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Mortality attributable to smoking in Vietnamese men in 2008

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ABSTRACT

Objective. Smoking prevalence among Vietnamese men is among the highest in the world. Our aim was to provide estimates of tobacco attributable mortality to support tobacco control policies.

Method. We used the Peto–Lopez method using lung cancer mortality to derive a Smoking Impact Ratio (SIR) as a marker of cumulative exposure to smoking. SIRs were applied to relative risks from the Cancer Prevention Study, Phase II. Prevalence-based and hybrid methods, using the SIR for cancers and chronic obstructive pulmonary disease and smoking prevalence for all other outcomes, were used in sensitivity analyses.

Results. When lung cancer was used to measure cumulative smoking exposure, 28% (95% uncertainty interval 24–31%) of all adult male deaths (>35 years) in Vietnam in 2008 were attributable to smoking. Lower estimates resulted from prevalence-based methods [24% (95% uncertainty interval 21–26%)] with the hybrid method yielding intermediate estimates [26% (95% uncertainty interval 23–28%)].

Conclusion. Despite uncertainty in these estimates of attributable mortality, tobacco smoking is already a major risk factor for death in Vietnamese men. Given the high current prevalence of smoking, this has important implications not only for preventing the uptake of tobacco but also for immediate action to adopt and enforce stronger tobacco control measures.

Introduction

Smoking prevalence among Vietnamese men is one of the highest in the world with smoking an integral part of male social behavior (Morrow and Barraclough, 2003; The Tobacco Atlas Online). Reliable smoking prevalence data are not available prior to 1990. A regional study in the 90s reported smoking prevalence of 70% (Jenkins et al., 1997) with the first national estimate of prevalence in excess of 60% for Vietnamese males (General Statistics Office, 1994). Given the very low smoking prevalence among women, per capita annual cigarette consumption implies an annual consumption of about 2600 cigarettes per adult male in the mid-90s (Guindon and Boisclair, 2003). Taken together these data suggest that past consumption has been substantial for men.

Over the last decade, Vietnam has implemented the National Tobacco Control Policy 2000–2010 (Government of Vietnam, 2000) aimed at reducing tobacco-related morbidity and mortality through a number of public interventions including excise tax and advertising bans, but the nation is in a relatively early stage in its tobacco control efforts (Levy et al., 2006). The paradox surrounding the tobacco control policy in Vietnam arises from the contradictory position of a government that benefits from manufacturing of tobacco products, and is also responsible for controlling tobacco consumption. Even with some evidence of success, limited resources and competing interests have impeded the effective implementation of the policy to its full potential. This is reflected in current smoking prevalence which has remained high among adult males at almost 50% (GATS Vietnam Working Group, 2010; General Statistics Office, 2007). Exposure to passive smoking also remains exceedingly high (67.6%) among non-smokers (GATS Vietnam Working Group, 2010). Despite some delays, recent passing of the Tobacco Harm Prevention Law is expected to strengthen implementation of the policy (Ministry of Health (Vietnam), 2012).

Such a policy framework can benefit from a better understanding of the current and future health effects of tobacco. This study applies the method of Peto and Lopez (Peto et al., 1992) to the first ever national estimates of causes of death for Vietnam (Ngo et al., 2010; Nguyen et al., 2011) in order to quantify mortality attributable to smoking in 2008. Given the low smoking prevalence among females the focus is on male smoking attributable mortality. Since smoking risks have not previously been published for Vietnam, the study provides analysis of uncertainty and sensitivity analyses. These estimates

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are provided to emphasize the urgency of strengthening tobacco control initiatives in Vietnam.

Methods

We used cause-specific mortality estimates from the first burden of disease and injury study for Vietnam in 2008 (Nguyen et al., 2011) based on a nationally representative cause of death survey using verbal autopsy methods (Ngo et al., 2010).

Relative risk estimates for cause-specific mortality related to tobacco use were derived from a re-analysis of the American Cancer Society Cancer Prevention Study, Phase II (CPS-II) which included adjustment for important covariates (Table 1) (Ezzati et al., 2005a; Ezzati et al., 2005b; Oza et al., 2011).

Base analysis

Following the Peto–Lopez method (Peto et al., 1992), we used estimated lung cancer mortality in Vietnam as an indirect indicator of the accumulated hazards of smoking taking into account the time lag between exposure and outcome. However, lung cancer diagnosis by verbal autopsy is difficult at older ages and with a small number of lung cancer deaths in the sample, the resulting lung cancer mortality age pattern in the first Vietnam burden of disease study was unstable. Consequently, we used the Vietnam burden of disease study to derive the level of lung cancer mortality for 2008 but the age pattern was smoothed by applying the age pattern for males in China 2004–2005 (Chinese Center for Disease Control, personal communication 2011).

Table 1
Relative risk estimates of disease specific mortality for CPS-II smokers relative to never-smokers.[a]

Disease outcome (ICD-10 codes)	Age group (years)	Males CPS-II RRs (95% CI)
Lung cancer (C33–C34)	≥30	21.3 (17.7–25.6)
Upper aerodigestive tract cancer (C00–C14, C15, C30–C32)	≥30	8.1 (5.7–11.7)
Other cancer		
Stomach cancer (C16)	≥30	2.2 (1.8–2.7)
Liver cancer (C22)	≥30	2.3 (1.5–3.8)
Pancreatic cancer (C25)	≥30	2.2 (1.7–2.8)
Bladder cancer (C67)	≥30	3.0 (2.1–4.3)
Myeloid leukemia[b] (C92)	≥30	1.9 (1.3–2.9)
Colorectal cancer (C18–C21)	≥30	1.3 (1.2–1.5)
Chronic obstructive pulmonary disease (J40–J44)	≥30	10.8 (8.4–13.9)
Other respiratory diseases (J00–J22, H65–H66, J30–J39, J45–J47, J60–J80, J82–J89, J91–J98)	≥30	1.9 (1.5–2.4)
Tuberculosis[c] (A15,A16,A19)	≥30	1.6 (1.2–2.3)
Cardiovascular diseases		
Ischemic heart disease (I20–I25)	30–44	5.51 (2.47–12.25)
	45–59	3.04 (2.66–3.48)
	60–69	1.88 (1.70–2.08)
	70–79	1.44 (1.27–1.63)
	≥80	1.05 (0.78–1.43)
Cerebrovascular disease (I60–I69)	30–44	No estimates (insufficient events)
	45–59	3.12 (2.10–4.64)
	60–69	1.87 (1.43–2.44)
	70–79	1.39 (1.09–1.77)
	≥80	1.05 (0.63–1.77)
Other cardiovascular diseases (I10–I15, I26, I28, I47–I49, I70–I84, I86–I89)	≥30	2.15 (1.94–2.38)
Diabetes mellitus (E10–E14)	≥30	1.42 (1.10–1.83)

The 95% confidence interval for the effect of smoking and cardiovascular disease (CPS-II) in a number of age groups crossed the null. We included all draws of the relative risk distribution including those that show a protective effect in the uncertainty analysis because the overall relationship for the risk factor across all ages for these diseases is statistically significant.
ICD-10 = International Classification of Diseases, 10th revision (World Health Organization, 1992).
[a] Source: Re-analysis of CPS-II data (Ezzati et al., 2005a, 2005b; Oza et al., 2011). RRs were estimated from Cox proportional hazard models with never smokers as the reference group. All risks were adjusted for age, race, education, marital status, "blue collar" occupation, weekly consumption of vegetables and citrus fruit, vitamin use, alcohol use, aspirin use, body mass index, exercise, dietary fat consumption. In addition, cancer RR were also adjusted for additional covariates including family history of cancer (Ezzati et al., 2005a) and cardiovascular RRs were also adjusted for hypertension and diabetes at baseline (Ezzati et al., 2005b).
[b] The relative risk for myeloid leukemia was applied to all leukemias (C91–C95).
[c] Relative risks for tuberculosis are from a separate meta-analysis (Lin et al., 2007) because there were too few cases in CPS-II to make estimates.

The smoothed lung cancer rate for Vietnam males in 2008 includes smokers and non-smokers and is considerably lower than the US CPS-II smoker lung cancer rates (from the CPS-II reanalysis) but is higher than 1986–88 China smoker lung cancer rates (Jill Boreham, personal communication 2011) at older ages (Fig. 1) as these rates are from an earlier phase of the tobacco epidemic in China. Non-smoker lung cancer rates in China are higher than in the CPS-II population, probably as a result of exposure to other lung cancer risk factors such as coal use for cooking and heating (Ezzati and Lopez, 2003).

The proportion of lung cancer attributable to smoking was estimated as the absolute difference between the smoothed Vietnam lung cancer death rate and the estimated level in non-smokers. In the absence of Vietnam non-smoker lung cancer rates, we used male non-smoker lung cancer mortality rates from the Global Burden of Disease Study 2010 (GBD 2010) where a negative binomial regression of pooled cohort studies was used to generate separate age–sex-specific non-smoker lung cancer mortality rates for 1) China, 2) countries in the high-income Asia-Pacific region, and 3) all other countries (Lim et al., 2012). We used the male non-smoker lung cancer mortality rate for the "all other countries" group as the non-smoker lung cancer rate for Vietnam.

For causes other than lung cancer, we calculated the Smoking Impact Ratio (SIR), defined as the Vietnam lung cancer mortality in excess of non-smokers, relative to excess lung cancer mortality for the reference group of smokers in the CPS-II population (Ezzati and Lopez, 2003):

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

where C_{LC} is the smoothed age–sex-specific lung cancer mortality rate for 2008 in Vietnam; N_{LC} is the age–sex-specific lung cancer mortality rate of non-smokers for all countries outside China and high-income Asia-Pacific region as estimated in GBD 2010. S^*_{LC} and N^*_{LC} are age–sex-specific lung cancer mortality rates for smokers and non-smokers, respectively, in the reference population CPS-II. The numerator and denominator are normalized with the respective non-smoker lung cancer mortality rates (Ezzati and Lopez, 2003).

Conceptually, the SIR converts the smokers in the Vietnam population with different smoking histories into equivalents of smokers in the CPS-II reference population, where hazards for smoking-related diseases have been measured (Ezzati and Lopez, 2003).

For each disease, the fraction of deaths attributable to smoking was estimated by using the standard population attributable fraction (PAF) formula (Greenland and Robbins, 1988):

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

with prevalence, *P*, set to SIR for each age group and *RR* the cause-specific relative risks from the CPS-II re-analysis (Table 1).

Sensitivity analysis

Prevalence-based method

A sensitivity analysis was also carried out using the conventional prevalence-based approach. PAFs were calculated by applying Vietnam current tobacco smoking prevalence data (Table 2) (GATS Vietnam Working Group, 2010) to relative risks from the CPS-II re-analysis. (Table 1).

Hybrid method

In addition, we followed the approach used in the GBD 2010 study (Lim et al., 2012) and used the Peto–Lopez method, which uses lung cancer mortality as a marker of cumulative population exposure to smoking for conditions where there is a long lag between exposure and outcome such as cancers and

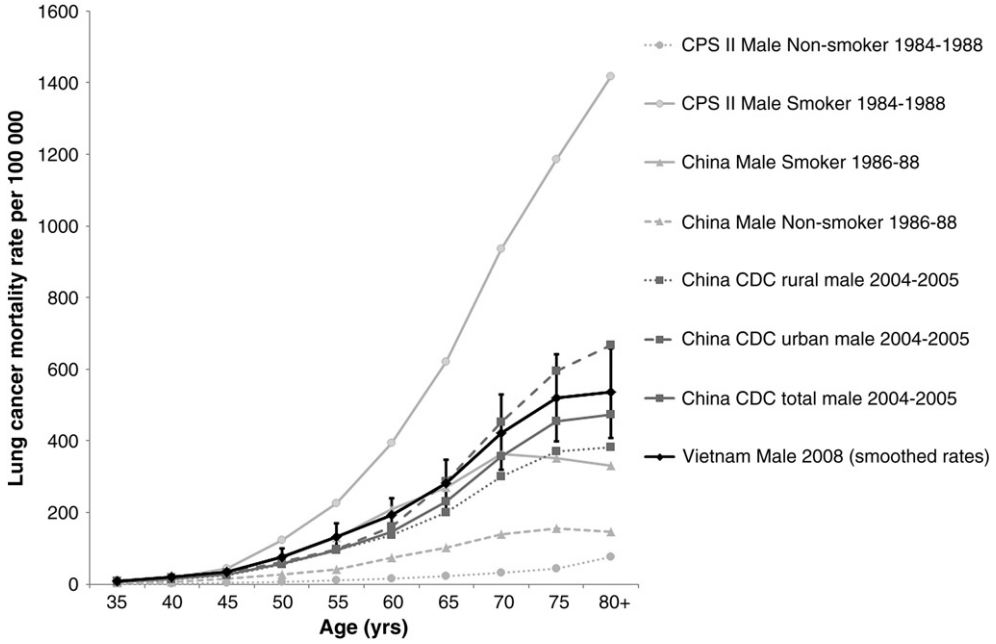

Fig. 1. Lung cancer mortality rates for Vietnam males 2008, China CDC males 2004-2005, CPS II male current smokers and non-smokers and Chinese male smokers and non-smokers 1986–88.

chronic obstructive pulmonary disease and then used tobacco smoking prevalence applied to CPS-II relative risks for cardiovascular diseases, tuberculosis, other respiratory diseases and diabetes where there is a shorter lag between exposure and outcome.

All PAFs were applied to mortality estimates for Vietnam in 2008 for the selected disease outcomes (Nguyen et al., 2011).

Uncertainty analysis

Monte Carlo simulation–modeling techniques were used to present uncertainty ranges around point estimates reflecting the main sources of sampling uncertainty in the calculations using Ersatz software version 1.2 (Barendregt, 2009–2012). Beta distributions were specified for smoking prevalence estimates. For the relative risk input variables we used the Ersatz random function *ErRelativeRisk* (Barendregt, 2010). For uncertainty around the CPS-II smoker and non-smoker lung cancer mortality rates, we modeled the uncertainty with a gamma distribution (Gelman et al., 2004).

Sampling uncertainty of lung cancer deaths in Vietnam verbal autopsy data was estimated by specifying a multinomial distribution. Based on data from a similar study in Thailand (Porapakkham et al., 2010) we assumed that the lung cancer deaths could vary by an additional 10% as a result of misclassification of deaths in the verbal autopsy sample from which the cause of death estimates were derived.

Table 2
Prevalence of smoking by age and sex in Vietnam.

	Prevalence of daily tobacco smoking*	
Age group (years)	Males	Females
35–39	47.9%	1.0%
40–44	49.4%	0.9%
45–49	55.0%	1.7%
50–54	53.2%	2.7%
55–59	52.4%	2.5%
60–64	41.5%	2.6%
65–69	38.2%	4.8%
70–74	28.6%	0.5%
75–79	21.1%	2.3%
80+	22.0%	2.8%
35+	47.4%	1.9%

Source: Global Adult Tobacco Survey (GATS) Viet Nam 2010 (GATS Vietnam Working Group, 2010).

* Daily smokers: Those who currently smoke cigarettes (includes hand-rolled and manufactured) on a daily basis.

Results

The SIR method using lung cancer to measure cumulative smoking exposure estimated 70,236 attributable deaths (95% uncertainty interval 60,900–77,800) accounting for 24% (95% uncertainty interval 21–27%) of all male deaths and 28% (95% uncertainty interval 24–31%) of all adult male deaths 35 years and older in Vietnam in 2008 (Table 3). Lower estimates of smoking attributable mortality were obtained in the prevalence-based sensitivity analysis where tobacco-attributable mortality accounted for 24% (95% uncertainty interval 21–26%) of all adult male deaths but with overlapping confidence intervals. The hybrid method yielded intermediate estimates with 26% (95% uncertainty interval 23–28%) of all adult male deaths attributable to smoking.

The cause-specific contributions to total attributable deaths varied slightly depending on the method used. PAFs for all outcomes were slightly lower when using the prevalence-based method compared with the Peto–Lopez method (Table 3).

Discussion

Despite inevitable uncertainty with regard to the precise level of mortality attributable to smoking in Vietnam, we estimate that tobacco is an important cause of preventable premature death among males. In Vietnam, as in developed countries, about half (52%) of those killed by tobacco were in middle age (35–69 years) (Peto et al., 1992) and a third were 35–60 years of age.

The prevalence-based method yielded lower smoking attributable deaths compared with baseline results estimated using the indirect Peto–Lopez method. It is important to mention that smoking prevalence and tobacco consumption may be underestimated in recent surveys in Vietnam and do not take into account smuggled cigarettes (Ha et al., 2006; Hoang et al., 2006).

Our estimates for Vietnam in 2008 are higher than previous estimates of tobacco attributable mortality using similar methods for developing regions of the Western Pacific (WPR-B), dominated by China in terms of population but which also includes Vietnam (15% of total adult male mortality) (Ezzati and Lopez, 2003) but closer to estimates for the South East Asia region in 2010 which includes Vietnam in GBD

Table 3
Estimated population attributable fractions (PAFs) and deaths attributable to smoking in Vietnamese men 2008.

Disease cause	Base analysis		Sensitivity analysis			
	Peto–Lopez method		Prevalence-based method		Hybrid method	
	PAFs	Attributable deaths	PAFs	Attributable deaths	PAFs	Attributable deaths
Lung cancer	90.9%	13,981	86.9%	13,367	90.9%	13,981
Upper aerodigestive tract cancer	78.0%	3829	72.7%	3572	78.0%	3829
Other cancer	36.5%	12,100	30.2%	9997	36.5%	12,100
Chronic obstructive pulmonary disease	79.3%	11,195	71.3%	10,055	79.3%	11,195
Tuberculosis	22.2%	2288	16.5%	1705	16.5%	1705
Other respiratory diseases	37.0%	4073	24.7%	2722	24.7%	2722
Cardiovascular diseases	23.8%	21,906	19.3%	17,796	19.3%	17,796
Diabetes mellitus	15.9%	864	11.8%	645	11.8%	645
Total tobacco attributable deaths		70,236		59,858		63,973
Uncertainty range total deaths		60,900–77,800		53,100–64,900		56,500–69,300
% Adult male deaths (>35 years)		28.2%		24.0%		25.7%
Uncertainty range % adult male deaths (>35 years)		24.4–31.2%		21.3–26.0%		22.7–27.8%
% All male deaths		24.2%		20.6%		22.0%
Uncertainty range % total male deaths		21.0–26.8%		18.3–22.3%		19.4–23.9%

Note: In uncertainty intervals the number of deaths has been rounded to the nearest 100.

2010 using the hybrid method (22% of all adult male deaths 35+) (Lim et al., 2012).

In our study, however, we assumed that no deaths classified to other medical causes were attributable to smoking, a category often included in studies of tobacco attributable mortality (Ezzati and Lopez, 2003; Groenewald et al., 2007; Peto et al., 1992). Other medical conditions is a rest category for the remainder of all conditions excluding those specified in Table 3 and other communicable, maternal, neonatal and nutritional disorders; neurological, mental and behavioral conditions; cirrhosis of the liver, congenital anomalies, and injuries. However, evidence of an association with smoking is considered insufficient for many of these conditions (English et al., 1995; Ridolfo and Stevenson, 2001). Furthermore, we considered that mortality estimates from verbal autopsy for these residual conditions were less reliable (Nguyen et al., 2011). We did, however, include diabetes as an outcome as in the GBD 2010 study.

There is also uncertainty around our estimates beyond sampling uncertainty, mainly because of the lack of reliable estimates of the risks of smoking in Vietnam. It could be argued that extrapolating overall risks from the US to a country such as Vietnam which may be at a different stage of the tobacco epidemic, could result in misleading information (Hunt et al., 2005).

CPS-II relative risks are from a population smoking an average of 20 cigarettes per day (Peto et al., 1992) while in Vietnam the average daily consumption is 11–13 cigarettes per person, similar to that in China (General Statistics Office, 1994, 2000; Ministry of Health, 2003). Nevertheless, the CPS-II relative risks estimates were used in the base analysis because they are considered robust, have published 95% confidence intervals, have been systematically and consistently adjusted for major covariates and enable comparisons with other studies using the same methodology (Ezzati et al., 2005a, 2005b; Thun et al., 2000) including the GBD 2010 study (Lim et al., 2012). The validity of tobacco attributable mortality estimates using the indirect method has been confirmed against alternative methods that account for accumulated hazards of smoking and existing evidence indicates that extrapolation of hazards from CPS-II to other populations is a valid option (Ezzati et al., 2005a, 2005b; Ezzati and Lopez, 2003). We felt that in the absence of epidemiological studies from Vietnam, extrapolation of CPS-II relative risks was necessary although it remains a source of additional uncertainty.

There are different approaches which may be used to calculate tobacco attributable mortality in Vietnam, including using relative risks from China instead of US risks. Even when comparing different sources from China, relative risks vary across several prospective cohort studies that have examined the relationship between tobacco smoking and mortality (Chen et al., 1997; Gu et al., 2009; He et al., 2002; Lam et al., 1997; Niu et al., 1998; Yuan et al., 1996). Nevertheless, most published studies have reported low relative risks in the range of 1.2–1.4 for males (Chen et al., 1997; Gu et al., 2009; He et al., 2002; Liu et al., 1998; Niu et al., 1998; Yuan et al., 1996). A similar, low effect of smoking on lung cancer mortality has also been observed in other Asian countries (Huxley et al., 2007). The lower relative risks undoubtedly reflect the shorter duration of smoking, lower numbers of cigarettes smoked in the past, the later age of smoking initiation, shorter duration of followup and greater exposure to other environmental carcinogens among non-smokers in some Asian countries (Gu et al., 2009; Huxley et al., 2007).

In China, although total solid fuel use is similar to that in Vietnam, coal use is more prevalent (World Health Organization, 2010). Since the evidence for a link between coal use and the development of lung cancer is much stronger than for biomass (Smith et al., 2004), in the GBD 2010 study, China non-smoker lung cancer mortality rates were assumed to apply specifically to China and background lung cancer rates in Vietnam were assumed to be the same as in all other countries.

Non-smoker lung cancer mortality rates for Vietnam from GBD 2010 were based on a pooled analysis of eleven cohort studies representing diverse demographic subpopulations, countries, and time periods. Studies were categorized as China, high-income Asia-Pacific, and all other countries (Lim et al., 2012). A limitation of this study, however, is that while this method has the benefit of drawing strength across many longitudinal studies with large sample sizes, the seven cohorts categorized as "all other countries" are exclusively North American studies and may not be appropriate for use in Vietnam.

We carried out these analyses for Vietnam using relative risks estimates from various sources including China and the US (data not shown) as well as various alternative background non-smoker lung cancer mortality rates resulting in a wide range of estimates. In the end we opted to use methods similar to those used in the GBD 2010 study to enable comparisons with other studies using this standardized methodology.

Levy and colleagues used a simulation model (SimSmoke) to predict deaths attributable to smoking in Vietnam. Using a higher overall prevalence of smoking (54.4% of the male population ages 15 and above) applied to all cause relative risks of 1.35 based on China the model predicted 33,472 deaths for males in Vietnam in 2008 (about 13% of adult male mortality) and 80,614 deaths (32% of adult male mortality) using relative risks of 2.4 based on US (Levy et al., 2006). This latter estimate by Levy et al. is comparable with estimates from the US and UK (about 30% of adult male mortality) at the height of their epidemics (Peto et al., 1992) but slightly higher than estimates for Vietnamese males in 2008 in our study using prevalence-based

methods and CPS-II relative risks. This could be due firstly to the higher overall smoking prevalence in the Levy et al. study compared to that used in our study. Secondly, effect sizes for all-cause mortality were applied to deaths at all ages in the Levy et al. study and this approach assumes the same age structure and cause distribution in Vietnam as in the US cohort and extends the effects to infants and children and causes not related to smoking.

There is a risk of overestimating the hazard with the indirect method if there has been a sharp decline in smoking prevalence in recent years. This is unlikely in Vietnam where recent surveys do not suggest an obvious declining trend (GATS Vietnam Working Group, 2010; General Statistics Office, 2007), although the potential underreporting and inconsistent definitions of smokers between studies make it difficult to assess change. Moreover, recent analyses based on US data suggest that this exaggeration is likely to be small (Oza et al., 2011).

Conclusion

Despite the different methodological options applied, we have obtained a remarkably consistent range of tobacco-attributable mortality in Vietnam, around a quarter of all adult male deaths. This suggests that tobacco is already a major risk factor for adult male survival in Vietnam. The high current smoking prevalence among Vietnam males has important implications not only for preventing the uptake of tobacco but also for developing and implementing effective smoking cessation policies. While Vietnam has made significant progress in tobacco control policy development and implementation, it still faces many challenges in addressing the health impacts of tobacco use and there is an urgent need to adopt and enforce stronger tobacco control measures. This national assessment provides important evidence for policy and health service planning as Vietnam moves forward with tobacco control initiatives.

Author contributions

Rosana Norman conceived, designed, and coordinated the study, analyzed the data and wrote the manuscript. Hideki Higashi, Emily Carnahan and Jan Barendregt contributed to data analysis and manuscript review. Bui Ngoc Linh and Nguyen Thanh Huong contributed to data interpretation and manuscript review. Theo Vos and Alan Lopez contributed to conception and design, data interpretation and revised the manuscript critically for important intellectual content. All authors approved the final version to be published.

Conflict of interest statement

JJB owns Epigear International, which sells the Ersatz software used in the analysis. Other authors declare no conflicts of interest.

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