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The future of smoking-attributable mortality: the case of England & Wales, Denmark and the Netherlands

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ABSTRACT

Aims We formally estimate future smoking-attributable mortality up to 2050 for the total national populations of England & Wales, Denmark and the Netherlands, providing an update and extension of the descriptive smoking-epidemic model. **Methods** We used smoking prevalence and population-level lung cancer mortality data for England & Wales, Denmark and the Netherlands, covering the period 1950–2009. To estimate the future smoking-attributable mortality fraction (SAF) we: (i) project lung cancer mortality by extrapolating age–period–cohort trends, using the observed convergence of smoking prevalence and similarities in past lung cancer mortality between men and women as input; and (ii) add other causes of death attributable to smoking by applying a simplified version of the indirect Peto–Lopez method to the projected lung cancer mortality. **Findings** The SAF for men in 2009 was 19% (44 872 deaths) in England & Wales, 22% (5861 deaths) in Denmark and 25% (16 385 deaths) in the Netherlands. In our projections, these fractions decline to 6, 12 and 14%, respectively, in 2050. The SAF for women peaked at 14% (38 883 deaths) in 2008 in England & Wales, and is expected to peak in 2028 in Denmark (22%) and in 2033 in the Netherlands (23%). By 2050, a decline to 9, 17 and 19%, respectively, is foreseen. Different indirect estimation methods of the SAF in 2050 yield a range of 1–8% (England & Wales), 8–13% (Denmark) and 11–16% (the Netherlands) for men, and 7–16, 12–26 and 13–31% for women. **Conclusions** From northern European data we project that smoking-attributable mortality will remain important for the future, especially for women. Whereas substantial differences between countries remain, the age-specific evolution of smoking-attributable mortality remains similar across countries and between sexes.

Keywords Age-period-cohort, Europe, lung cancer mortality, Peto-Lopez method, projection, smoking-attributable mortality, smoking-epidemic.

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INTRODUCTION

Smoking is a life-style with a considerable effect on health, mortality and trends therein over time. Within Europe, smoking is the leading risk factor of premature mortality [1]. However, smoking behaviour and, consequently, smoking-attributable mortality (i.e. the number of all deaths in a population caused by smoking) differ strongly by country and cause a major gender gap in mortality [2,3].

The smoking-epidemic model by Lopez *et al.* in 1994 [3] described that, in general, men in Anglo-Saxon countries were the first to take up smoking in the early 20th

century. After a rapid rise lasting two to three decades, male smoking prevalence started to decline. Smoking-attributable mortality followed the increase and subsequent decline in smoking prevalence some 30–40 years later. For women, the increase in smoking started about 20 years later than men but, depending on the country, this period may be shorter or longer [4]. The maximum levels in female smoking prevalence would be considerably lower than for men and, consequently, female smoking-attributable mortality would be lower than that for men.

In the last stage of the original smoking-epidemic model, similar (declining) levels of smoking prevalence

for men and women were put forward, suggesting that smoking-attributable mortality for men and women will converge in the future [2,3]. Smoking-attributable mortality for women, however, still increased during this last stage. Currently, some countries have already experienced the peak in smoking-attributable mortality for women, e.g. England & Wales [4]. In other countries in northern and western Europe, such as Denmark and the Netherlands, this peak is also approaching, due to the past peak in smoking prevalence for women. An update of the smoking-epidemic model is therefore warranted.

A previous update of the smoking-epidemic model by Thun *et al.* [4] in which the experience of developing countries was added, and previous projections of smoking-attributable mortality [5,6], however, only included the short-term future. Whereas Thun *et al.* [4] qualitatively suggested a parallel future decrease in smoking-attributable mortality for men and women, and Pampel [5] also revealed the equalization of smoking mortality rates for men and women, the long-term future evolution of the gap between the sexes in smoking-attributable mortality has not formally been studied previously. Furthermore, in the original smoking-epidemic model and its update [4], little information is provided concerning differences by age groups.

Our objective is to update and extend the smoking-epidemic model by estimating future levels of smoking-attributable mortality up to 2050 for England & Wales, Denmark and the Netherlands, three countries that are ahead in the smoking-epidemic. We shall formally estimate the peak and subsequent decline in smoking-attributable mortality for women, and will provide information on the differences by sex and age groups for the long-term future. Our results will aid policymakers and public health professionals in setting goals for tobacco control programmes and can provide important input to all-cause mortality projections.

ESTIMATION METHODOLOGY

We studied past trends in age- and sex-specific smoking prevalence, lung cancer mortality rates and smoking-attributable mortality for England & Wales, Denmark and the Netherlands during the period 1950–2009.

Data on smoking prevalence by sex and age group were obtained from Cancer Research UK [7] for England & Wales for 1950–2009 and The Dutch Expert Centre on Tobacco Control (STIVORO) [8] for the Netherlands for 1958–2009. For Denmark, data on smoking prevalence among adults by sex was obtained from International Smoking Statistics WEB Edition [9], Organization for Economic Co-operation and Development (OECD)

Health Data [10] and the World Health Organization (WHO) [11] for 1950–69, 1970–93 and 1994–2009, respectively.

Annual lung cancer mortality deaths [International Classification of Diseases (ICD)-9: 162; ICD-10: C33–C34] by age (40–44, 45–49, . . . , 80+) and sex were obtained through the WHO Statistical Information System [12] for England & Wales (1950–2009), Denmark (1951–2006) and the Netherlands (1950–2009). For Denmark, additional death numbers for 2007–09 were obtained through the Nordic Cancer Statistics Database NORDCAN [13]. Rates were calculated by dividing the deaths by population exposure data from the Human Mortality Database [14].

To estimate the smoking-attributable mortality fraction (SAF), i.e. the proportion of all deaths due to smoking, an adapted and simplified version of the indirect Peto–Lopez method [15] was used. Our method, like Peto *et al.* [16], uses observed lung cancer mortality—controlled for background lung cancer mortality—as an indicator of the accumulated damage from smoking. That is, the observed national lung cancer mortality rates are compared with the rates of smokers and never-smokers of the American Cancer Society’s Cancer Prevention Study II (ACS CPS-II) study to obtain the proportion of the population that is exposed to smoking (p) [16]. We combined this indicator with relative risks (RR) for all-cause mortality for smokers versus non-smokers from the ACS CPS-II study to obtain the age- and sex-specific SAF: $\text{SAF} = p(\text{RR}-1)/(p(\text{RR}-1) + 1)$ [17]. The RRs were smoothed by applying a second-level polynomial and the excess risk was reduced by 30% to allow for confounding [18].

Lung cancer mortality and the SAF for all ages combined were directly age-standardized using sex- and country-specific population and death numbers, respectively, in 2009 as the standard.

To summarize the past trends more formally, age-period-cohort (APC) analysis was applied to lung cancer mortality. We chose an APC model with drift [19], defined as:

$$y_{a,p} = N_{a,p} \exp(\delta * p + \alpha_a + \beta_p + \gamma_{p-a}) + \epsilon_{a,p} \quad (1)$$

where $y_{a,p}$ is the number of deaths in age group a in period p which follows a Poisson distribution, $N_{a,p}$ is the number of person-years at risk in age group a in period p , and $\epsilon_{a,p}$ is the error term. δ , α_a , β_p , γ_{p-a} are the drift, age (non-linear) period and (non-linear) cohort effect, respectively. The model is applied to data by 5-year age groups (45–49, . . . , 80+) and 5-year calendar periods (1950–2009). We set the first and last cohort and first and last period to 0 to ensure identifiability [19]. The model is fitted in R version 2.10 using the function `glm`.

PAST TRENDS

For men, smoking prevalence in the 1950s was very high: 60% in England & Wales, 80% in Denmark and 90% in the Netherlands (Fig. 1). During the period 1950–2009, smoking prevalence for men declined in all three countries, reaching a level of 30% in the Netherlands and approximately 20% in the other two countries. For women, smoking prevalence in the 1950s was between 30 and 40%. After reaching a maximum of approximately 45% between 1970 and 1980, smoking prevalence for women also started to decline. From 1990 onwards the decline in smoking prevalence for women

was parallel with the decline for men in all three countries. In 2009, smoking prevalence for women was almost 20% in England & Wales and Denmark and approximately 24% in the Netherlands.

For men, lung cancer mortality and the corresponding age-standardized SAF reached its maximum around 1975 in England & Wales and almost 10 years later in Denmark and the Netherlands (Fig. 1). The SAF was 33 (90 087 deaths), 29 (9167 deaths) and 37% (25 578 deaths), respectively. Thereafter, the SAF showed a steady decline in all three countries, leading to a level of SAF in 2009 of 19 (44 872 deaths), 22 (5861 deaths) and 25% (16 385 deaths), respectively. For women, lung cancer

Smoking prevalence

Standardised lung cancer mortality rate

Smoking-attributable mortality fraction

England and Wales

Denmark

The Netherlands

Figure 1 Smoking prevalence (%), age-standardized lung cancer mortality rate (per 1000) and age-standardized smoking-attributable mortality fraction (SAF) for Denmark, England & Wales and the Netherlands between 1950 and 2009, by sex

mortality and the SAF increased during the whole period in all three countries and converged to the level of men. The female SAF in 2009 was 14% (36 479 deaths) in England & Wales, 19% (5249 deaths) in Denmark and 12% (8099 deaths) in the Netherlands.

For men, the age-specific lung cancer mortality rates (Fig. 2) show a clear cohort pattern in the timing of the maximum, reflecting the uptake of smoking. The maximum is followed by a more period pattern after the peak, reflecting the quitting of smoking as a result of, for instance, tobacco control or changes in life-style when there is a decline in the lung cancer mortality rates at the same time for different age groups. The declines after the peak show parallel trends at the log scale for the different age groups, indicating that the age-specific patterns converge. For women, the cohort pattern in lung cancer mortality is less clear, but visible at the moment the lung cancer mortality starts to rise for each successive age group, and at the moment the increase for the youngest age groups ceases. For the youngest age groups we can observe that the moment the rates for women cross the rates for men, the rates start to decline at the same pace. The rates for women at higher ages show a steady increase over time. These observations also hold for the age-specific SAF's (results not shown).

Our APC analysis shows that men with the highest lung cancer mortality are born around 1900 in England & Wales, around 1925 in Denmark and around 1910 in the Netherlands (see Supporting information, Online Resource 1). The increase in lung cancer mortality among the oldest cohorts is very similar for the three countries, as well as the decline after the maximum. For women, differences in the timing of the increase in lung cancer mortality show England & Wales to be the fore-runner. Women in England & Wales born around 1930 experienced the highest lung cancer mortality. For Denmark and the Netherlands no such maximum occurred.

PROJECTION METHODOLOGY

Based on our study of past trends (see previous section), we were able to formulate the basic assumptions behind our projection methodology:

- convergence of smoking prevalence and lung cancer mortality between men and women;
- a similar decline in age-specific lung cancer mortality rates for women as for men after the age-specific rates for women reached the age-specific rates for men; and
- a cohort approach for the increase in lung cancer mortality and a period approach for its decrease.

We projected lung cancer mortality up to 2050, making qualitative use of the predictive value that current smoking prevalence has on mortality for the next

30–40 years. We then apply indirect estimation techniques to estimate the future SAF. For our main results we use the same simplified Peto–Lopez estimation technique. In addition, we performed a sensitivity analysis including four additional indirect estimation techniques (see Supporting information, Online Resource 3).

For men, the observed decline in lung cancer mortality for different age groups is projected to continue into the future. That is, we first estimated the maximum cohort exposed to smoking using an APC model applied to the lung cancer mortality data, and then projected the drift from the APC model applied to the lung cancer mortality data after this estimated maximum cohort (see Supporting information, Online Resource 1).

For women, we needed to estimate the year and level of the maximum in lung cancer mortality as well as the trend up to and after this maximum. We extrapolated the age-specific increase through an APC model with drift using the drift and non-linear cohort component. The peak years for the separate age groups were obtained by estimating the year in which the age-specific trends for women would reach the age-specific trends for men. The long-term decline after the maximum for women has been set equal to the drift from the model of men.

The limited reliability of historical smoking prevalence—due mainly to changed definitions and samples [20]—and the fact that smoking prevalence is a poor proxy of smoking intensity—mainly because it does not include dosage and age at onset [18]—are important restrictions of incorporating smoking prevalence directly in any projection methodology. Smoking prevalence is thus used merely to generate assumptions, i.e. the similarities in current smoking prevalence for men and women and its main effect on mortality 30–40 years later [3].

We project lung cancer mortality and not smoking-attributable mortality, because of the different indirect estimation techniques that exist to estimate smoking-attributable mortality, and the probable impact on the projection.

FUTURE LEVELS OF SMOKING-ATTRIBUTABLE MORTALITY

Figure 3 shows the projected age-standardized lung cancer mortality and SAF. For men in England & Wales, the SAF is estimated to decline from 19% in 2009 to 6% in 2050. The maximum SAF for women in England & Wales was already reached in 2008 (14%, 38 883 deaths), and the SAF is estimated to decline from 14% in 2009 to 9% in 2050. The SAF for men in Denmark is estimated to drop from 22% in 2009 to 12% in 2050. The level for Danish women is estimated to first increase from 19% in 2009 to 22% in 2028 and then decline to 17% in

Figure 2 Lung cancer mortality rate (log-scale) for Denmark, England & Wales and the Netherlands between 1950 and 2009, by sex and age group (the 10-year age groups are weighted averages of two 5-year age groups)

Standardised lung cancer mortality rate

England & Wales

Smoking-attributable mortality fraction

Denmark

The Netherlands

Figure 3 Age-standardized lung cancer rate (per 1000) and age-standardized smoking-attributable mortality fraction for Denmark, England & Wales and the Netherlands for 1950–2009 (observations) and 2010–2050 (projections), by sex

2050. For men in the Netherlands, the SAF is estimated to decline from 25% in 2009 to 14% in 2050. For Dutch women, the SAF is estimated to increase from 12% in 2009 to 23% in 2033 and then decline to 19%.

Figure 4 presents the future SAF by age (see Supporting information, Online Resource 2 for the projected lung cancer mortality by age). The results show the continuing convergence between the age groups and the (more pronounced) cohort pattern in the trend up to the maximum for women. For each country and each age group, it is expected that the SAF in 2050 for women is higher than the SAF for men.

When we apply five different indirect estimation methods (see Supporting information, Online Resource 3)—including using the National Health Interview Survey–Linked Mortality Files (NHIS-LMF) cohort study and the recent regression methods [21–23]—the SAF's for men in 2050 range from 1 to 8% (England & Wales), from 8 to 13% (Denmark) and from 11 to 16% (the Netherlands). For women the ranges are 7–16%, 12–26% and 13–31%, respectively. Note that without the outliers, method 2 (NHIS-LMF cohort study) for men and the regression method 3 [21] for women, the ranges were much lower.

Figure 4 Smoking-attributable mortality fractions for Denmark, England & Wales and the Netherlands for 1950–2009 [age–period–cohort (APC)-estimates] and 2010–2050 (projected), by sex and age group (the 10-year age groups are weighted averages of two 5-year age groups)

DISCUSSION

Summary of the results

The SAF for men in 2009 was 19% in England & Wales, 22% in Denmark and 25% in the Netherlands. In our projections, these fractions decline to 6, 12 and 14%, respectively, in 2050. The SAF for women peaked at 14% in 2008 in England & Wales, and is expected to peak in 2028 in Denmark (22%) and in 2033 in the Netherlands (23%). By 2050, a decline to 9, 17 and 19%, respectively, is foreseen.

Update and extension of the smoking-epidemic model

The original smoking-epidemic model assumes that, after a rapid rise, the SAF among women could be expected to peak at approximately 20–25% of all deaths, significantly lower than experienced by men (33%) and occurring approximately 20 years later. Thereafter, smoking-attributable mortality for both sexes would decline progressively [3].

Our projected maximum levels of SAF for women in Denmark (22%) and the Netherlands (23%) correspond with the expected peak of SAF for women in the smoking-epidemic model. However, the observed maximum level for women in England & Wales (14%) is clearly lower. The difference in the timing of the maximum level between men and women, which amounts to 20 years in the smoking-epidemic model, is much greater in England & Wales (35 years), Denmark (43 years) and the Netherlands (48 years), and supports earlier findings of differential results for different countries [4].

Our observed differences between countries in the future level of smoking-attributable mortality and in sex differences in the (timing of the) smoking-epidemic are related clearly to differences in historical smoking prevalence, especially for women. These differences in smoking prevalence can be related to differences in cultural, political and economic determinants that led to differences in tobacco control and life-style [4]. For instance, in England & Wales tobacco companies began the pursuit of female smokers after World War I [24]. In other countries the government promoted traditional social roles for women that, among other things, discouraged tobacco use [25].

Our analyses also highlighted some important differences and commonalities between the different age groups. The SAF by age is characterized by a clear cohort pattern, and starts to rise, to peak and subsequently to decline first at younger ages. The SAF for younger age groups is higher than for older age groups, but after the maximum there is convergence between the age groups. These age patterns are similar across countries and sexes.

In spite of the observed convergence in smoking prevalence and lung cancer mortality rates between men

and women, the SAFs in 2050 for women are higher than for men. This is because of lower relative risks and lower all-cause mortality rates for women compared to men in each age group.

Reflection on the projection methodology

Previous projections of smoking-attributable or smoking-related mortality consisted mainly of methods incorporating lagged smoking prevalence or different smoking scenarios [5,6]. Probably because of the limited historical data on smoking prevalence, these projections were limited to a short projection period. Our methodology can be used for a longer projection period.

Previous projections of lung cancer mortality all used APC methodologies, although in different ways (e.g. [26–29]). Most of these methods do not perform well in a situation where the past trend in lung cancer mortality does not continue in the future, as we expect to happen with the trend for women. An exception is Shibuya *et al.* [28], who replaced the period variable by lagged information on smoking. Their method might project changes in the trend in lung cancer mortality due to changes in smoking habits, although to obtain projections for the long term the smoking habits themselves need to be projected. Thus, previous projection methods of lung cancer mortality were relevant only for short-term projections.

Our methodology—differently from earlier studies—takes into account the expectation that future smoking-attributable mortality will first increase and then decline among women. Our assumption, and subsequent estimation, of the maximum level in lung cancer mortality for women resulted from the observed similar smoking prevalences for men and women and our assumption that this would result in similar lung cancer mortality rates 30–40 years later (as described by the smoking epidemic model by Lopez *et al.* [3] and already observed for the youngest age groups). Applying our methodology to part of the data for England & Wales (1950–99), our assumption and methodology proved able to predict the observed maximum in 2008, justifying the use of the trend and level in lung cancer mortality of men to determine the maximum for women.

Reflection on the indirect estimation method

The adapted and simplified Peto–Lopez method that we used to estimate SAF has the advantage of a low demand of data, is easy to use and is widely used [30]. Furthermore, potential benefits of smoking cessation and probable effects of second-hand smoking are taken into account indirectly, because of the use of lung cancer mortality. The results of the simplified method are comparable to the results of the original Peto–Lopez method [17].

A limitation of the (adapted and simplified) Peto–Lopez method is the use of the ACS CPS-II study, which may not be representative for the population under consideration due, for instance, to generally lower lung cancer mortality rates for female smokers. Furthermore, Mehta & Preston [31] show a continuing increase over time in the relative risk of death for current and former smokers. Finally, the Peto–Lopez method assumes that the temporal relationship between accumulated exposure (including cessation) and risk will be similar between lung cancer and other smoking-determined risks (e.g. vascular disease, chronic respiratory disease).

In recent years additional indirect estimation methods have been developed, making use of regression analysis [21–23]. These methods rely only on observed lung cancer mortality and all-cause death rates. The two most recent methods [22,23] showed a large similarity with the method we used, showing the validity of the three methods. Because differences at higher age groups had the largest effect on the SAF of all ages combined, its estimation should receive special attention.

OVERALL CONCLUSION AND IMPLICATIONS

Our results for England & Wales, Denmark and the Netherlands illustrate clearly that smoking-attributable mortality will remain important for the future, especially for women. Substantial differences between countries are expected, both in the future level of smoking-attributable mortality and in the sex difference in the (timing of the) smoking-epidemic. However, because of similarities in smoking prevalence, the similar age-specific evolution of smoking-attributable mortality across countries and between sexes, with convergence between the age groups, is also likely to occur for other countries currently at the fourth stage of the smoking epidemic.

Because our projection methodology requires a limited amount of data, it can be applied easily to other countries where lung cancer is dominated by smoking. The methodology would be suitable especially for countries where (i) the maximum level of lung cancer mortality for men was reached quite some time ago (e.g. Finland, Ireland, Italy, Sweden and Switzerland) and (ii) recent smoking prevalence is similar for men and women. In countries where the maximum for men was reached only recently (e.g. France, Norway, Portugal and Spain), an APC model would be more difficult to estimate and information from forerunners would also be needed. In addition, for countries at an earlier stage of the smoking epidemic, detailed information on smoking prevalence would be necessary.

Our formal quantification of future health effects of past smoking behaviour and differences therein by age

and sex can aid policymakers and public health professionals in setting goals for tobacco control programmes. The effect of recent control measures, such as the WHO Framework Convention on Tobacco Control [32], is expected to have its main effect on mortality after 2050. Moreover, it is essential to take into account the non-linear development of the smoking-epidemic to project all-cause mortality correctly for the future.

Declaration of interests

None.

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Supporting information

Additional Supporting information may be found in the online version of this article at the publisher's web-site:

Online Resource 1 Age–period–cohort (APC) estimation.

Online Resource 2 Projected lung cancer mortality.

Online Resource 3 Sensitivity of (future) smoking-attributable mortality to different indirect estimation techniques.