Global Report on Mortality Attributable to Tobacco, 2004

Technical note

The global burden of tobacco use

Tobacco is the only legal drug that kills many of its users when used exactly as intended by manufacturers. Tobacco smoking and exposure to second-hand smoke in non-smokers are currently responsible for the deaths of almost six million people across the world each year, equating to one death every six seconds of every hour of every day, with many of these deaths occurring prematurely. Tobacco kills more than tuberculosis, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), and malaria combined. In the next two decades, the annual death toll from tobacco is expected to rise to over 8 million, with more than 80% of those deaths projected to occur in low- and middle-income countries (Mathers and Loncar, 2006). If effective measures are not urgently taken, tobacco could, in the 21st century, kill more than 1 billion people. (Peto and Lopez, 2001)

Although often associated with ill-health, disability and death from non-communicable chronic diseases such as lung cancer, heart disease, stroke and respiratory diseases, tobacco smoking is also associated with an increased risk of death from communicable diseases causes including respiratory infections and tuberculosis. Furthermore, exposure to tobacco smoking negatively impacts on health across the life-course. Examples include increased rates of stillbirth and selected congenital malformations during fetal life, death attributed to the sudden infant death syndrome in infancy, disability from respiratory diseases in childhood and adolescence and young adulthood, increased rates of cardiovascular death in relatively young middle-aged adults, and of cancers especially lung cancer particularly later in life.

The adverse repercussions of tobacco use and exposure, however, extend well beyond the health risks to individuals. For families, communities and governments, tobacco use and exposure to second hand smoke represents a significant social and economic handicap, but also importantly represents a major risk factor in a looming epidemic of non-communicable diseases that threatens to undo much of the global health gains so difficultly attained over the past fifty years.

Tobacco use contributes to family poverty cycles whereby expenditure on tobacco can consume a substantial proportion of total household income, displaces other goods and services important for health and wellbeing (such as healthy nutrition or education for children), and reduces the prospects of future family prosperity, and results in debilitating diseases and conditions with high medical costs. Social dislocation represents a considerable burden for families and communities who must care for and cope following the loss of loved ones and valued community members due to tobacco. For governments, significant expenditure of health care to treat tobacco related diseases, and reduced national productivity due to premature death or disability limits government capital for investment in other public services or infrastructure to serve the public good.

Use of tobacco among adults in developing countries is increasing and has now surpassed that of developed countries, where prevalence of tobacco use has begun to decline. Globally, rates of tobacco use, and tobacco attributable mortality are higher in men then women. In many low income countries tobacco is almost exclusively used by males. Of concern, however, is accelerating rates of tobacco use among women. If such trends in tobacco use continue global increases in deaths due to tobacco will largely be driven by increasing tobacco use of women.

The Framework Convention on Tobacco Control

To address the global burden of tobacco, the World Health Assembly, in 2003, unanimously adopted the WHO Framework Convention on Tobacco Control (WHO FCTC). In force since 2005, the main objective of the WHO FCTC is to protect present and future generations from the devastating health, social, environmental and economic consequences of tobacco consumption and exposure. Ratified by over 170 countries as at December 2010, the WHO FCTC currently covers about 90% of the world's population. It is a legally binding treaty which commits Parties to the Convention to develop and implement a series of evidence-based tobacco control measures to regulate tobacco industry marketing activities and sales reach, reduce the demand for tobacco, and provide agricultural alternatives for those involved in farming and producing tobacco (WHO, 2005).

Surveillance of Global Mortality Attributable to Tobacco

Ever since the seminal work by Doll and colleagues in the 1950s (Doll et al., 1950; Doll et al., 1956), there has been substantial interest in measuring the impact of tobacco use on health outcomes at the population level. Article 20 of the WHO FCTC requires Parties to adopt standard methods of data collection to measure both the magnitude of tobacco use and exposure, as well as consequences of tobacco use (WHO, 2005).

Information on tobacco use and exposure have been collected in the WHO STEPwise surveys, the WHO World Health Surveys, and in partnership with the US Centers for Disease Control and Prevention and Ministries of Health through the Global Youth Tobacco Survey, Global School Health Survey, Global School Personnel Survey, Global Health Profession Student Surveys, and the Global Adult Tobacco Survey

WHO is now aiming to expand on its prevalence work with Member States to monitor regularly mortality outcomes associated with tobacco use and exposure. The availability of these data and future updates will add to the capacity of Member States to monitor and evaluate better the impact of their tobacco control strategies.

Method of calculating tobacco attributable mortality

This section will describe the population attributable fraction (PAF) method, one commonly used to estimate mortality that can be attributed to tobacco smoking. Only three pieces of information are required to enable this calculation to be made:

1. the prevalence of tobacco use.
2. the risk of death related to specific causes among tobacco users compared with the risk of death of these same causes among non-users; and
3. vital statistics information on the number of deaths in a population by cause of death, age at death, and sex of the deceased.

The PAF is defined as the proportion of deaths that may be attributed to exposure to tobacco (or any other risk factor). Alternatively, the PAF can also be thought of as the proportional reduction in population disease or mortality that would occur if nobody was exposed to tobacco. Multiplying the number of cause-specific deaths by the PAF results in the number of deaths attributable to tobacco smoking:

$$PAF = \frac{P(RR-1)}{[P(RR-1)+1]}$$

The population attributable fraction (PAF) formula is intuitively simple to understand. It is made up of only two factors: (i) the relative risk (RR) of developing a disease among those exposed to tobacco smoking

compared with those who do not smoke tobacco; and (ii) the prevalence (P) of smoking in the population in question.

The relative risk (RR) measures the risk of dying from a specific cause among those exposed to a factor relative to those not exposed to the same factor. If the risk of dying from a specific disease, when exposed to tobacco smoking, is equal to the risk among those not exposed to tobacco smoking, then the ratio of the two risks will be equal to one. If the risk is higher among those exposed then the relative risk will be greater than one. Therefore the higher the value of (RR-1), the higher the PAF as long as prevalence of tobacco smoking is not zero.

The prevalence of smoking measures the proportion of people in a population who smoke tobacco. As with the relative risk, the higher the prevalence (P), the higher the PAF as long as RR is not equal to 1.

The PAF can only take the value zero when either the relative risk is exactly equal to 1 or prevalence of tobacco use is zero (i.e., nobody uses tobacco).

As an illustration, if the risk of dying from a disease among smokers was 20% and the risk of dying from the same disease among non-smokers was 4%, then the relative risk would be 20% ÷ 4% = 5, i.e. the risk of dying from lung cancer among smokers is five times higher than among non-smokers. If the proportion of smokers in that population was say 30%, then the PAF would be given by

$$PAF = \frac{0.30 \times (5-1)}{((0.30 \times (5-1)) + 1)}$$

yielding a PAF value of 0.55. Multiplying the total number of deaths in a country or to cause specific deaths by the PAF gives the number of deaths that can be attributed to tobacco use among them. It is important to note that information on the smoking status of each deceased person is not necessary for the calculation. What is needed is the prevalence of smoking and the relative risk of death from a specific disease that is caused by tobacco.

Although simple at face value, the dual absences of reliable smoking history and prevalence data in many countries, as well as an accurate count mortality by cause of death makes it difficult to estimate tobacco attributable deaths.

Estimating prevalence: The Smoking Impact Ratio (SIR) method

In this section, we present a method, proposed by Peto *et al.* (1992), to derive proxy estimates of prevalence for use in the PAF formula. This method, known as the Smoking Impact Ratio (SIR) method, is particularly useful for countries that lack good historical data on smoking in their populations.

Using data from a well conducted study in the United States, Peto *et al.* (1992)calculated lung cancer death rates for smokers and never-smokers. Although the SIR method was derived using smoking history measures from CPSII data, any other well conducted cohort study with similar indicators could also be used.

Using lung cancer death data from another country, Peto *et al.* (1992) estimated the Smoking Impact Ratio (SIR) which they defined as the excess mortality from lung cancer in smokers in that country's population relative to the excess mortality in smokers in the reference population (CPSII). SIR can be expressed as:

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

where C_{LC} and N_{LC} are lung cancer rates in the population and in never smokers in a country's population; $S^{\bullet}_{LC}$ and $N^{\bullet}_{LC}$ are the lung cancer rates in smokers and never smokers of the reference population.

The SIR method is useful because it circumvents the need for good data on age at initiation, duration and intensity of smoking - smoking history data that are often lacking in many countries. The only data therefore required to calculate SIR are cause specific death rates for countries.

As the CPS II relative risks used by Peto *et al.* (1992) were not adjusted for potential confounding factors, the level of the calculated risk may theoretically be biased and could in theory result in upwardly biased relative risks. To minimize this potential source of bias, Peto *et al.* (1992) conservatively halved the excess mortality in smokers from all diseases other than lung cancer.

The SIR method has been well received and has been applied and refined in a variety of reports and publications that have produced tobacco related burden of disease estimates at regional and global levels. These refined methods have been reviewed in greater detail by Khanna and Stevens (2011).

The proportion of smokers in a reference population is equal to the SIR of that reference population. In specific, the lung cancer rates in the underlying mix of smokers and non-smokers in the CPSII study were matched for each five-year age interval with those of the country population to obtain the SIR. Since lung cancer in non-smokers is rare and large studies are needed to accurately determine non-smoker lung cancer mortality, Peto *et al.* (1992) used the lung cancer rates of the CPSII population (i.e., they assumed NLC = N*LC). Relative risks were obtained from the CPSII study.

To estimate tobacco-attributable deaths, population attributable fractions (PAF) for each country-age-sex group were calculated using equation 2:

$$PAF = \frac{P(RR-1)}{[P(RR-1)+1]}$$

with prevalence (P) set equal to the SIR for each age and sex. The PAFs were applied to national mortality statistics, by age and sex, to estimate tobacco-attributable deaths for each category.

Relative Risks for the various causes of death

	Tobacco related disease *	Males	Females
1	Upper aerodigestive cancer	8.1	6.0
2	Stomach cancer	2.2	1.5
3	Liver cancer	2.3	1.5
4	Pancreas cancer	2.2	2.2
5	Cervix uteri cancer	-	1.5
6	Bladder cancer	3.0	2.4
7	Myeloid leukemia	1.9	1.2
8	Kidney and other urinary cancer	2.5	1.5
9	Ischaemic heart disease		
	30-44 years	5.5	2.3
	45-59	3.0	3.8
	60-69	1.9	2.5
	70-79	1.4	1.7
	80 years & over	1.1	1.4
10	Stroke		
	30-44 years	3.1 [a]	4.6
	45-59	3.1	4.6
	60-69	1.9	2.8
	70-79	1.4	2.0
	80 years & over	1.1	1.0 [b]
11	Hypertensive heart disease	2.0	2.1
12	Other cardiovascular diseases	2.2	2.0
13	Chronic obstructive pulmonary disease	10.8	12.3
14	Other respiratory diseases	1.9	2.2
15	Tuberculosis	1.6	1.6

Notes: a - Estimate for 45-59 used for this age group
b - Set to 1 since a relative risk of less than 1 is implausible

As the CPS II relative risks used by Peto *et al.,* (1992) were not adjusted for potential confounding factors, the level of the calculated risk that they used was criticised as producing upwardly biased relative risks. To minimize this potential source of bias, Peto *et al.* (1992), had conservatively halved the excess mortality in smokers from all diseases other than lung cancer. To address this criticism, Thun *et al.* (2000) using the same CPSII data produced relative risks for tobacco after adjusting for a range of demographic and behavioural confounders. These adjusted relative risks have been used to produce the deaths attributable to tobacco provided in this report.

Quality of vital statistics data on deaths by cause of death, age and sex of deceased

To assist countries classify deaths to allow for meaningful and valid comparison groupings, the WHO has developed the International Classification of Diseases (ICD) and encourages countries to use the classification (WHO 1992). The data presented in this report makes use of the ICD classified data provided to WHO by countries. In addition this report only provides information for communicable and non communicable causes known to be related to tobacco. Deaths from external causes (e.g., death from fires) have not been included in the analyses for this report.

Countries were divided into those with excellent vital registration, those which required medium level modelling and those countries whose data had to be modelled for the analysis. The methods used for this division by quality of the data have been published in the 2008 WHO report titled "The Global Burden of Disease 2004 Update".

Vital registration data were used to estimate deaths by cause in countries where coverage was 85% or higher. Vital registration data is provided to WHO on an annual basis. Where registration data was not available for the year 2004, the most recent data available since 1980 (up until 2004) were used to project the cause distribution for 2004. For countries with less then 85% coverage, cause of death modelling was used to adjust proportions of deaths by cause age and sex.

For countries without usable vital registration data, cause of death modelling was applied at the country level to estimate deaths by cause age and sex based on all cause mortality levels, gross national income per capita and region.

Example of calculation for PAF using SIR

The example below works through the methods described above and show how to calculate tobacco attributable deaths in country X using hypothetical data in males. The objective of this exercise is to calculate SIR and PAF (with SIR used as proxy for P in the PAF formula):

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

$$PAF = \frac{P(RR - 1)}{[P(RR - 1) + 1]}$$

Table 1: Example of calculation of number, proportion and rate of deaths attributable to tobacco

Age group (years)	Population size of Country X	Number of lung cancer deaths for Country X	Country X lung cancer death rates	Lung cancer mortality rates in Reference Population		SIR	Cause A relative risk of death from tobacco use	Population Attributable Fraction for cause A for Country X
				Current Smoker	Never Smoker			
	(1)	*(2)*	*(3)= (2)/(1)*	*(4)*	*(5)*	*(6)= (3-5)/(4-5)*	*(7)*	*(8)= (6*(7-1)/(6*(7-1)+1)*
30-44	3,650,000	150	4.1	10	2	0.26	5.5	0.5427
45-59	2750000	1600	58.2	120	7	0.45	3.0	0.4753
60-69	1200000	2200	183.3	500	17	0.34	1.9	0.2366
70-79	750000	2000	266.7	1000	30	0.24	1.4	0.0889
80+	275000	700	254.5	1200	46	0.18	1.1	0.0178
Total	8,625,000	6650	77.1					

Table (continued)

Age group (years)	Population Attributable Fraction for cause A for Country X	Number of Cause A deaths as per Vital Registration or modeled	Number of cause A deaths attributed to tobacco for Country X	Age specific death rate for all cause A deaths	Age specific death rate attributable to tobacco for cause A
	(8)= (6(7-1)/(6*(7-1)+1)*	*(9)*	(10) = (8) * (9)	(11) = ((9) / (2))	*(12) = (9) / (1) *100*
30-44	0.5427	450	244	12	7
45-59	0.4753	4000	1901	145	69
60-69	0.2366	5000	1183	417	99
70-79	0.0889	7250	645	967	86
80+	0.0178	4500	80	1636	29
Total		21200	4053	246	47

Note: All rates expressed per 100,000 population

Columns 1 and 2 provide population and mortality data from lung cancer in broad age intervals for males in Country X and lung cancer mortality rates in smokers ($S_{LC}^{\bullet}$) and never smokers $N_{LC}^{\bullet}$ in a reference population.

Column 3 provides an estimate of age-specific lung cancer death rates - calculated by dividing the number of lung cancer deaths by the population at each age.

Columns 4 and 5 provide lung cancer mortality rates for never smokers and current smokers in the reference population (in the absence of data on lung cancer rates in never smokers in Country X, it is assumed that lung cancer mortality rates in never smokers in the reference population is the same as lung cancer rates in never smokers in country X i.e. NLC = N*LC).

Column 6 presents the calculated Smoking Impact Ratio (SIR) for Country X.

Column 7 presents the relative risks for cause of death A

Column 8 provides estimates of the population attributable fractions for cause A in country X.

Column 9 provides the number of deaths from Cause A in country X (either from the vital registration system of Country X or as a result of modelling by WHO)

Column 10 provides information on the number of Cause A deaths attributed to tobacco for Country X

Columns 11 provides the age specific death rate for all cause A deaths for Country X

Column 12 provides the age specific death rate attributable to tobacco for cause A for Country X

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