Demography (2011) 48:461–479
DOI 10.1007/s13524-011-0020-9

Estimating the Effect of Smoking on Slowdowns in Mortality Declines in Developed Countries

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Published online: 26 April 2011

Abstract Declines in mortality rates for females at older ages in some developed countries, including the United States, have slowed in recent decades even as decreases have steadily continued in some other countries. This study presents a modified version of the indirect Peto-Lopez method, which uses lung cancer mortality rates as a proxy for smoking exposure, to analyze this trend. The modified method estimates smoking-attributable mortality for more-specific age groups than does the Peto-Lopez method. An adjustment factor is also introduced to account for low mortality in the indirect method's study population. These modifications are shown to be useful specifically in the estimation of deaths attributable to smoking for females at older ages, and in the estimation of smoking-attributable mortality more generally. In a comparison made between the United States and France with the modified method, smoking is found to be responsible for approximately one-half the difference in life expectancy for females at age 65.

Keywords Mortality · Smoking · Life expectancy

Introduction

Slowdowns in gains in life expectancy have been observed in recent decades in the United States and some other developed countries, particularly for females at older ages, even as increases have continued to be robust in other countries. Meslé and Vallin (2006) noted that life expectancy at age 65 for females increased only slightly from 1984 to 2000 in the United States and the Netherlands, although female e_{65} increased steadily in France and Japan in this period. Janssen et al. (2004, 2007)

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found similar slowdowns in mortality declines at advanced ages in some European countries (e.g., Denmark and the Netherlands) as well as continued strong declines in other countries (e.g., France).

Numerous causes for these trends have been suggested, but the effects of previous cigarette smoking merit particular attention. Decades of medical and epidemiological research have demonstrated that cigarette smoking is the largest cause of preventable mortality in the United States and most other developed countries (DHHS 2000; Ezzati et al. 2002).

Research has also shown that changes in mortality differences by sex within developed countries are due in large part to smoking. Pampel (2002) examined ratios of male and female mortality rates in high-income countries and found that changes in these ratios were largely due to changes in mortality attributable to smoking. Preston and Wang (2006) showed that mortality sex differences changed in the United States on a cohort basis, and that cohorts with the largest sex differences for all-cause mortality rates also had the largest sex differences for lung cancer mortality rates and smoking prevalence.

Various methods have been proposed and used to measure mortality attributable to smoking in populations (CDC 2005; Ezzati and Lopez 2003). These methods generally employ vital statistics or survey data and a variety of statistical techniques, and they produce a range of estimates. One of the most commonly used methods to estimate mortality attributable to smoking is the indirect method presented by Peto et al. (1992). This method was further explained by Lopez (1993) and is commonly known as the Peto-Lopez method. This method uses observed lung cancer mortality in a population as a proxy for previous cigarette use and then estimates smoking-attributable mortality based on the relative risks of mortality for various causes for smokers and nonsmokers. The method has been used to estimate smoking-attributable mortality for many countries over time, and updates to these estimates are made periodically on the collaborators' website (Peto et al. 2006). The Peto-Lopez method has the advantages of using vital statistics data that are readily available for many countries and a standardized measure of smoking exposure based on its impact on mortality. At the same time, however, the method is also somewhat limited with respect to the age groups that are used and the precision with which smoking-attributable mortality can be estimated.

Many studies have therefore shown that cigarette smoking is an important cause of preventable mortality in developed countries and that cigarette smoking explains much of the change in mortality sex differences within these countries. This study presents a modified version of the indirect Peto-Lopez method and uses this modified method to estimate the effect of smoking on mortality differences between countries. The study emphasizes results for females at older ages, generally defined here as ages 65 and older, because of research interest in trends for this group. Its analyses, however, are relevant to the use of the indirect method with all population groups. The modified version of the indirect method presented here estimates smoking exposure and relative risks for more-specific age groups than does the Peto-Lopez method. As a result, it produces improved estimates of smoking-attributable mortality, particularly at older ages. The study also introduces an adjustment factor to account for low mortality levels in the indirect method's study population. Overall, the use of the modified indirect method with this adjustment factor is shown to be useful specifically in the estimation of smoking-attributable mortality for U.S. women at older ages and in the estimation of smoking-attributable mortality for the U.S. population more generally.

Estimating the Effect of Cigarette Smoking on Mortality Trends

Recent slowdowns in gains in life expectancy for females at older ages can be observed in various developed countries, as suggested by Meslé and Vallin (2006). Figure 1 shows e_{65} values for females over time for England and Wales, France, Japan, and the United States from the Human Mortality Database (HMD) (UCB-MPIDR 2009). The United States performed well in female mortality at older ages compared with other developed countries prior to 1980, but gains in e_{65} for U.S. women slowed after this time. Gains in female e_{65} slowed in a somewhat earlier period in England and Wales than in the United States, although by 2000, the gap in female e_{65} between the two countries had narrowed. Similar slowdowns in gains in female e_{65} occurred in other developed countries, including Denmark and the Netherlands, according to HMD data.

Smoking trends can help explain these differences among countries, given that women began smoking in large numbers in various countries at different times. For example, national surveys show that in 1965, the prevalence of smoking among women aged 25 to 29 was approximately 50% in the United Kingdom, 45% in the United States, 15% in France, and less than 10% in Japan. By 1990, smoking prevalence at these ages was approximately 35% in France and the United Kingdom, 30% in the United States, and 20% in Japan (Forey et al. 2002).

The effect of cigarette smoking on life expectancy at older ages can be estimated with the indirect Peto-Lopez method, which uses lung cancer mortality as a proxy for smoking (Peto et al. 1992). Pampel (2005) provided a useful summary of the procedure as well as a review of criticisms of its methodology and support from

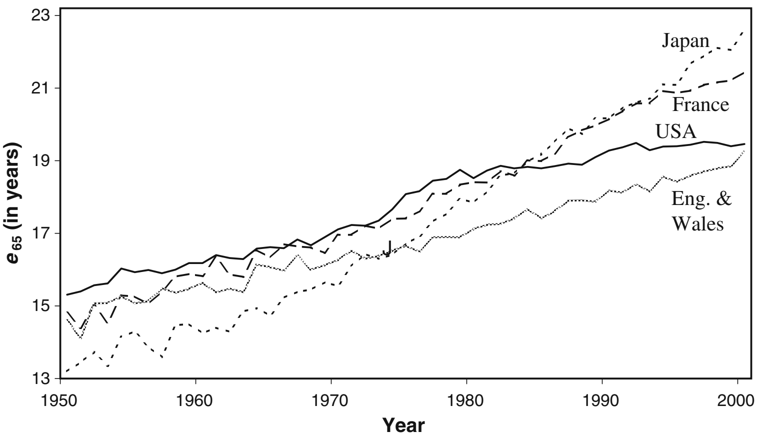

Fig. 1 Life expectancy at age 65 for females in selected countries. Data are from the Human Mortality Database (2009)

some empirical studies for the accuracy of its estimates of smoking-attributable mortality (Sterling et al. 1993; Valkonen and van Poppel 1997). This study employs the indirect method as presented by Peto, Lopez, and their colleagues with certain modifications, particularly the use of more-specific age groups, and this implementation of the method will be referred to as the "modified indirect method" in the remainder of the article. The study also introduces an adjustment factor to account for low mortality in the Peto-Lopez method's study population. When the adjustment factor is used with the modified indirect method in this article, the method will be referred to as the "modified indirect method with adjustment."

Estimating Smoking

The modified indirect method was implemented in this analysis by first estimating standardized cigarette smoking exposure in a given country and year for men and women by age group. All mortality and population data used in this analysis came from the WHO Mortality Database (2009). Table 1 shows the codes from the relevant revisions of the International Classification of Diseases for the classes of cause of death that were used with the method. Following the procedure of Peto et al. (1992), smoking exposure was estimated for a population group, defined by sex and age, by calculating the proportion of smokers and nonsmokers that would produce the observed lung cancer mortality rate for that group. It was assumed that smokers and nonsmokers by population group had the same lung cancer mortality rates as their counterparts in the American Cancer Society Cancer Preventive Study-II (CPS-II), a large prospective cohort study that included more than 1 million adults

Table 1 Classification of causes of death for the modified indirect method according to detailed lists of revisions of the International Classification of Diseases

Causes	ICD-7	ICD-8	ICD-9	ICD-10
Lung Cancer	162–163	162	162	C33–C34
Upper Aerodigestive Cancer	140–150, 161	140–150, 161	140–150, 161	C00–C15, C32
Other Cancer	151–160, 164–209	151–160, 163–209	151–160, 163–209	C16–C31, C35–C97
Respiratory Disease[a]	470–527	460–519	460–519	J00–J98
Vascular Disease[b]	400–468	390–458	390–459	I00–I99
Cirrhosis, Accidents, and Violence	581, E800–E999	571, E800–E999	571, E800–E999	K70, K74, W00–Y89
Other Medical Causes	Rest of 001–799	Rest of 000–799	Rest of 000–799	Rest of A00–R99

Source: ICD codes from WHO Mortality Database (2009) documentation

[a]Respiratory diseases were classified as a single, distinct class of causes of deaths, as opposed to the separation of COPD from other medical causes in Peto et al. (1992), because of the large number of empty cells for COPD at younger ages in CPS-II data.

[b]Relative risks for vascular disease were calculated from the CPS-II data for these causes that were presented in the appendix of Peto et al. (1992). Peto et al. used relative risks for other medical causes, which in their classification included vascular disease, but showed that the relative risks for vascular disease and other medical causes were very similar.

in the United States in the mid-1980s. This standardized calculation of exposure can be expressed as

$$M_{lc} = P \cdot M_{lc}^{S} + (1 - P) \cdot M_{lc}^{N}, \qquad (1)$$

where M_{lc} is the lung cancer mortality rate for a population group; P is the proportion exposed as smokers in that population group; and M_{lc}^{S} and M_{lc}^{N} are lung cancer mortality rates for smokers and nonsmokers in a study population group, in this case, the CPS-II sample. CPS-II lung cancer mortality rates came from the rates presented in the appendix of the Peto et al. paper. Peto et al. (1992) calculated mortality rates for CPS-II nonsmokers from data for individuals who reported at the beginning of the study that they had never smoked regularly and rates for CPS-II smokers from data for individuals who reported at the beginning of the study that they were current smokers. Peto et al. noted that most of these current smokers were lifelong adult smokers who smoked, on average, approximately 20 cigarettes per day. These CPS-II lung cancer mortality rates for smokers and nonsmokers were then smoothed using a Loess procedure in the modified indirect method, producing results similar to the smoothed nonsmoker lung cancer mortality rates presented by Peto et al. Population groups for which observed lung cancer mortality rates were lower than the lung cancer mortality rates of nonsmokers in the corresponding CPS-II study group were assumed to have had no smoking exposure. Former smokers and persons with passive exposure to cigarette smoke contributed to estimates of smoking exposure in populations to the extent that they had higher lung cancer mortality rates than nonsmokers in the CPS-II study.

This estimation procedure in the modified indirect method is similar to the procedure of the Peto-Lopez method, but has certain substantive differences in its implementation. Smoking exposure was consistently estimated in the modified indirect method for populations by five-year age groups from 35–39 to 75–79, whereas the Peto-Lopez method estimates exposure for the age group of 35–59 and then for five-year age intervals from 60–64 to 75–79. Exposure was also estimated in the modified indirect method for the age groups 80–84 and 85+, using CPS-II lung cancer mortality rates for those aged 80 and older for both groups. This procedure differs from the one employed in the Peto-Lopez method, which attributes the same proportion of mortality to smoking by cause for persons aged 80+ as was estimated for persons aged 75–79, because of concerns about the reliability of lung cancer mortality rates at older ages. Classification of cause of death at advanced ages is often considered to be somewhat unreliable because multiple medical conditions often contribute to the person's death (Nusselder and Mackenbach 2000). Mortality from malignant neoplasms such as lung cancer, however, tends to be more accurately identified than mortality from other causes because of the specific nature of these conditions (Kircher et al. 1985). In this case, more-specific estimates of smoking exposure for older age groups were calculated as part of the modified indirect method because of the particular focus on mortality at older ages and because of changes in smoking prevalence over time for cohorts. These changes in smoking experience for cohorts can lead to appreciable differences in smoking exposure for different age groups at older ages on a period basis.

Table 2 provides estimates from the modified indirect method of standardized smoking exposure for females in three developed countries or regions by age group between 1955 and 2000. Lung cancer mortality rates among U.S. nonsmokers tended to be rather consistent during this period, according to results from the American Cancer Society's CPS-I and CPS-II (Thun et al. 2006), suggesting that smoking exposure can be reasonably estimated for these years. This period is also similar to the interval for which Peto et al. (1994, 2006) estimated the effects of smoking on mortality for various developed countries. Estimates of standardized smoking exposure in these countries for age groups 80–84 and 85+ are consistent with trends for younger age groups, in spite of concerns about the accuracy of lung cancer mortality rates at these advanced ages from study and national population data. Standardized smoking exposure may not be accurately estimated for the youngest age groups in some countries, particularly those with small populations, because of the low levels of lung cancer mortality generally found among smokers and nonsmokers at these ages.

Trends in estimated standardized smoking exposure for these countries are generally consistent with survey results. Smoking exposure estimated with the modified indirect method does, however, tend to be higher for females in the United States and some other developed countries than self-reported smoking prevalence figures from survey data (Forey et al. 2002). According to survey data, smoking among young women in the United States appears to have peaked at around 45% for cohorts born in the 1930s and then declined. To some extent, variation in these two sets of estimates may occur because of differences in the way in which smoking exposure is measured. Survey data often provide an estimate of smoking prevalence

Table 2 Proportion of females exposed as smokers as estimated by the modified indirect method, by year and age group in selected countries

Country and Year	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+
England and Wales									
1955	0.17	0.13	0.12	0.08	0.07	0.04	0.00	0.00	0.00
1970	0.34	0.34	0.28	0.22	0.18	0.15	0.12	0.04	0.04
1985	0.31	0.27	0.42	0.46	0.43	0.39	0.32	0.24	0.17
2000	0.26	0.27	0.34	0.32	0.39	0.50	0.48	0.40	0.27
France									
1955	0.03	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.00
1970	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1985	0.03	0.04	0.05	0.02	0.02	0.01	0.00	0.00	0.00
2000	0.24	0.15	0.12	0.06	0.06	0.05	0.03	0.00	0.00
United States									
1955	0.07	0.04	0.03	0.02	0.01	0.00	0.00	0.00	0.00
1970	0.35	0.28	0.22	0.13	0.09	0.06	0.02	0.00	0.00
1985	0.55	0.56	0.56	0.48	0.43	0.37	0.27	0.18	0.10
2000	0.36	0.40	0.52	0.55	0.60	0.62	0.62	0.58	0.43

Source: WHO Mortality Database (2009)

at a particular time, whereas the modified indirect method estimates cumulative exposure to smoking as measured by its impact. On the other hand, these differences may also result from certain characteristics of the indirect method's study population. The indirect method standardizes smoking exposure based on the mortality of CPS-II nonsmokers and smokers, but all-cause mortality rates for both current smokers and nonsmokers in the CPS-II study were, as noted by Peto et al. (1992), lower than all-cause mortality rates for the U.S. population of the time. Lower mortality in the CPS-II could have resulted from a general tendency of people in good health or concerned about their health to participate in such a study, as well as the specific nature of the CPS-II study, in which American Cancer Society volunteers recruited friends and neighbors to participate (Malarcher et al. 2000). Sterling et al. (1993) noted that CPS-II lung cancer mortality rates for nonsmoking males were also substantially lower than the rates for nonsmoking males in the U.S. population, as calculated from more representative data from the National Mortality Followback Survey (NMFS) and National Health Interview Survey (NHIS), sometimes by as much as 69% by age group. Low lung cancer mortality in the CPS-II study group could bias estimates of smoking made with the indirect method upward, and thus some adjustment might be needed to estimate smoking exposure more accurately for other populations.

Such an adjustment can be made by introducing a factor into the indirect method to increase mortality rates from the CPS-II study to levels that approximate those of the U.S. population at the time of the study. One way to do this is to assume that CPS-II mortality rates for lung cancer and all causes were lower by a constant factor for smokers and nonsmokers in a sex and age group compared with rates at the time for the corresponding U.S. population group. U.S. mortality rates for lung cancer and all causes, M, at the time can then be expressed as

$$M = \dot{P} \cdot \lambda M^S + (1 - \dot{P}) \cdot \lambda M^N \tag{2}$$

and

$$M_{lc} = \dot{P} \cdot \lambda M_{lc}^S + (1 - \dot{P}) \cdot \lambda M_{lc}^N, \tag{3}$$

where λ is an adjustment factor that is applied to mortality rates from the CPS-II study group to produce rates equal to those in the U.S. population at the time, and $\dot{P}$ is an adjusted measure of smoking exposure in the U.S. population group. The equations imply that estimates of the population smoking exposure P are, in some sense, inflated in the absence of such an adjustment. The equations can be solved for the adjusted exposure $\dot{P}$

$$\dot{P} = \frac{M_{lc}\dfrac{M^N}{M} - M_{lc}^N}{M_{lc}^S - M_{lc}^N - \dfrac{M_{lc}}{M}(M^S - M^N)} \tag{4}$$

and adjustment factor λ

$$\lambda = \frac{M}{\dot{P} \cdot M^S + (1 - \dot{P}) \cdot M^N} = \frac{M_{lc}}{\dot{P} \cdot M_{lc}^S + (1 - \dot{P}) \cdot M_{lc}^N} \tag{5}$$

to produce estimates of exposure for the United States at the time of the CPS-II study. λ can be estimated using U.S. data for 1986, approximately the midpoint of the CPS-II study. Values for females and males are as follows:

	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+
Females	1.62	1.97	1.73	2.11	1.95	2.04	1.95	2.06	1.72
Males	1.70	1.98	1.98	1.87	1.82	1.72	1.48	1.36	1.21

The adjustment factor λ can also be used with other national populations or the United States in other years to produce comparable adjusted estimates of smoking exposure, denoted by P^*:

$$M_{lc} = P^* \cdot \lambda M_{lc}^S + \left(1 - P^*\right) \cdot \lambda M_{lc}^N. \tag{6}$$

Evidence suggests that this adjustment factor improves baseline estimates of lung cancer mortality and thus improves estimates of smoking exposure when used with the indirect method. CPS-II lung cancer mortality rates can be compared with more recent U.S. rates estimated by using NHIS data linked to death records for mortality follow-up (NCHS 2009). Lung cancer mortality rates were estimated for NHIS participants from 1997, when the survey was revised to include smoking information as part of the Adult Core questionnaire, to 2000 with mortality follow-up through the end of 2002. Figure 2a shows rates obtained from the NHIS for female nonsmokers, defined as persons who reported that they had smoked fewer than 100 cigarettes in their lives. The figure also presents lung cancer mortality rates for nonsmokers from the CPS-II study group and these CPS-II rates multiplied by the adjustment factor. Mortality rates from the CPS-II from the mid-1980s can be compared with more recent data because lung cancer mortality for nonsmokers has remained fairly constant in the United States over time (Thun et al. 2006). Rates from the CPS-II study are much lower than those estimated from the NHIS for the U.S. population, particularly at older ages. Adjustment increases the CPS-II rates, although they are still lower than rates from NHIS data for some ages. A similar trend is observed for female current smokers in the comparable comparison between CPS-II and NHIS lung cancer mortality rates, shown in Fig. 2b. Lung cancer mortality rates for current smokers in the CPS-II study are similar to rates in the U.S. population at middle ages but are lower at some advanced ages, even when adjusted. Aspects of smoking exposure, such as the duration and intensity of smoking, may have been somewhat different for current smokers in the two periods, but the figure again shows that lung cancer mortality rates in the CPS-II study were much lower than rates observed in the U.S. population, especially at older ages.

Use of the adjustment factor also appears to produce improved estimates of smoking for cohorts over time. Figure 3 shows smoking exposure for female cohorts in the United States estimated at various ages by using the modified indirect method with (Fig. 3b) and without (Fig. 3a) the adjustment factor. Use of the adjustment factor significantly decreases the variability of the estimates for specific cohorts and demonstrates that consistent estimates of smoking exposure can be obtained from lung cancer mortality data from various periods.

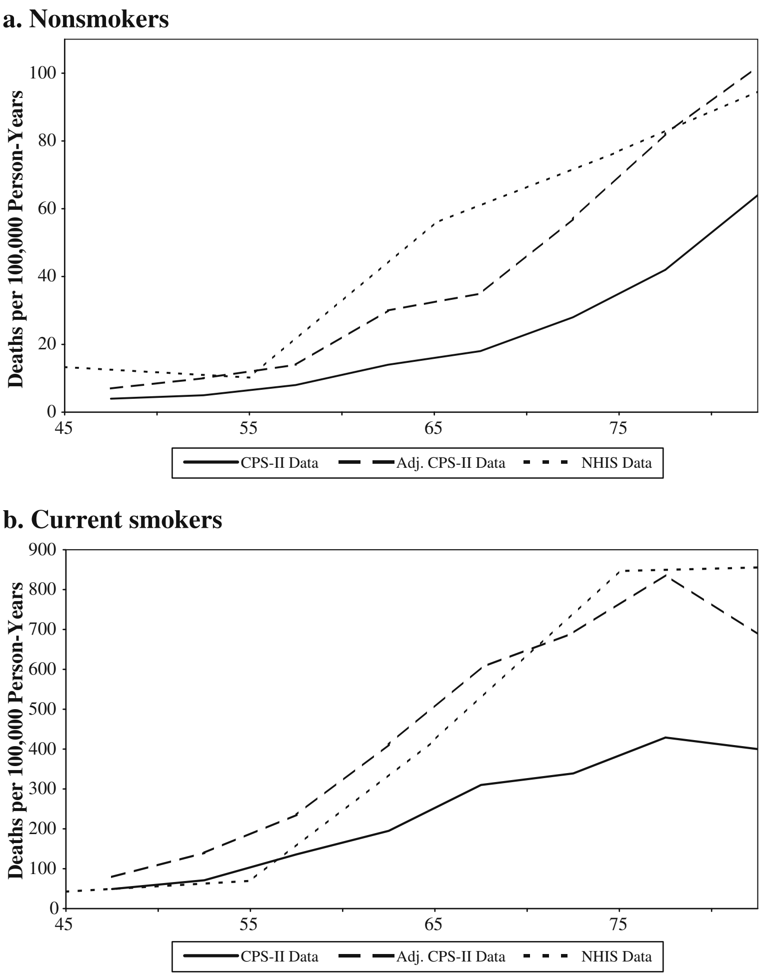

Fig. 2 Lung cancer mortality rates for females from selected data sources, by age and smoking status. Rates from CPS-II data came from Peto et al. (1992) and were for the years 1984–1988. Rates from adjusted CPS-II data were obtained by multiplying the CPS-II rates by the adjustment factor presented in this study. U.S. rates from NHIS data were estimated from data from 1997–2002

Estimating Smoking-Attributable Mortality

The second half of the modified indirect method was then implemented to calculate smoking-attributable mortality. Estimates of smoking exposure found with the first half of the method were used in standard population attributable-risk calculations (Kahn and Sempos 1989) with relative risks of mortality associated with smoking for various causes. Relative risks were calculated from detailed data in the appendix of Peto et al. (1992) for CPS-II smokers and nonsmokers. This procedure is similar to the one in the Peto-Lopez method, although five-year age groups were again consistently used with data and estimates because of the modified indirect method's emphasis on mortality at older ages. Following the Peto-Lopez method, relative risks of mortality for causes were assumed to be constant over time. Similarly, only one-half of the

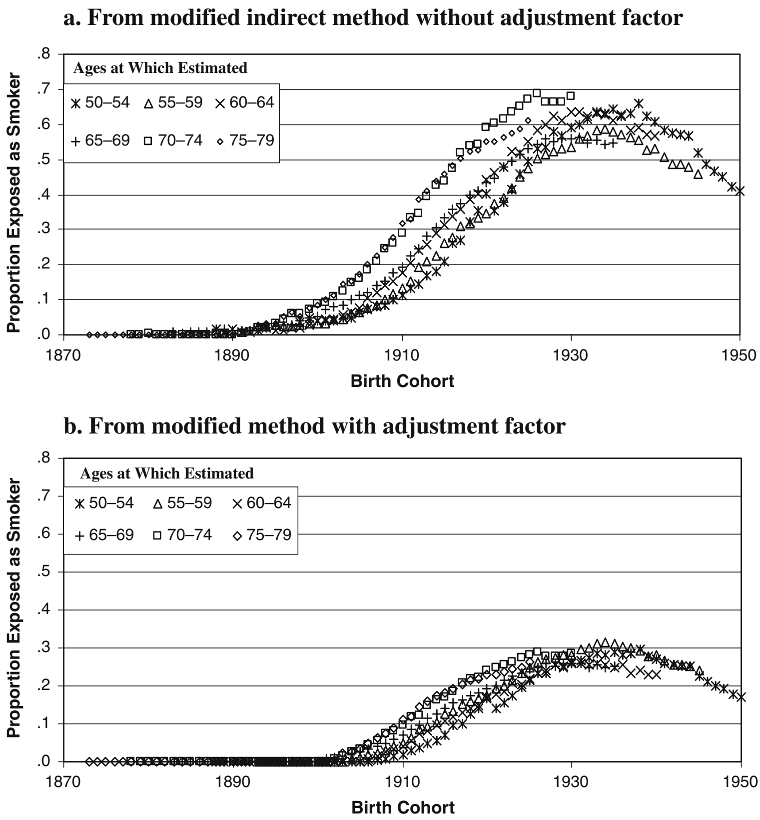

Fig. 3 Estimated smoking exposure for U.S. females, by cohort. Data are from the WHO Mortality Database (2009)

excess relative risk for smokers for causes other than lung cancer was attributed to smoking, due to the possible confounding effect of other risk factors associated with smoking, such as alcohol consumption. It was also assumed that smoking did not increase the risk of mortality from external causes and cirrhosis of the liver, as is assumed in the Peto-Lopez method.

Alternative estimates of life expectancy in the absence of all or some fraction of smoking can be calculated, using estimates of smoking exposure from the modified indirect method. In this case, life expectancy for countries was calculated for females at older ages under the assumption that smoking rates by age group had stayed the same in these countries from one period to another, a method chosen to try to understand the divergence in mortality trends among countries that occurred over time. Figure 4 presents observed e_{65} values for females in England and Wales, France, Japan, and the United States, as well as adjusted e_{65} values for England and Wales and the United States that were calculated with the modified indirect method and WHO data. Adjusted values for these countries were calculated with the assumption that smoking exposure had remained at estimated 1970 levels in subsequent years. The figure shows adjusted estimates for the United States made with and without the adjustment factor. The plot shows an appreciable increase in e_{65}

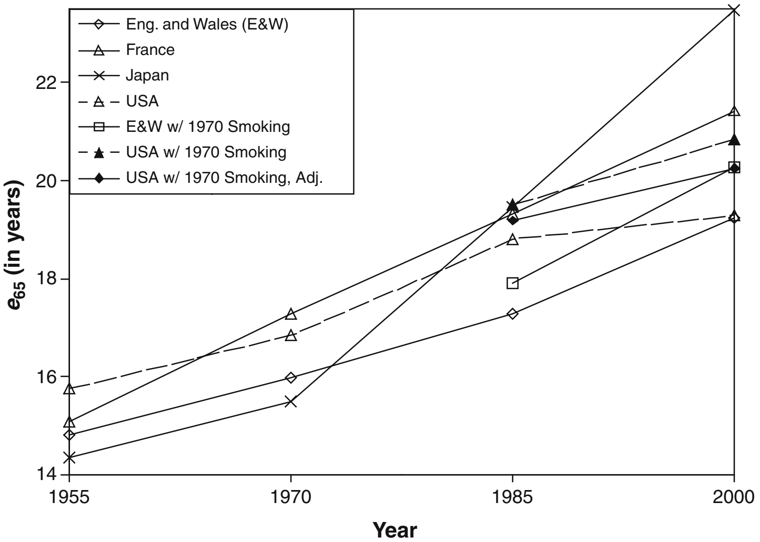

Fig. 4 Life expectancy at age 65 for females in selected countries with constant 1970 smoking exposure. Alternative values for e_{65} with constant 1970 smoking exposure by age group were estimated using the modified indirect method with and without adjustment. Data are from the WHO Mortality Database (2009)

for females in England and Wales and the United States in 2000 if smoking exposure had remained at the same levels by age group as in 1970, although the improvement estimated using the adjustment factor for the United States is more modest.

These methods and results can be evaluated with reference to another analysis of the effect of smoking on mortality for females at older ages in the United States in 2000, conducted by Rogers et al. (2005). Rogers et al. calculated mortality risks of smoking for different lengths and intensities, controlling for possible confounding variables, using a discrete-time hazard model with data from the 1990 NHIS Health Promotion and Disease Prevention supplement (NHIS-HPDP) linked to seven years of mortality follow-up. These mortality risks were then applied to the number of people in each smoking category in the United States in 2000, based on smoking prevalence figures from the NHIS, to estimate the number of deaths attributable to smoking by sex and age group. Removing the number of deaths attributed to smoking by Rogers et al. for U.S. women aged 65 years and older in 2000 produces an estimate of female e_{65} of approximately 20.1 years. The comparable values of female e_{65} without smoking deaths are 20.26 years from the modified indirect method with adjustment, 20.95 years from the modified indirect method without adjustment, and 21.51 years from the Peto-Lopez method. These results suggest that the modified indirect method with adjustment produces more accurate estimates of smoking exposure and smoking-attributable mortality for females at older ages than do the Peto-Lopez method and the modified indirect method without adjustment.

A similar analysis can be performed for life expectancy at older ages for males in developed countries. HMD data show that values of e_{65} for males in many countries, including Australia, Canada, Denmark, England and Wales, Italy, and the United States, either did not increase significantly or in fact decreased between 1955 and

1970, although e_{65} for men did increase in France and Japan. The effects of changes in smoking exposure on mortality can again be estimated using attributable risk calculations. Figure 5 presents observed e_{65} values over time for males in England and Wales, France, Japan, and the United States. The figure also presents adjusted e_{65} values for U.S. males that were calculated with the estimated smoking exposure for 1955 applied to later periods. The graph shows that male e_{65} in the United States would have been higher over time if smoking exposure for older males had remained at the moderate levels estimated for 1955. The graph also shows that with constant smoking levels e_{65} for males would have increased in the United States from 1955 to 1970 at a rate similar to the increase observed in Japan, instead of remaining relatively flat, and that U.S. male e_{65} from 1970 to 1985 would have increased at a somewhat greater rate than the observed appreciable increase. The figure also graphically illustrates that trends in life expectancy for older males in developed countries in recent decades have been quite distinct from trends for females. Male e_{65} values in the United States and England and Wales, although generally at lower levels than in France and Japan, increased at an appreciable rate from 1970 to 2000.

Overall, this analysis suggests that differences in previous smoking trends account for an important portion of the observed differences across countries in life expectancy at older ages. It also suggests that use of the modified indirect method with adjustment improves estimates of the effect of smoking on mortality at these ages in countries such as the United States. As an example, e_{65} for females calculated from WHO data was 2.14 years higher in France than in the United States in 2000. The modified indirect method with adjustment estimates that 45% of this difference would have been eliminated if U.S. females had had the same smoking exposure as French females by age group, whereas the estimates from the modified indirect method without adjustment and Peto-Lopez method are 73% and 93%,

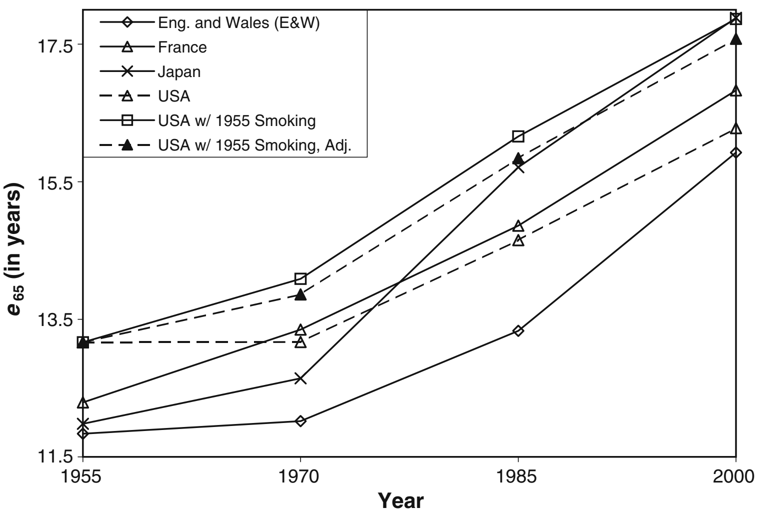

Fig. 5 Life expectancy at age 65, males in selected countries with constant 1955 smoking exposure. Alternative values for e_{65} with constant 1955 smoking exposure by age group were estimated using the modified indirect method with and without adjustment. Data are from the WHO Mortality Database (2009)

respectively. Because of the evidence suggesting that the modified indirect method with adjustment improves estimates of smoking-attributable mortality, it would appear that the first figure is the best estimate. Regardless of the estimation method, however, it is apparent that previous trends in female smoking have had large effects on differences in mortality trends for females at older ages in developed countries.

Evaluation of the Proposed Method

Evidence suggests that use of the modified indirect method with adjustment improves estimates of both smoking exposure and smoking-attributable mortality. For smoking exposure, estimates made with the adjustment factor are more consistent with self-reported smoking prevalence than estimates made without it. For example, the 1975 Adult Use of Tobacco Survey (AUTS) conducted by the U.S. Department of Health, Education, and Welfare and Public Health Service found that 36% of U.S. women in their 30s, 33% of women in their 40s, and 26% of women in their 50s reported that they were smokers (Forey et al. 2002). As seen in Fig. 3, these proportions by cohort are much closer to estimates of smoking exposure from the modified indirect method with adjustment than to estimates without adjustment. For males, the comparable prevalence figures from the 1975 AUTS are 47% for men in their 30s, 41% for men in their 40s, and 34% for men in their 50s. The modified indirect method without adjustment also appears to overestimate smoking exposure for males, producing estimates for male cohorts who were in their 40s in 1975 of up to 80%, compared with estimates made with adjustment of around 40%.

The modified indirect method with adjustment also produces estimates of the mortality attributable to smoking that are similar to detailed national estimates of mortality for various causes and age groups. Table 3 presents estimates of deaths due to smoking in the United States from 1997 to 2001 produced by the CDC's National Center for Chronic Disease Prevention and Health Promotion (CDC 2005). These figures were obtained by multiplying estimates of the smoking-attributable fractions of deaths by the total numbers of deaths for 18 adult and four infant causes of death. Smoking-attributable fractions of deaths for causes were calculated using relative risks of mortality for smokers obtained from CPS-II data and the prevalence of current and former smokers by age group as reported in NHIS data. Results show that the modified indirect method with and without adjustment produces estimates of lung cancer mortality attributable to smoking that are close to the estimates produced by the CDC. The figures also indicate that estimates of total mortality from smoking made with the modified indirect method without adjustment are closer to CDC estimates than estimates made with the method with adjustment.

Some researchers have suggested, however, that estimates by the CDC may sometimes overestimate the overall mortality effects of smoking. Rogers et al. (2005) produced detailed estimates of mortality attributable to smoking in the United States from data from the 1990 NHIS-HPDP supplement with mortality follow-up, and found that 338,000 deaths could be attributed to smoking in the United States in 2000—a figure that is substantially lower than the CDC estimates. The estimates from Rogers et al. (2005), unlike those from the CDC, were also presented broken down by age group, although not by cause of death. Estimates of deaths attributable

Table 3 Estimated average annual number of deaths attributable to smoking, by sex and cause of death, United States, 1997–2001

Causes of Death	CDC Estimates	Modified Indirect Method	Modified Indirect Method with Adjustment
a. Females			
Neoplasms	54,310	63,734	48,916
Lung	44,810	53,265	43,743
Circulatory diseases	53,612	41,421	21,872
Cardiovascular diseases	44,719	33,909	17,906
Cerebrovascular diseases	8,893	7,512	3,966
Respiratory diseases	47,135	45,898	25,282
Other diseases	23,351	36,688	17,487
Total	178,408	187,742	113,557
b. Males			
Neoplasms	104,219	114,137	96,922
Lung	79,026	81,861	76,513
Circulatory diseases	84,367	71,736	43,339
Cardiovascular diseases	75,824	62,794	37,815
Cerebrovascular diseases	8,543	8,942	5,524
Respiratory diseases	54,319	41,459	31,788
Other diseases	16,589	29,435	15,854
Total	259,494	256,767	187,904

Notes: As explained in the text, estimates from the modified indirect method were obtained using a procedure that is similar to the Peto-Lopez method but that uses data for more specific age groups. Estimates from the modified indirect method with adjustment were obtained with this procedure and the adjustment factor introduced in this study.

Sources: CDC (2005); WHO Mortality Database (2009)

to smoking for the United States in 2000 by age group from Rogers et al. (2005) are shown in Table 4 along with similar estimates from the modified indirect method, with and without adjustment. Estimates produced for this study from WHO data by using the Peto-Lopez method, with and without use of the adjustment factor to estimate smoking exposure, are shown as well. Estimates produced for this study using the Peto-Lopez method without adjustment for the United States in 2000 are very consistent with the comparable estimates produced by Peto et al. (2006). For example, they estimated 243,000 total deaths from smoking for females and 269,000 deaths for males in the United States in 2000, compared with 243,000 deaths for females and 272,000 deaths for males estimated with the Peto-Lopez method as part of this study. Estimates produced by Rogers et al. (2005) do not include deaths attributable to passive smoking exposure. Deaths from this type of exposure account for approximately 10% of deaths attributed to smoking in the CDC estimates.

Figures in Tables 3 and 4 show considerable variation in the estimated levels of mortality attributed to smoking by different methods but suggest that use of the modified indirect method and adjustment factor produce reasonable estimates,

Table 4 Estimated number of deaths attributable to smoking by sex and age group, United States, 2000

Ages	Rogers et al. Estimates	Modified Indirect Method	Modified Indirect Method with Adjustment	Peto-Lopez Method	Peto-Lopez Method with Adjustment
a. Females					
35–64	59,000	47,743	31,520	47,145	29,762
65+	75,000	143,393	83,855	195,578	125,089
Total 35+	134,000	191,136	115,375	242,723	154,851
b. Males					
35–64	83,500	88,517	55,289	84,402	52,662
65+	105,500	166,259	130,408	187,718	147,474
Total 35+	189,000	254,777	185,698	272,120	200,136

Notes: Estimates from the Peto-Lopez method were obtained using this method with data from the WHO Mortality Database (2009), as well as the adjustment factor described in this study for estimates with adjustment.

Sources: Peto et al. (1992); Rogers et al. (2005); WHO Mortality Database (2009)

particularly at older ages. Estimates produced with the Peto-Lopez method are higher than estimates from other methods, with approximately 510,000 deaths for those 35 and older compared with about 440,000 annual deaths at all ages estimated by the CDC for the period and about 325,000 deaths for those 35 and older estimated by Rogers et al. (2005). It is useful to note that all of the 52,000 difference in deaths for females and 17,000 difference for males between the Peto-Lopez method and the modified indirect method without adjustment are found for ages 80 and older. These differences indicate that use of the same proportion of mortality attributable to smoking for those 80 and older as estimated for those aged 75–79 in the Peto-Lopez method tends to significantly increase estimates of total deaths attributable to smoking when smoking exposure is increasing for successive cohorts. The difference in estimates is more pronounced for females in this case because of the substantial increase in smoking prevalence over time for female cohorts reaching older ages.

These results also support use of the adjustment factor, particularly with the modified indirect method. Table 4 shows that use of the adjustment factor, whether with the modified indirect method or the Peto-Lopez method, produces estimates of total deaths for both sexes that are closer to the detailed estimates calculated by Rogers et al. (2005) than are estimates made without adjustment. Of the four versions of the indirect method presented in Table 4, the indirect method with adjustment produces estimates of deaths attributable to smoking for both sexes that are closest to the estimates from Rogers et al. (2005). For females aged 65 and older —the group that is the focus of this study—the modified indirect method with adjustment produces estimates that are quite similar to estimates from Rogers et al. (2005): 84,000 deaths compared with 75,000.

The indirect method, whether in the Peto-Lopez or modified form, does produce in this case estimates of mortality attributable to smoking for younger ages that are low relative to estimates for older ages, based on comparison to results from Rogers et al. (2005). One possible cause of this relative underestimation at younger ages, particularly for the method with adjustment, could be that lung cancer mortality rates in the CPS-II study were closer at younger ages than at older ages to comparable rates in the U.S. population, as suggested by data in Fig. 2. Additional research comparing lung cancer mortality rates and relative risks of smoking for other causes from the CPS-II and data from studies with more representative populations is needed to understand this trend more fully.

Discussion

This study has presented a modified version of the indirect Peto-Lopez method and used it to examine the effect of smoking on mortality trends for females at older ages, given observed differences in mortality for this group in developed countries in recent decades. The modified indirect method presented here estimates mortality from smoking for more-specific age groups than does the Peto-Lopez method, a change that appears to improve estimates at older ages when smoking exposure differs substantially for successive cohorts. An adjustment factor has also been introduced for use with the modified indirect method to account for low mortality in the Peto-Lopez method's study population. Results from the modified indirect method with this adjustment have been shown to be similar to those in published studies from Rogers et al. (2005) and the CDC for U.S. females at older ages according to numerous measures, including differences in life expectancy and the number of deaths overall and by specific causes that are attributable to smoking. Overall, the modified indirect method with adjustment estimates that smoking accounts for approximately one-half of the difference in life expectancy for females at age 65 between the United States and France, two countries with fairly similar levels of economic development but different smoking levels for women.

This work has also evaluated use of the modified indirect method and adjustment factor to estimate smoking exposure and smoking-attributable mortality more generally. Results presented here suggest that the Peto-Lopez method tends to overestimate the mortality effects of smoking for U.S. men and women, sometimes by as much as 50% compared with other published estimates. This study has found that use of the modified indirect method and adjustment factor tends to improve the accuracy of estimates of smoking exposure and smoking-attributable mortality for these groups.

This finding of mortality overestimation by the Peto-Lopez method is generally consistent with previous research. Sterling et al. (1993) noted various limitations in the Peto-Lopez method, including low lung cancer mortality rates for nonsmokers in its study population. They also demonstrated that the relative risks of mortality for smokers for causes other than lung cancer tended to be higher in the CPS-II study population than in the U.S. population of the period, particularly for males. Malarcher et al. (2000) also found that use of relative risks from CPS-II data for four important causes overestimated deaths attributable to smoking from these causes in the United States by 19% compared with use of NHIS and NMFS data. These higher relative risks could produce an upward bias in estimates obtained from both the Peto-Lopez and CDC methods, given that the CDC methodology uses relative risks from CPS-II data and does not adjust for possible confounding effects from other health behaviors, such as alcohol consumption (CDC 2008). It should be noted, however, that some researchers have found little effect from controlling for confounding factors in estimates of mortality attributable to smoking (Malarcher et al. 2000), although other researchers have found the effects of such adjustment to be modest but appreciable (Rogers et al. 2005). To some extent, the conservative halving of excess relative risks for smokers for causes other than lung cancer in the Peto-Lopez method mitigates the possible effect of higher relative risks in the CPS-II study population, but any downward bias introduced by the halving of these risks appears to have less influence on the estimation of mortality attributable to smoking in this case than does the upward bias caused by overestimation of smoking exposure. Smoking-attributable mortality can be reestimated with the modified indirect method with adjustment and 75% of excess relative risk for smokers attributed to smoking. This figure is less conservative than the halving of excess relative risks but still accounts for effects of confounding factors and overestimation of relative risks for smokers in the CPS-II data. This modification produces an estimate of 142,000 smoking-attributable deaths for U.S. females in 2000, of which 104,000 are at ages 65 and older. The comparable estimate for U.S. males in 2000 is 221,000 deaths, of which 158,000 are at ages 65 and older.

Some researchers have found greater agreement between estimates from the Peto-Lopez method and estimates from other sources, although other estimation techniques may also present methodological issues. Brønnum-Hansen and Juel (2000), for example, obtained similar estimates for smoking-attributable mortality in Denmark using a simulation model and the Peto-Lopez method, although the two methods are similar in that they both use relative risks for smoking calculated from CPS-II data. More generally, Valkonen and van Poppel (1997) compared estimates of smoking-attributable mortality for five European countries from the Peto-Lopez method with estimates from data from national epidemiological studies, and found general agreement between the two sets of estimates. The authors noted, however, that they did not control for confounding factors in their calculation of relative risks and smoking-attributable mortality from these national studies and that the Peto-Lopez method tended to overestimate smoking in these countries compared with the known numbers of smokers. They concluded that the Peto-Lopez method would be more likely to overestimate than underestimate the mortality effects of smoking.

Additional research needs to be conducted to further evaluate these modifications and improve estimates. The degree to which mortality was lower in the CPS-II study group compared with mortality in more representative populations probably varies to some extent by sex, age, smoking group, and cause of death. The adjustment factor introduced here serves to adjust for differences by sex and age group, but this process appears to work better for some age groups than for others. Results presented here suggest that the modified indirect method without adjustment produces plausible estimates of smoking-attributable mortality at middle ages but inflates estimates at older ages and that the method with adjustment produces reasonable estimates at older ages but low estimates at middle ages. Additional study is needed to verify this finding and identify the elements of the method that produce these results, perhaps such as differences by age in mortality bias between lung cancer and all-cause mortality in the CPS-II data. More generally, additional analysis of large numbers of health survey participants with extensive mortality follow-up needs to be performed to improve estimates of lung cancer mortality rates and relative risks for mortality from other causes by smoking group, preferably controlling for possible confounding factors. These data would be particularly useful for very advanced ages, results for which have been considered somewhat unreliable in previous research.

At the same time, this study has also shown the usefulness of the indirect method, particularly for comparisons between countries and over time. The Peto-Lopez method and the modified indirect method presented here contain various procedures and assumptions that need to be analyzed further. Even so, results produced by the modified indirect method are generally plausible and consistent with published findings. The indirect method, whether in the form presented by Peto et al. (1992) or in the modified form presented here, has been shown to be particularly useful in cases in which detailed, accurate, and comparable information on smoking exposure and relative risks of smoking may be difficult to obtain but mortality data by cause are readily available. The indirect method thus makes possible the estimates presented here of male mortality in the 1950s and 1960s and female mortality in the 1980s and 1990s with different levels of smoking exposure.

Finally, these results confirm the importance of previous smoking behavior on trends in mortality and life expectancy. Beginning in the 1970s, mortality declines began to slow for females at older ages in countries such as the United States, the United Kingdom, the Netherlands, and Denmark, in large part due to previous increases in the number of women smoking at younger ages in these countries. To the extent that smoking in successive female cohorts in these countries has already reached a peak—or, in some cases, declined—then the effect of smoking on mortality for females at older ages should also stabilize or decrease. As an example, lung cancer mortality rates peaked for U.S. women in their 50s around 1990 and for U.S. women in their 60s in the late 1990s, and have since declined somewhat (WHO 2009). These trends, which are closely related to previous smoking behavior, are mirrored by improvements in mortality more generally. Female e_{65} in the United States increased from 19.3 to 19.9 years from 2000 to 2005, after increasing by only 0.2 years in the preceding decade (UCB 2009). Conversely, an eventual slowdown in gains in life expectancy should be expected in countries such as France, Italy, and Spain, where women began smoking in large numbers at a later date, thus eventually producing trends similar to those that have already been observed in other countries.

Acknowledgments The authors would like to thank Ron Lee, Ken Wachter, and Griff Feeney for helpful suggestions and comments. The authors are also grateful for support for this research from the National Institute of Aging (Grant Nos. T32 AG000246-14 and R01 AG11552).

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