin concentrations in subjects with primary insomnia and matched controls and predicted that the subjects with insomnia would have lower melatonin concentrations.

Subjects, methods, and results

Cases and controls were recruited predominantly by advertisement, but two cases were referrals from general

practice. The 10 men and 10 women with insomnia had a mean age of 53.9 years (range 40-68), and the 20 controls matched for sex and age (within five years) had a mean age of 54.7 (40-69). The cases and controls were recruited continuously over two years, and all but three of the controls were studied within three months of their matched case. We used a supplemented structured interview to ensure that the cases met criteria for primary insomnia according to *Diagnostic and Statistical Manual of Mental Disorders*, third edition, revised (DSM-III-R). Their mean duration of insomnia was 18 years (range 2-50), and they had no other current axis 1 disorder according to DSM-III-R. The controls had no current axis 1 disorder. None of the subjects had taken psychotropic drugs or β adrenoceptor antagonists for at least one month, and all gave their informed consent to the study, which was approved by the local ethics committee.

Subjects came to the laboratory at 6 pm, when we inserted an indwelling venous cannula under dim light