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Regional Lung Cancer Death Rates Unrelated to Smoking? The Case of The Netherlands

Anton E. Kunst and Johan P. Mackenbach

It has been observed in various countries that regional variation in lung cancer mortality can hardly be explained by differences in current smoking. This paper addresses the question of whether mortality variation within The Netherlands in 1980–1984 is due to differences in past instead of current smoking. A first indication of the role of past smoking is that, within male birth cohorts, regional mortality patterns have been very stable for over 30 years. Reliable data on smoking in 1972 explain 40% of the mortality variation among women, but only 2% of that among men. A crude indicator on smoking in 1930 explained 43% of the mortality variation among men aged 75+ years (correlation=0.66). The lack of a relationship with smoking in 1972 appears to be due to a radical change in regional smoking differences, which caused smoking in 1972 to be unrelated to smoking in 1930; long time lags, so that these changes were not yet followed by changes in regional mortality differences. It is concluded that the explanation of regional lung cancer death rates sometimes has to go far back in time. Studying determinants of lung cancer by means of regional analyses requires a more detailed control for smoking history than has been usual.
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INTRODUCTION

In most countries, lung cancer death rates vary markedly between regions. An example is The Netherlands, where a belt of high mortality contrasts with much lower mortality in surrounding areas (see Fig 1).

It seems plausible to attribute such a pattern to regional differences in tobacco consumption. However, we found that regional mortality differences were not related to the percentage of inhabitants currently smoking in 1983 [1]. Correlations were very low for women (0.07) and even negative for men (−0.10). In several other countries too it was found that only a small part of regional differences in lung cancer mortality can be explained by differences in current tobacco consumption [2–7].

In this paper, we attempt to explain regional differences in lung cancer mortality in The Netherlands by applying data on past instead of current smoking. The time lag between smoking and the occurrence of lung cancer is at least 10 years, and the risk of dying from lung cancer is closely related to the cumulative exposure to tobacco smoke over the entire lifetime [8–10]. Until now, however, regional studies have not used data on past regional differences in smoking because of the limited availability of such data.

This analysis was made possible thanks to the availability of detailed and reliable data on regional cigarette consumption in 1972, and an approximate indicator of regional tobacco consumption in 1930.

The analysis consists of two steps: firstly regional differences in lung cancer mortality in 1980–1984 are compared with mortality differences in earlier periods. If regional mortality differences are determined by smoking several years before, it may be expected that regional mortality patterns have been stable over time. Secondly, it is examined to what extent mortality differences in 1980–1984 can be explained by data on smoking in 1972 and 1930. A distinction will be made by sex and birth cohort. Since in The Netherlands sex and birth cohorts have different smoking histories [11, 12], they might also differ with respect to the contribution that smoking in 1930 and 1972 make to the explanation of mortality differences in 1980–1984.

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MATERIALS AND METHODS

Numbers of deaths from lung cancer by age, sex, year of death and region of residence were extracted from a large data file. All deaths from cancer of the trachea, bronchus and lung were selected. Three age groups (45–64, 65–74, 75+) and four 5-year periods (1950–1954, 1960–1964, 1970–1974, 1980–1984) were distinguished. The data refer to 39 so-called COROP-regions. Corresponding numbers of population-at-risk were obtained from the national continuous population register. The mortality level in a region was measured by means of standardised mortality ratios (SMR), with national death rates by 10-year age group as the standard.

Smoking data for 1972 were obtained from the National Press Survey of 1972. The total number of respondents (30 746) was sufficiently large for regional disaggregation. Regional samples of respondents were representative of the total population according to age, sex, household size and size of municipality. For each sex and age group separately, the mean number of cigarettes smoked per respondent was calculated. Younger age-groups (35–54, 55–64, 65+) were distinguishable with the mortality data, because the survey data refer to a time approximately 10 years before 1980–1984.

In 1930, an extensive inventory of the Central Bureau of Statistics registered, among others, the number of enterprises that sold tobacco [13]. From this data the number of selling points of tobacco per head of the population was calculated. This measure is considered to be an indicator of the amount of tobacco consumed by the adult population in 1930, that is, those 75 years and older in 1980–1984.

Smoking measures were related to SMR by means of least squares regression analysis. SMR were transformed to their

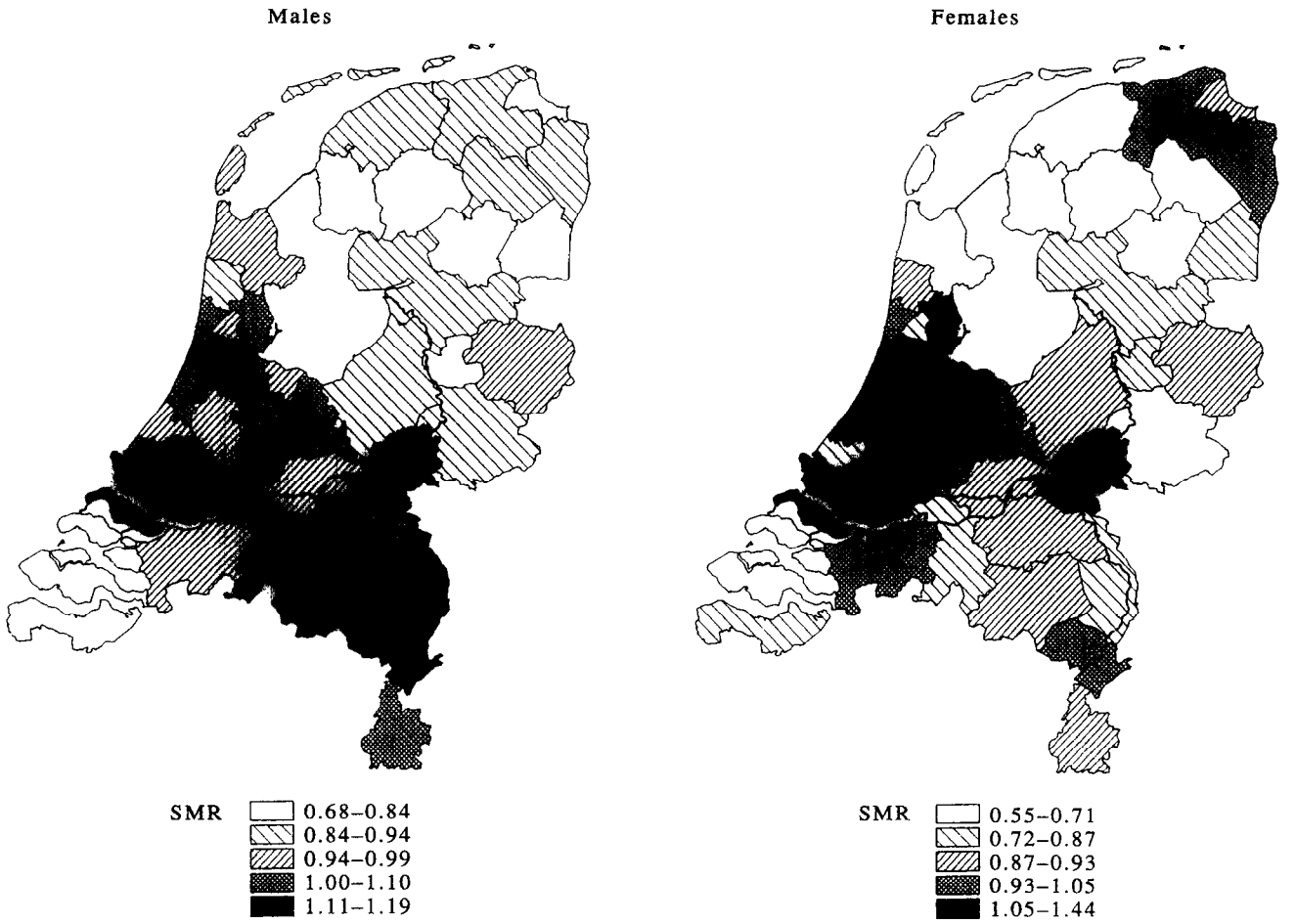

Fig. 1. Spatial distribution of age-standardised ratios of lung cancer mortality, The Netherlands, 1980–1984. All ages. SMR, Standardised mortality ratios.

natural logarithms so as to normalise the distribution of residuals. Regions were weighted according to their population size in order to reduce effects of random fluctuations in numbers of (age-specific) deaths and in smoking measures.

RESULTS

In Table 1 the pattern of regional mortality variation in 1980–1984 is compared with the pattern in previous periods. Younger birth cohorts were excluded because of large fluctuations in regional numbers of deaths in earlier years. Among females, the low correlations with 1960–1964 and especially with 1950–1954 may be attributable to large random fluctuations in the small numbers of deaths in earlier periods. The strong correlations for males are remarkable, and indicate quite stable mortality patterns over time.

Table 1. *Correlation between regional mortality variation in* 1980–1984 *among men and women aged* 75–94 *years, with regional mortality variation in previous periods within the same birth cohorts*

Period	Product-moment correlation* Females	Males
1970–1974	0.45	0.87
1960–1964	0.24	0.85
1950–1954	0.07	0.86

*Product-moment correlation between log-transformed SMR, weighted by population size, n = 39 regions.

In Table 2 it is shown to what extent mortality variation in 1980–1984 can be explained by cigarette consumption in 1972. Positive relationships between smoking and mortality explain about 40% mortality variation among women in the youngest age group and in all age groups together. Significant relationships are also found for older women, but explain only a modest part of mortality variation. For men, most relationships are insignificant and the part of mortality variation that can be explained is nil.

In Table 3, mortality variation among men and women 75 years and older is related to the crude indicator of smoking in 1930. For men, but not for women, the 1930 measure adds substantially to the explanation of mortality variation in 1980–1984. The corresponding product-moment correlation for men is 0.66, a surprisingly high value in view of the very approximate nature of the smoking indicator. After control for this indicator, smoking in 1972 has no significant relationship with mortality among men 75 years and older.

The measure for smoking in 1972 among men 75 years and older could not have picked up the effect of smoking in 1930 (see Table 1) because these smoking measures are not strongly correlated. Their low correlation (0.25) is due to a radical change

Table 2. Association between lung cancer mortality in 1980–1984 and cigarette consumption in 1972

Age group	Regression coefficient*	%Variance explained
Females		
45+	0.1883‡	39.8
45–64	0.1973‡	42.7
65–74	0.1159†	9.7
75+	0.1862†	11.0
Males		
45+	0.0138	1.6
45–64	− 0.0072	1.1
65–74	0.0103	0.9
75+	0.0596†	13.7

*From multiple regression analysis of ln (SMR) on average number of cigarettes smoked, weighted by population size, n = 39 regions.
†$P<0.05$, ‡$P<0.01$.

in smoking in The Netherlands. While in 1930 high tobacco consumption was limited to prosperous areas in the centre of The Netherlands, in 1972 it was also high in other parts of the country.

DISCUSSION

The aim of this paper was to explain regional differences in lung cancer mortality in 1980–1984 by data on past smoking. Regional differences in cigarette consumption in 1972 explained a substantial part of regional mortality variation among women, but not among men. For men 75 years and older, a strong relationship was found with a crude indicator on tobacco consumption in 1930.

The analysis was limited by scarce data on regional tobacco consumption, which covered only two moments in time (1930 and 1972) and which were very crude in the case of 1930. It may be expected that more complete and accurate data would have explained a much larger part of regional mortality differences.

The question should be addressed of whether data problems are responsible for the weak correlations between cigarette smoking in 1972 and lung cancer mortality among men in 1980–1984. A data problem is under-reporting of the amount of cigarettes smoked, which has been estimated for the 1972 survey to be about 23% in the whole country [11]. If the degree of under-reporting varied largely by region, this would have led to biased estimates of regional differences in cigarette consumption. However, there are no indications of regional variation in the degree of under-reporting. For example, the same results were obtained with a measure that is less susceptible to under-reporting of tobacco consumption, the percentage of respondents currently smoking cigarettes.

Instead of being an artifact, the finding that, among men, lung cancer mortality is hardly related to smoking 10 years before, appears to be a real phenomenon that can be explained as follows: (1) a radical change in regional smoking differences caused smoking in 1972 to be unrelated to smoking in 1930, but (2) due to long time lags these changes have not yet been followed by changes in regional mortality differences.

The fact that changes in regional smoking differences have not led to changes in mortality differences suggests that these mortality differences have already been determined long before. The relationship between mortality in 1980–1984 and smoking in 1930 does not necessarily indicate a time lag of 50 years, but may be reflective of smoking in more recent years. But the fact that regional differences in lung cancer mortality have been stable since 1950–1954 suggests that at least a part of the relevant tobacco exposure had already occurred in the forties or before.

The lack of a relationship between regional lung cancer death rates and current or recent smoking is in striking contrast with the results of studies using individual-level data, which consistently find excess lung cancer mortality among current smokers and persons who have stopped smoking recently [8–10]. This discrepancy is an extreme example of the bias that may occur in making a causal inference on individual phenomena on the basis of observations of regions ('ecological bias' or 'cross-level bias') [14, 15]. This study reveals one condition under which ecological bias may occur: when time lags are long and when there are substantial changes in the distribution of risk factors among population groups.

Regional variation in lung cancer mortality is relevant to the study of the causes of lung cancer, because this variation may be reflective of factors other than tobacco consumption, and it may point to regions where in-depth research on such factors would be particularly fruitful. It is remarkable, for example, that most areas of exceptionally high lung cancer mortality are heavily urbanised and industrialised [2–4, 16–18]. The finding that geographical mortality differences cannot be explained by current smoking had been considered as further evidence for the role of factors other than smoking [5, 7, 19, 20]. However, not only current smoking, but several aspects of smoking such as life-time exposure should be taken into account. This study offers an example in which consideration of only current and recent smoking would not just be incomplete, but even superfluous.

Table 3. Association between lung cancer mortality in 1980–1984 and tobacco consumption in 1972 and in 1930

Age group	Regression coefficient* 1930	Regression coefficient* 1972	%Variance explained by smoking in 1930 and 1972 together
Females			
75+	0.0655	0.1184	14.8
Males			
75+	0.1284†	0.0373	43.1

*From multiple regression analysis of ln (SMR) on the two smoking measures at the same time, weighted by population size, n = 39 regions. Measure for 1930: number of selling points of tobacco per 1000 population. Measure for 1972: average number of cigarettes smoked per respondent.
†$P<0.05$.

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Feature Articles

Black (Air-cured) and Blond (Flue-cured) Tobacco and Cancer Risk II: Pharynx and Larynx Cancer

H. Sancho-Garnier and S. Theobald

Two case–control studies have examined the relationship between black or blond tobacco smoking and the occurrence of pharynx or larynx cancer. The first study was carried out in several European countries. Tobacco smoking was found to be associated with higher risks for supraglottic and epilarynx cancer localisations than for pharynx, glottic and subglottic localisation. In all localisations, risk was twice as high again in users of black tobacco after adjusting for alcohol and for lifetime average daily dose of tobacco. The other study was carried out in Uruguay. After taking into account age, age at start of smoking, duration of smoking, years since stopping smoking and filter use, risks were found to be higher in black tobacco smokers than in blond tobacco smokers. All known studies which have been performed in countries where blond tobacco is generally smoked showed lower risks even when adjusted for alcohol. Use of black tobacco appears to be associated with higher risks of cancer of the pharynx and larynx than blond tobacco use.
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THE FREQUENCY of larynx and pharynx cancer throughout the world is characterised by great variability. Table 1 presents countries associated with the highest and lowest incidence rates of these cancer localisations. The incidence of pharynx (oropharynx and hypopharynx) and larynx cancers is very high in the southern part of Europe: France, Spain, Italy, Switzerland (see Table 2). In these countries (except Italy) up until the present time, black tobacco has been more frequently consumed than blond tobacco. The consumption of black tobacco varies from 65% in Geneva (Switzerland) to 90% in Calvados (France) [1]. Inversely, low rates of the above cancer localisations are observed in the UK and Denmark where blond tobacco is widely smoked. However, another important risk factor is alcohol consumption which is very different between northern and