Articles

# Estimates of global mortality attributable to smoking in 2000

*Majid Ezzati, Alan D Lopez*

## Summary

**Background** Smoking is a risk factor for several diseases and has been increasing in many developing countries. Our aim was to estimate global and regional mortality in 2000 caused by smoking, including an analysis of uncertainty.

**Methods** Following the methods of Peto and colleagues, we used lung-cancer mortality as an indirect marker for accumulated smoking risk. Never-smoker lung-cancer mortality was estimated based on the household use of coal with poor ventilation. Relative risks were taken from the American Cancer Society Cancer Prevention Study, phase II, and the retrospective proportional mortality analysis of Liu and colleagues in China. Relative risks were corrected for confounding and extrapolation to other regions.

**Results** We estimated that in 2000, 4·83 (uncertainty range 3·94–5·93) million premature deaths in the world were attributable to smoking; 2·41 (1·80–3·15) million in developing countries and 2·43 (2·13–2·78) million in industrialised countries. 3·84 million of these deaths were in men. The leading causes of death from smoking were cardiovascular diseases (1·69 million deaths), chronic obstructive pulmonary disease (0·97 million deaths), and lung cancer (0·85 million deaths).

**Interpretation** Smoking was an important cause of global mortality in 2000. In view of the expected demographic and epidemiological transitions and current smoking patterns in the developing world, the health loss due to smoking will grow even larger unless effective interventions and policies that reduce smoking among men and prevent increases among women in developing countries are implemented.

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**Department of Population and International Health, Harvard School of Public Health, Boston, MA, USA** (M Ezzati PhD)**; and School of Population Health, University of Queensland, Brisbane, Australia** (Prof A D Lopez PhD)

**Correspondence to:** Dr M Ezzati, Department of Population and International Health, Harvard School of Public Health, 665 Huntington Avenue, Boston, MA 02115, USA
(e-mail: mezzati@hsph.harvard.edu)

## Introduction

Smoking is a risk factor for mortality from several medical causes.[1] The hazards of smoking depend on factors such as the age at which smoking began, number of cigarettes smoked per day, cigarette characteristics, such as tar and nicotine content or filter type, and smoking behaviour, such as degree of inhalation.[2] Many of these factors vary over time and across generations because of changes in the socioeconomic determinants of smoking, such as income, and tobacco control efforts, including tobacco trade and advertising laws, and prices (including taxes). Therefore, current smoking prevalence or tobacco consumption alone would be insufficient indicators of the accumulated risk from smoking, even if detailed data were available in all countries.

To strengthen the scientific evidence for national and global tobacco control efforts, a consistent method is needed to estimate the health effects of smoking across different populations and different points in time. In this paper, we extend the indirect Peto-Lopez method[3] for estimation of mortality attributable to smoking to developing countries, with emphasis on factors that affect lung-cancer mortality among non-smokers. The emphasis on developing countries is particularly important because of shifting global smoking patterns, with an estimated 930 million of the world's 1·1 billion smokers living in low-income and middle-income countries.[4] Despite recent improvements in the data required for the method, substantial uncertainty still remains about the levels of smoking-attributable mortality, especially in developing countries. We addressed this issue by providing a quantitative analysis of uncertainty.

## Methods

### Smoking impact ratio

Following the methods of Peto and colleagues,[3] we used lung-cancer mortality as an indirect indicator of the accumulated hazards of smoking. Background-adjusted smoking impact ratio (SIR) was defined as population lung-cancer mortality in excess of never-smokers, relative to excess lung-cancer mortality for a known reference group of smokers, adjusted to account for differences in never-smoker lung-cancer mortality rates across populations.[5] Conceptually, by using excess lung-cancer mortality as the indicator of the accumulated hazards of smoking in both study and reference populations, SIR converts the smokers in the study population—who may have different smoking histories—into equivalents of smokers in the reference population, where hazards for other diseases have been measured.[3] A detailed description of the use of SIR as a measure of exposure to accumulated smoking hazards with emphasis on developing countries is provided elsewhere[5] and summarised below as appropriate:

$$SIR=\frac{C_{LC}-N_{LC}}{S^{*}_{LC}-N^{*}_{LC}}\times\frac{N^{*}_{LC}}{N_{LC}}$$

$C_{LC}$ is age-sex-specific lung-cancer mortality rate for 2000 in the study population (eg, country of analysis) from WHO's Global Burden of Disease database; see online report[6] for methods. $N_{LC}$ is age-sex-specific lung-cancer mortality rate of never-smokers in the same population as $C_{LC}$. $S^*_{LC}$ and $N^*_{LC}$ are age-sex-specific lung-cancer mortality rates for smokers and never-smokers, respectively, in a reference population.

The age groups used in the analysis were 0–4, 5–14, 15–29, 30–44, 45–59, 60–69, 70–79, and 80 years and older. No deaths before the age of 30 years were attributed to smoking. SIR values were calculated for each age-group and sex and for individual countries, and then averaged (population-weighted) in each of 14 epidemiological subregions of the world (see previous work[7] for the list of countries in each subregion).

Peto and colleagues[3] used the same lung-cancer mortality for never-smokers in the study and reference populations (numerator and denominator of the equation), when applying the method to developed countries. Liu and colleagues[8] noted that non-smokers in different geographical regions of China had lung-cancer mortality rates that varied by a factor of 10. (see figure 1 in reference 5 and figure 4 in reference 8) The different non-smoker lung-cancer mortality rates in China are largely a result of patterns of household energy use in China over the past few decades. Coal, a common household fuel in China and traditionally burned in stoves and buildings with poor ventilation, has been associated with increased risk of lung cancer.[9,10] Never-smoker lung-cancer mortality in the SIR equation for different regions was estimated based on the household use of coal in poorly-vented stoves.[5] The remaining risk factors for lung-cancer mortality (ambient air pollution, occupational hazards, indoor air pollution from radon or biomass smoke, and so on) affect all populations to varying degrees. The net effects of these other risk factors were included as sources of uncertainty in never-smoker lung-cancer mortality.

Following Peto and colleagues' methods,[3] we used the American Cancer Society Cancer Prevention Study, Phase II (CPS-II) for the reference population (see below for description). This is a prospective study of smoking and death in more than 1 million Americans aged 30 years and older when they completed a questionnaire in 1982, with the latest published follow-up in 1998. Complete descriptions of the study and analysis have been provided previously.[3,11–13] We took our reference population from CPS-II because this was one of the few studies of smoking and cause-specific mortality undertaken when the full effects of the smoking epidemic were apparent, especially for men. Therefore, most (male) current-smokers included in CPS-II had been lifelong cigarette smokers, with a mean consumption of about 20 cigarettes per day.[3] Further, the estimates of increased risk of mortality among smokers were available for both men and women and for smaller age groups than in other studies.

## Hazard estimates

Lung-cancer mortality attributable to smoking, by definition, is the difference between lung-cancer mortality rates in the study population and among never-smokers. To estimate mortality attributable to smoking from causes other than lung cancer, a composite population consisting of reference population (ie, CPS-II) smokers and non-smokers was established so as to give an SIR equal to that of the study population (it is simple to show that the share of CPS-II smokers in the mixture equals the SIR of the study population).[3] This composite population was then used together with cause-specific relative risks from CPS-II[3] to estimate the smoking-attributable fraction of mortality for each medical cause. The exception to the use of CPS-II was China, for which attributable fractions for diseases other than lung cancer were obtained using relative risks from Liu and colleagues.[8]

We reduced the excess risk attributed to smoking in the CPS-II relative risks by constant correction factors, to avoid overestimation of mortality due to confounding in CPS-II risk estimates (which were initially adjusted for age and sex only) as well as extrapolation to other populations, where exposure to other risk factors could modify the effects of smoking in a non-multiplicative way.[3] The correction factor used by Peto and colleagues[3] was 50% of excess risk. In subsequent studies, the overall effect of confounding from factors such as diet and alcohol has been estimated as substantially less than half of the excess risk for cardiovascular diseases (including evidence of negative confounding for some causes).[14–17] In response to criticism about lack of empirical evidence for confounding correction,[18,19] CPS-II data have been reanalysed with adjustment for potential confounders.[13,20] In one reanalysis, apart from cerebrovascular disease among men (where the fraction attributable to smoking decreased from 16% to 10%), adjustment for confounding had no or little effect on smoking-attributable mortality (the next largest decreases were for lung cancer among men from 91% to 89%, and chronic obstructive pulmonary disease among women from 70% to 68%), or even resulted in a slight increase in risk for some causes.[20]

In a more detailed analysis, Thun and colleagues[13] adjusted for age, race, education, marital status, occupation ("blue collar" worker), and total weekly consumption of citrus fruits and vegetables, in their estimation of the increased risk of mortality from a range of neoplasms, cardiovascular diseases, and respiratory diseases as a result of smoking. The analysis also adjusted for current aspirin use, alcohol consumption, body-mass index, physical activity at work or leisure, and weekly consumption of fatty foods for cardiovascular diseases, and for occupational exposure to asbestos for lung cancer and chronic obstructive pulmonary disease. With the exception of stroke among men, for which the relative risk decreased from 2·9 (95% CI 2·3–3·7) to 2·4 (1·8–3·0) for the 35–64 year age group and from 1·8 (1·6–2·2) to 1·5 (1·2–1·8) for those older than 64 years, excess risks increased, remained unchanged, or decreased by small amounts. Overall, adjustment for confounding reduced the estimates of mortality attributable to smoking in the USA by about 1%.[13]

Based on this new evidence on the robustness of CPS-II relative risks to adjustment for confounding, we used a correction factor of 30% (about equal to the largest reduction in excess risk after adjustment in the reanalysis of CPS-II) to reduce the excess risk for all cause-specific risks other than lung cancer. This choice continues to be conservative to account for residual confounding or potential overestimation from extrapolation across regions. For the category "other medical causes", where the extent of confounding was unknown, we attributed only half of the excess mortality estimated by CPS-II, as did Peto and colleagues.[3] The excess risk in China was reduced by 5% to account for residual confounding. The proportional mortality method used by Liu and colleagues[8] is not affected by confounding due to any risk factor that increases mortality in the study and reference categories proportionally.

| | Men | Women | Total† |
|---|---|---|---|
| Developing (1874 million)* | 2·02 (1·56–2·50) | 0·38 (0·25–0·65) | 2·41 (1·80–3·15) |
| Industrialised (795 million)* | 1·81 (1·62–2·02) | 0·61 (0·52–0·75) | 2·43 (2·13–2·78) |
| Total (2669 million)*† | 3·84 (3·17–4·53) | 1·00 (0·76–1·40) | 4·83 (3·94–5·93) |

Values are millions of deaths (uncertainty range). *Numbers in parentheses= population aged 30 years and older. Industrialised countries include GBD subregions AMR-A, EUR-A, EUR-B, EUR-C, and WPR-A (see reference 7 for the list of countries in each subregion). Developing countries include all other subregions. †Three significant digits are reported to limit discrepancies between components and totals as a result of rounding. The precision of estimates is lower, as shown by the uncertainty ranges.

Table 1: **Estimated mortality attributable to smoking in developing and industrialised countries in 2000**

## Analysis of uncertainty

Uncertainty was estimated separately for each of the input variables. Uncertainties of individual variables were used in a stratified sampling simulation[21] to obtain combined uncertainty distribution for the fraction of cause-specific mortality attributable to smoking. The uncertainty reported here is the 95% range of the combined distribution. The analysis of uncertainty for causes other than lung cancer does not include uncertainty of mortality data from the Global Burden of Disease (GBD) project,[6] which is expected to be higher in developing countries, where vital registration is absent or incomplete, than in industrialised countries.

### *Population lung cancer mortality*

In countries with good vital registration and medical certification of deaths (about 75 countries),[6,22] lung-cancer mortality is diagnosed with a high degree of accuracy. For example, microscopic confirmation of diagnosis against the cause reported on death certificates has suggested a 95% or higher confirmation rate.[23] In about 50 other countries, vital registration of mortality is incomplete and medical certification of cause-of-death less reliable. Standard demographic techniques were used in the GBD project[6,22] to correct all-cause death rates by age for these populations, and recorded rates of lung cancer were adjusted accordingly. For countries without vital registration, overall age-specific death rates are first determined from model life-tables.[22] Total cancer death rates are then estimated on the basis of regional information about proportionate cancer mortality. Within this death rate, the distribution by site is based on regional incidence patterns from cancer registries reporting to the International Agency for Research on Cancer.[24] We assigned each country into one of four uncertainty categories on the basis of the quality of available mortality data. Lung cancer mortality for the four categories were assigned uncertainty ranges equal to 10%, 20%, 40%, and 80% of the best estimate, with a triangular distribution. In countries with good vital registration, 10% is double the observed uncertainty level. 80% uncertainty for the most uncertain countries (ie, those with no mortality reporting) implies that we have allowed nearly all of estimated lung-cancer mortality to be due to misclassification. Countries with less complete or less reliable data were classified as having 20% or 40% uncertainty around the best estimate.

### *Never-smoker lung cancer mortality*

For China, estimates of uncertainty for non-smoker lung-cancer mortality rates from the proportional mortality study of Liu and colleagues[8] were used. For populations where never-smoker lung-cancer mortality rates were based on CPS-II, we assumed a standard error equal to the sampling uncertainty of CPS-II plus 15% of its central estimates. The additional 15% is nearly equivalent to the whole (never-smoker) population being exposed to levels of air pollution, such as that in the centre of the industrial city of Cracow, Poland, which resulted in a 14% increase in lung-cancer mortality during 1980–85,[25] or the whole (never-smoker) population being exposed to more than 10 μg/m$^3$ of particles smaller than 2·5 μm in diameter in CPS-II.[26] Because the net difference between accumulated exposure to additional lung-cancer risk factors (radon, ambient air pollution, biomass smoke) in any two countries is less than the whole population, 15% is a relatively large uncertainty range for never-smoker lung cancer mortality. For reference population smoker and never-smoker lung cancer mortality, the sampling uncertainty of CPS-II was used.

| | Male (1·31 billion) | | Female (1·35 billion) | |
|---|---|---|---|---|
| | Age 30–69 years (1·21 billion) | Age ≥70 years (109 million) | Age 30–69 years (1·20 billion) | Age ≥70 years (156 million) |
| **Cause (ICD-9)** | | | | |
| Lung cancer (162) | 398 (77%) | 294 (82%) | 77 (44%) | 79 (54%) |
| Upper aerodigestive cancer (mouth, oropharynx, or oesophagus) (140–150)* | 152 (46%) | 66 (42%) | 17 (12%) | 15 (13%) |
| Other cancer (151–161, 163–209) | 195 (15%) | 135 (13%) | 17 (1%) | 24 (2%) |
| Chronic obstructive pulmonary disease (490–492, 495, 496)* | 269 (54%) | 433 (52%) | 86 (24%) | 178 (19%) |
| Other respiratory diseases (460–466, 480–487, 381–382) | 274 (22%) | 93 (11%) | 34 (4·8%) | 32 (4%) |
| Cardiovascular diseases | 848 (24%) | 476 (12%) | 143 (6%) | 223 (4%) |
| Infectious and parasitic diseases (001–139, 320–323, 614–616, with the exception of those above), maternal and perinatal conditions (630–676, 760–779), neuro-psychiatric conditions (290–319, 324–359), cirrhosis of the liver (571), congenital anomalies (740–759)† | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Other medical causes (remainder of 000–799) | 145 (17%) | 57 (8%) | 36 (5%) | 35 (4%) |
| Total medical | 2280 (22%) | 1556 (18%) | 410 (6%) | 587 (5%) |
| Non-medical (accidents and injuries) (E800–999)‡ | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Total mortality | 2280 (19%) | 1556 (18%) | 410 (5%) | 587 (5%) |

Values are number (in thousands) of deaths from each cause and the fraction of total mortality from that cause in the specified age group. Population numbers correspond to the respective age-sex group. *In CPS-II, ICD 161 was included with upper aerodigestive cancer and ICD 495 with other medical causes. In this analysis, ICD 161 is included with other cancers and ICD 495 with chronic obstructive pulmonary disease, to be consistent with disease categories used in the GBD project.[6] †Peto and colleagues[3] included the medical (non-injury) causes of death listed here with the category other medical causes. We assumed that none of deaths in this category were attributable to smoking. There has also been growing evidence of the effects of maternal smoking on maternal and child health. Specific outcomes include stillbirths and neonatal deaths, low birthweight, primary and secondary infertility, ectopic pregnancy and spontaneous abortion, and other child and maternal conditions.[1,27] ‡Many deaths from burns and other injuries from fires are also attributable to smoking. For example pooled studies from Australia, UK, and USA show a population attributable fraction of 0·23 for fire-related injuries and smoking.[28]

Table 2: **Estimated global mortality attributable to smoking by age, sex, and cause of death in 2000**

| | Adult population (millions) | | Smoking-attributable mortality (thousands of deaths [uncertainty range]) | | Proportion of total adult mortality | |
|---|---|---|---|---|---|---|
| | M | F | M | F | M | F |
| **Subregion** | | | | | | |
| AFR-D | 41 | 43 | 43 (23–80) | 7 (2–20) | 5% | 1% |
| AFR-E | 47 | 50 | 83 (58–122) | 25 (16–46) | 6% | 2% |
| AMR-A | 91 | 98 | 352 (296–429) | 294 (237–372) | 28% | 22% |
| AMR-B | 85 | 92 | 163 (123–214) | 58 (34–93) | 15% | 6% |
| AMR-D | 12 | 12 | 5 (2–9) | 1 (0–4) | 3% | 1% |
| EMR-B | 25 | 22 | 43 (27–63) | 10 (2–20) | 15% | 5% |
| EMR-D | 52 | 52 | 114 (70–167) | 19 (6–46) | 13% | 2% |
| EUR-A | 125 | 137 | 531 (451–644) | 145 (103–202) | 27% | 7% |
| EUR-B | 50 | 54 | 255 (206–304) | 53 (38–82) | 28% | 6% |
| EUR-C | 63 | 80 | 548 (461–632) | 73 (45–123) | 32% | 4% |
| SEAR-B | 61 | 62 | 167 (89–240) | 12 (1–44) | 19% | 1% |
| SEAR-D | 244 | 235 | 746 (328–1112) | 110 (18–308) | 18% | 3% |
| WPR-A | 47 | 51 | 128 (105–162) | 49 (35–71) | 22% | 10% |
| WPR-B | 374 | 367 | 658 (500–822) | 143 (58–238) | 15% | 3% |

M=male. F=female. See reference 7 for list of countries in each subregion.

Table 3: **Estimated mortality attributable to smoking in people aged 30 years and older by GBD subregion in 2000**

*Hazard correction factor*

We allowed the 30% correction factor to vary between 10% and 50%, with a triangular distribution. 10% corresponds to the typical reduction in excess risk seen after adjustment for covariates in the re-analysis of CPS-II[13] and other studies;[14] 50% is the correction used by Peto and colleagues[3] before the CPS-II reanalysis, and larger than the largest effect of confounding estimated in the re-analysis.[13] Uncertainties in relative risks themselves were taken from the CPS-II and Chinese mortality study.

### Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

## Results

Table 1 shows the estimated number of smoking-attributable deaths, divided into causes and age groups in table 2, and into 14 epidemiological subregions of the world as defined in the GBD project[6,7] in table 3. The 4·83 (uncertainly range 3·94–5·93) million deaths attributable to smoking were 12% of the estimated total global adult (those older than 30 years) mortality in 2000. 18% and 5% of total adult male and female mortality, respectively, were attributable to smoking. Smoking killed 3·0 and 6·7 times more men than women in industrialised and developing countries, respectively. 2·69 million deaths were in people aged between 30 and 69 years, resulting in a substantial number of life years lost to premature mortality.

Lung cancer was the disease with the highest fraction attributable to smoking. 71% of all lung cancers or 0·85 million deaths (79% or 0·69 million deaths among men and 48% or 0·16 million deaths among women) were attributable to smoking. Cardiovascular diseases, however, were the most common cause of death from smoking: 1·69 million deaths (1·32 million among men and 0·37 million among women), or 35% of all smoking-attributable deaths (35% among men and 37% among women). 11% of all adult cardiovascular deaths worldwide were attributable to smoking (17% among men and 4% among women). Only when all cancers were considered together did they approach cardiovascular diseases as the largest cause of death attributable to smoking. 1·47 million deaths from cancer (22% of all deaths from cancer in adults; 1·24 million or 33% of all deaths from cancer in men and 0·23 million or 8% of all deaths from cancer in women) were attributable to smoking, accounting for 32% of all smoking-attributable deaths (34% among men and 24% among women).

In 2000, smoking caused an estimated 2·43 (uncertainty range 2·13–2·78) million deaths in adults in industrialised countries; 19% of total adult mortality (table 4). 1·81 (1·62–2·02) million of these deaths were among men (28% of total mortality of adult men) and 0·61 (0·52–0·75) million among women (9% of total mortality of adult women). 1·19 million (about half) of these deaths were between ages 30 and 69 years.

Among industrialised regions the fraction of smoking-attributable mortality among men was highest in the EUR-C (dominated by Russia in terms of population) and AMR-A (North America) subregions, with 0·55 million and 0·37 million smoking-attributable deaths in men, respectively, or 32% and 28% of all deaths in adult men. Among women, the highest fraction of smoking-attributable mortality was in AMR-A, where 0·29 million adult deaths (22%) were attributable to smoking. The lowest fraction of smoking-attributable mortality among men was in the industrialised countries of the western Pacific region (22%) and among women in eastern Europe (4–6%).

The estimated number of adult deaths attributable to smoking in developing countries in 2000 was 2·41 (uncertainty range 1·80–3·15) million, accounting for 9% of total adult mortality (table 5). 2·02 (1·56–2·50) million deaths were among men (14% of total mortality in adult men) and 0·38 (0·25–0·65) million among women (3% of total mortality in women). 1·49 million deaths were in people aged between 30 and 69 years and 0·91 million in those older than 69.

There was larger variation in the mortality attributable to smoking among different regions of the developing

| | Male (375 million) | | Female (420 million) | |
|---|---|---|---|---|
| | Age 30–69 years (329 million) | Age ≥70 years (47 million) | Age 30–69 years (342 million) | Age ≥70 years (78 million) |
| **Cause** | | | | |
| Lung cancer | 216 (91%) | 187 (92%) | 50 (70%) | 67 (72%) |
| Upper aerodigestive cancer | 52 (72%) | 24 (66%) | 5 (39%) | 9 (41%) |
| Other cancer | 97 (21%) | 88 (16%) | 11 (2%) | 18 (3%) |
| Chronic obstructive pulmonary disease | 63 (84%) | 142 (77%) | 20 (62%) | 86 (61%) |
| Other respiratory | 67 (44%) | 38 (16%) | 9 (15%) | 23 (8%) |
| Cardiovascular diseases | 455 (40%) | 298 (17%) | 77 (13%) | 192 (7%) |
| Other attributable medical causes | 55 (32%) | 33 (13%) | 17 (14%) | 28 (7%) |
| Other medical causes | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Total medical | 1005 (39%) | 810 (24%) | 189 (13%) | 423 (9%) |
| Non-medical (accidents and injuries) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Total mortality | 1005 (33%) | 810 (24%) | 189(12%) | 423 (9%) |

See table 2 for definitions of categories.

Table 4: **Estimated mortality (thousands of deaths) attributable to smoking in industrialised countries by age, sex, and cause of death in 2000**

| | Male (939 million) | | Female (934 million) | |
|---|---|---|---|---|
| | Age 30–69 years (877 million) | Age ⩾70 years (62 million) | Age 30–69 years (856 million) | Age ⩾70 years (78 million) |
| **Cause** | | | | |
| Lung cancer | 181 (65%) | 108 (69%) | 27 (26%) | 12 (22%) |
| Upper aerodigestive cancer | 100 (38%) | 42 (35%) | 12 (10%) | 6 (7%) |
| Other cancer | 98 (11%) | 48 (9%) | 7 (1%) | 6 (1%) |
| Chronic obstructive pulmonary disease | 206 (49%) | 290 (45%) | 65 (20%) | 93 (12%) |
| Other respiratory | 207 (18% | 55 (9%) | 26 (4%) | 9 (1%) |
| Cardiovascular diseases | 393 (17%) | 178 (8%) | 66 (4%) | 31 (1%) |
| Other attributable medical causes | 90 (14%) | 25 (5%) | 19 (3%) | 7 (1%) |
| Other medical causes | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Total medical | 1275 (16%) | 746 (14%) | 221 (4%) | 164 (3%) |
| Non-medical (accidents and injuries) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Total mortality | 1275 (14%) | 746 (14%) | 221 (3%) | 164 (3%) |

See table 2 for definitions of categories.

Table 5: **Estimated mortality (thousands of deaths) attributable to smoking in developing countries by age, sex, and cause of death in 2000**

world than in industrialised regions. The fraction of total adult mortality attributable to smoking in developing regions ranged from a low of 2–4% in sub-Saharan Africa and parts of Latin America to a high of 9–11% in other parts of Latin America, southeast Asia, and the western Pacific. In men, the lowest fraction of total mortality attributable to smoking was in sub-Saharan Africa and parts of Latin America (3–6%). The highest fractions of mortality attributable to smoking in men were in other parts of Latin America, the eastern Mediterranean, southeast Asia and the western Pacific (15–20%). For women, the fraction of total mortality attributable to smoking was lowest in sub-Saharan Africa and parts of Latin America and the eastern Mediterranean (⩽2%) and highest in other parts of Latin America and the eastern Mediterranean (5–6%), reflecting more recent increases in smoking among women in these regions with modernisation and economic development.

## Discussion

By using lung cancer mortality as an indirect indicator of the accumulated hazards of smoking, we estimated that 4·83 (uncertainty range 3·94–5·93) million premature deaths in the world were attributable to smoking in the year 2000. Numbers of deaths were almost equal in developing and industrialised regions of the world, and were greater in men than in women, especially in developing countries.

The reliability of mortality estimates based on the indirect SIR method has been confirmed against other methods.[29] Nevertheless, there is large uncertainty, especially in developing countries where both complete mortality records and detailed studies of smoking risks are less common. Additionally, use of lung cancer—which has a longer lag than cardiovascular disease and some other diseases caused by smoking—as the marker for accumulated smoking hazard, can result in an overestimation of risk where there have been sharp declines in smoking, and underestimation of risk where there has been large increases in smoking. The former case is likely to apply in North America and some countries in western Europe where smoking has declined, although this is partly or fully offset by continued choice of a conservative hazard correction factor. On the other hand, the hazards of smoking may be underestimated in most developing countries, where smoking has been on the rise over the past few decades.[30] The work of Gajalakshmi and colleagues[31] provides an example from India.

Due to differences in methodology and presentation, the estimates reported here are not fully comparable with those for previous years. Data on tobacco consumption and prevalence of tobacco use show that smoking has declined among men in many industrialised countries.[30] Even after accounting for methodological differences, in most of these countries the accumulated hazards of smoking among women have increased in the past decade. Compared with the estimates of Peto and colleagues,[3] industrialised countries have also seen a small decline in the share of smoking-attributable mortality in people aged 30–69 years compared with those aged 70 years and older, suggesting that in these countries as a whole, the effects of the smoking epidemic are shifting towards older age groups (with the exception of younger women in many countries).

Mortality from smoking varied greatly among different regions of the developing world (table 3) because the smoking epidemic is highly affected by diverse demographic, economic, and cultural determinants. A few general statements can nonetheless be made about the hazards of smoking in developing countries. First, mortality attributable to smoking is highly concentrated among men (84% of smoking-attributable deaths). Second, compared with industrialised countries, developing countries have a higher proportion of smoking-attributable mortality at age 30–69 years, than at older ages (62% in developing versus 49% in industrialised countries).

The results of this analysis suggest a transition to an era in which smoking kills about as many people in developing countries as in industrialised nations. Even at the current stages of the tobacco epidemic, more men die from smoking in developing countries (2·02 million) than in the industrialised nations (1·81 million). As the hazards of smoking accumulate among those who began smoking in developing countries over the past few decades, coupled with population growth and ageing, mortality as a result of smoking will rise substantially in these countries unless effective interventions and policies that reduce smoking among men and prevent increases among women are implemented.

*Contributors*

Both authors contributed to adaptation of the Peto-Lopez method to developing countries, designed the analysis, and wrote the paper. M Ezzati did data analysis.

*Conflict of interest statement*

None declared.

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