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REVIEW

Secondhand Smoke and CVD in Low- and Middle-Income Countries

A Case for Action

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Secondhand tobacco smoke (SHS) is an environmental toxin and an established cause of cardiovascular disease in nonsmokers. Smoke-free laws reduce SHS and its downstream cardiovascular disease, but until recently, evidence to support smoke-free law implementation in low- and middle-income country settings was limited. In 14 low- and middle-income nations surveyed by the Global Adult Tobacco Survey, active smoking prevalence in adults (⩾15 years old) was universally higher in men (range 21.6–60.2%) than in women (0.5–24.4%), and the highest burden of SHS exposure was in women (strong positive association between male/female active smoking ratio and female SHS exposure prevalence). A systematic review was conducted of MEDLINE-indexed studies of self-reported SHS exposure and cardiovascular harms in low- or middle-income nations. Eight papers reported the association of SHS with ischemic heart disease, and four reported the association of SHS with stroke. For all the studies, and almost all sources of SHS surveyed, a strong positive association between SHS and ischemic heart disease (main relative odds ratio range 1.17–2.36) and SHS and stroke (odds ratio or hazard ratio: 1.41–1.49). Prevalence of SHS exposure is high in low- and middle-income nations, especially among women. Epidemiologic evidence supports the conclusion that SHS harms are the same across low-, middle-, and high-income nations. Governments have an obligation to protect citizens from SHS exposure, enforcing smoke-free legislation and providing public education about SHS harms.

Involuntary exposure to secondhand tobacco smoke (SHS) increases the risk of ischemic heart disease (IHD) and lung cancer in nonsmoking adults and likely increases stroke risk [1,2]. Reduced myocardial infarction rates after implementation of smoke-free policies in specific jurisdictions support the hypothesis that IHD risk declines rapidly when SHS exposures are reduced [3]. Therefore, SHS is a cause of cardiovascular disease (CVD) preventable by public health policy.

Most past studies of the public health burden attributable to tobacco smoking have underestimated tobacco's contribution to global morbidity and mortality by neglecting SHS [4,5]. Likewise, past tobacco-control policy analyses have often underestimated the policy impact of workplace and public space smoking bans by projecting reductions in active smoking exposures alone [6–9].

One in 10 CVD deaths are attributable to active smoking, and approximately 40% of the global tobacco-related CVD burden is borne by

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low- and middle-income nations [4]. Furthermore, many of the low- and middle-income nations have high male smoking rates, but substantially lower female rates so that nonsmoking women may be more likely to be exposed in the home. A 2010 study of the burden of disease attributable to SHS in 192 countries estimated that 603,000 deaths, including 379,000 IHD deaths and 1% of global mortality were due to SHS exposures in 2004 [10]. That study relied on incomplete exposure data in adults and SHS effects on IHD estimated mostly from high-income nation studies, gaps filled in part by recent publication exposure estimates from the Global Adult Tobacco Survey (GATS) [11], and recent epidemiologic studies of the association between SHS and IHD and stroke in low- and middle-income nations [12–18].

Smoke-free laws are a cornerstone policy arm of global tobacco-control policy, incorporated in the World Health Organization (WHO) Framework Convention for Tobacco Control [19]. In this paper, we review adult SHS prevalence data from the GATS and studies of SHS and CVD in low- and middle-income nations in order to present the case for preventing CVD by implementing smoke-free laws worldwide. We present evidence that SHS is an important public health problem in low- and middle-income nations, where women are often the main "innocent victims" of SHS.

PREVALENCE OF SECONDHAND SMOKE EXPOSURES IN LOW- AND MIDDLE-INCOME NATIONS: THE GLOBAL ADULT TOBACCO SURVEY

In the United States, in 2010, 19.3% of adults $\geqslant$18 years were active smokers [20]. When a sensitive biomarker such as serum cotinine $\geqslant$5 ng/ml was used to define SHS exposure, approximately 37% of U.S. adults were estimated to be exposed to SHS (prevalence was higher in ages <20 years, the poor, and African Americans) [21]. However, SHS exposure has declined along with active smoking in high-income nations [21].

Active smoking declines have not been replicated in many low- and middle-income nations, and until recently, SHS prevalence was unknown in these nations. In 2007, WHO sponsored the nationally representative GATS in 16 low- and middle-income nations (Bangladesh, Brazil, China, Egypt, India, Indonesia, Mexico, Pakistan, Philippines, Poland, Russian Federation, Thailand, Turkey, Ukraine, Uruguay, and Vietnam). Data from only 14 sites were available for this review (Pakistan and Indonesia data not available) [11]. GATS comprised multistage stratified samples of urban and rural men and women $\geqslant$15 years of age in each country. Prevalence of self-reported active smoking and SHS exposures were weighted in order to provide nationally representative estimates (Table 1, Supplemental Table 1). Most countries elicited self-reported public place SHS exposure among persons visiting those places within the prior 30 days.

Active smoking prevalence was higher in men than in women in all the GATS nations, but home SHS exposures were common in men and women alike (Table 1, Supplemental Table 1). Though the exposure denominator in Table 1 was smokers and nonsmokers, a similar prevalence was found in nonsmokers (Supplemental Table 2). The GATS nations with the lowest levels of SHS have the most active tobacco-control policies (Brazil, Mexico, Thailand, and Uruguay). The nations listed as having smoke-free legislation have expanded the scope of their laws to cover more public spaces since GATS was conducted [22].

Male active smoking was the driver of female SHS exposures at home or at work, especially in countries with high male and low female active smoking prevalence (high male/female active smoking ratios) (Figs. 1 and 2). The same strong association between male/female active smoking ratio and SHS among female nonsmokers was observed in the nations reporting SHS exposures in nonsmokers only (Supplemental Fig. 1). Variability in female SHS among nations with similar male/female ratios, such as Mexico and Turkey, could be explained by different male smoking patterns, relatively higher rates of both male and female smoking in some nations (e.g., Turkey), or SHS under- or over-reporting.

HOW DOES SHS CAUSE CVD?

SHS is also known as environmental tobacco smoke or passive smoking. SHS is a combination of mainstream smoke exhaled by active smokers and side stream smoke given off by smoldering cigarettes or other smoked tobacco sources. Human subjects studies have documented that SHS exposure leads to both acute and chronic damage to the cardiovascular system. Acutely, SHS causes platelet activation, causes coronary artery endothelial dysfunction [23,24], and impairs heart rate variability [25] similar to the effects of active smoking

Table 1. Active smoking and prevalence of selected SHS exposures (%) in 14 low- and middle-income nations, the Global Adult Tobacco Survey, 2007–2009 [11]. Smoke-free workplace or public space laws status obtained from the 2011 World Health Organization, Tobacco Control Country Profiles report (reporting on laws as of December 31, 2010) [22]

		SHS exposures among those visiting these places		
	Active smoking	Home	Workplace	Restaurants
Bangladesh				
Smoke-free laws			No	No
Men	44.7	N/A	67.8	53.4
Women	1.5	N/A	30.4	2.2
Brazil				
Smoke-free laws			Yes[†]	Yes[†]
Men	21.6	28.9	28.5	[‡]
Women	13.1	27	20.4	[‡]
China				
Smoke-free laws[§]			No	No
Men	52.9	70.5	71.1	91.8
Women	2.4	63.9	53.2	83.3
Egypt				
Smoke-free laws			Yes	No
Men	37.7	82.5	62.4	75.6
Women	0.5	80.5	54	62.1
India				
Smoke-free laws			Yes	No
Men	24.3	52.2	32.2	19.2
Women	2.9	52.5	19.4	2.8
Mexico				
Smoke-free laws[¶]			Yes	Yes
Men	24.8	17.2	23.3	30.9
Women	7.8	17.4	13.9	28.1
Philippines				
Smoke-free laws			No	No
Men	47.7	58.1	43.3	38.3
Women	9.0	50.6	28.8	28.6
Poland				
Smoke-free laws			No	No
Men	36.9	44.9	41.3	53.4
Women	24.4	43.6	24.9	54.3
Russian Federation				
Smoke-free laws			No	No
Men	60.2	36.7	45.7	78.3
Women	21.7	33.0	25.7	78.8
Thailand				
Smoke-free laws			Yes	Yes
Men	45.6	43.4[‖]	34.9	[‡]
Women	3.1	35.1[‖]	18.9	[‡]
Turkey				
Smoke-free laws			Yes	Yes
Men	47.9	56.1	41.5	57.7
Women	15.2	56.5	28.3	52.3

(*continued on next page*)

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Table 1. continued

	Active smoking	SHS exposures among those visiting these places		
		Home	Workplace	Restaurants
Uruguay				
Smoke-free laws			Yes	Yes
Men	30.7	32.0‖	21.4	N/A
Women	19.8	26.7‖	11.8	N/A
Vietnam				
Smoke-free laws			Yes	No
Men	47.4	77.2	68.7	90.9
Women	1.4	69.2	41.4	75.2

N/A, not available; SHS, secondhand smoke.
† Brazil did not have a national smoke-free policy, but does have complete smoke-free legislation in seven jurisdictions that govern almost 40% of the national population: Amazonas, Paraiba, Parana, Rio de Janeiro, Rondonia, Roraima, and Sao Paolo.
‡ Brazil and Thailand reported public place SHS exposures using total adult population as the denominator (unlike the other countries in this table that used population visiting the selected public place in the prior 30 days as the denominator). See Supplemental Table 3 for the Brazil and Thailand data using total population as the denominator.
§ The exception for China is that the Hong Kong Administrative Region had comprehensive smoke-free laws.
¶ Mexico City and Tabasco had comprehensive smoke-free laws (covering 4% of Mexico's population).
‖ Thailand and Uruguay did not use the same monthly threshold for measuring exposure in the home as the other countries did. Thailand included exposure that occurs less than monthly, and Uruguay reported exposure that occurs at least weekly.

exposure. Chronically, SHS leads to increased arterial stiffness [26,27] and atherosclerosis progression [28], perhaps mediated by raised and oxidized low-density lipoprotein cholesterol [29], lowered high-density lipoprotein cholesterol [30], and increased inflammatory response [31]. The pathological effects of SHS occur abruptly at low exposure levels—there is no "safe" level of passive smoke exposure [1,23,32].

SHS CAUSES CVD IN NONSMOKERS: EVIDENCE FROM OBSERVATIONAL STUDIES

Similar to active smoking, health hazards from secondhand smoking may occur decades after exposure. Therefore, the epidemiologic evidence comes from case–control studies and observational

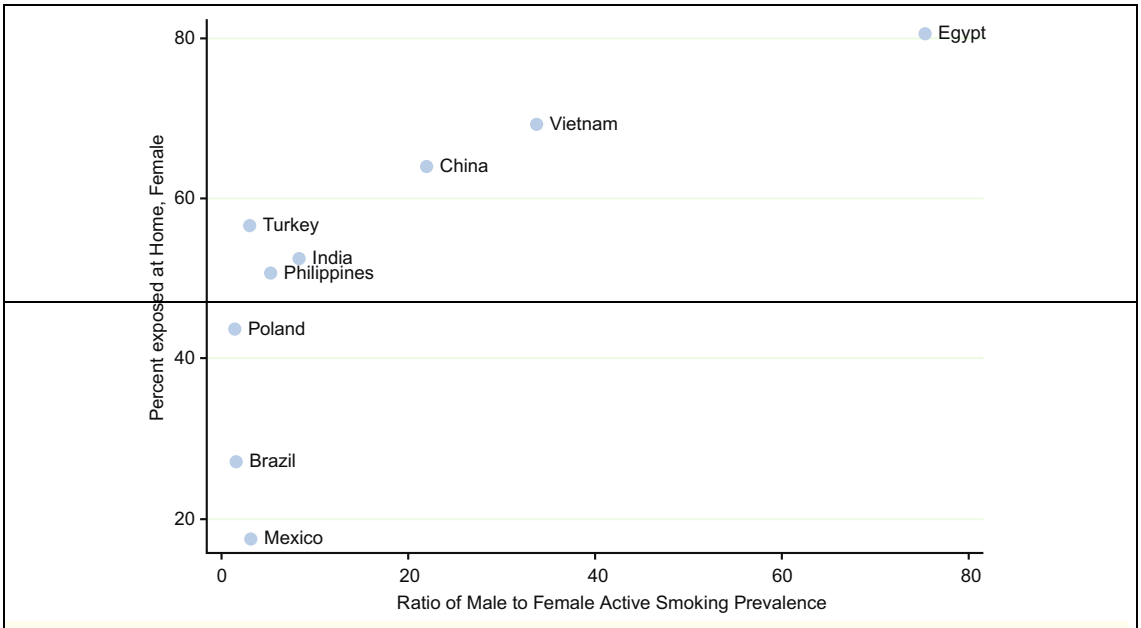

Figure 1. Ratio of male/female active smoking and home secondhand smoke exposure in women, in nine nations surveyed for the Global Adult Tobacco Survey, 2007–2009 (GATS). Reasons for excluding five GATS countries: (1) Thailand was excluded because it included smoking that occurs in the home less than monthly, which was a lower threshold than the other countries have; (2) Uruguay reported smoking that occurs in the home at least weekly, which was a higher threshold than the other countries; (3) Bangladesh did not report home exposure; (4) Russia; and (5) Ukraine were excluded because they appeared to be outliers.

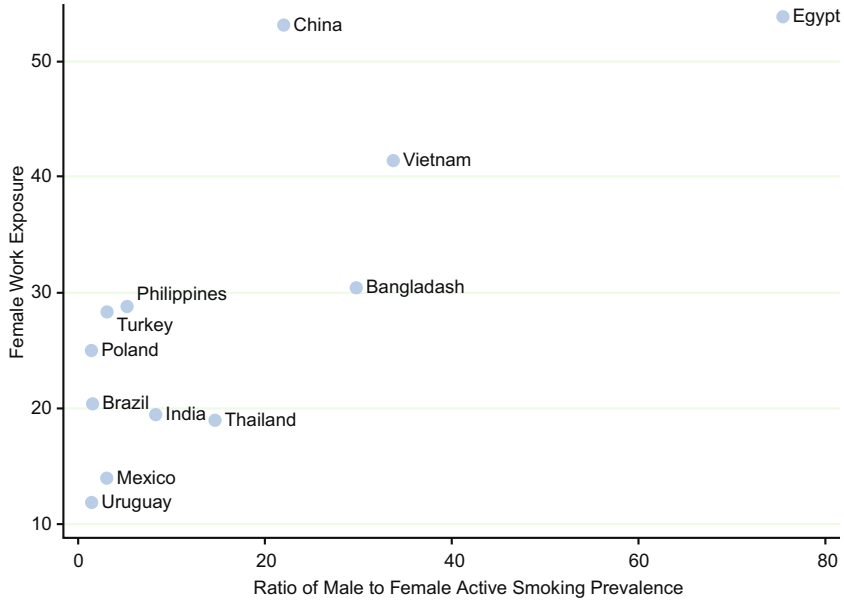

Figure 2. Ratio of male/female active smoking and indoor workplace secondhand smoke exposure in women, in 12 nations surveyed in the Global Adult Tobacco Survey, 2007–2009 (GATS). Two GATS countries, Russia and Ukraine, appeared to be outliers and therefore were excluded.

cohort studies with long-term follow-up. A problem specific to SHS is misclassification bias: most epidemiologic studies are based on self-reported SHS exposure, which could lead to under- or over-reporting exposure duration or intensity. However, under-reporting has likely been more common, because background involuntary secondhand exposure has been common in the past. This leads to misclassifying SHS exposed individuals as "nonexposed" and biasing hazard estimates toward the null (or "no harm").

The 2006 U.S. Surgeon General's report [1] summarized the evidence of SHS effect on CVD by reviewing prior meta-analyses and pooling estimates from original observational studies. Of the 19 studies pooled, all were based on self-reported SHS exposure. The overall relative risk of coronary heart disease in nonsmokers exposed to SHS was 1.26 (95% confidence interval [CI]: 1.19–1.36) compared with unexposed nonsmokers. The relative hazard estimate did not vary substantially according to sex, exposure location, or study type (case control vs. cohort). The pooled relative risk estimate for studies that adjusted for other IHD risk factors was higher than the estimate for unadjusted studies. Analysis restricted to studies quantifying exposure intensity (number of actively smoked cigarettes exposed to daily) suggested a dose–response relationship between SHS and IHD risk. Only 6 studies of secondhand smoking and stroke were reviewed by the Surgeon General's report. Exposure measurement, adjustment for confounders, and definitions of stroke varied among the studies. Two studies showed a statistically significant association between secondhand smoking and stroke; other studies produced estimates with 95% confidence intervals that crossed the null (i.e., included the possibility of no harm). The 2006 report concluded that causal evidence for the link between SHS and IHD was "sufficient," but evidence of a causal link between SHS and stroke was "suggestive, but not sufficient." A number of stroke and SHS epidemiology studies have been completed since the Surgeon General's report review. Oono et al. [33] reviewed 20 stroke studies in 2011 and found a pooled relative risk of 1.25 (95% CI: 1.12–1.38) and evidence of a dose–response relationship for the association of stroke with SHS.

How might misclassification bias have affected the IHD relative risk estimate from the Surgeon General's report and other estimates based on self-reported SHS exposure? One solution to the problem of misclassification resulting from self-reporting of SHS exposure has been to measure exposure using serum or salivary cotinine levels obtained from nonsmokers. Cotinine is the principal metabolite of nicotine and is a sensitive and specific biomarker of SHS exposure in nonsmokers [34]. Whincup et al. [35] studied the association of

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SHS exposure, defined as a baseline serum cotinine of 0.8–14.0 ng/ml categorized as "exposed" and ⩽7 ng/ml categorized as "unexposed." Defined as having elevated baseline cotinine, SHS had a relative risk of IHD of 3.73 (95% CI: 1.32–10.58) during the first 4 years of follow-up, a relative risk of 1.95 (95% CI: 1.09–3.48) in years 5–9, and the risk continued to decline toward the null after 20 years of follow-up (because baseline exposure measurement represented future exposure less and less over time or because of a secular trend toward less active smoking in Britain). The effect remained significant after adjustment for other IHD risk factors and showed a (cotinine) dose–response relationship. No significant association was found between stroke and SHS. The Whincup study demonstrates an IHD relative risk affect size related to SHS that is substantially higher when misclassification bias is eliminated.

Little is known about CVD risk associated with SHS in low- and middle-income countries (e.g., the U.S. Surgeon General's 2006 meta-analysis [1] included an IHD study from Argentina [36] and another from China [37]), and whether the association differs in these populations. Though biological effects of SHS are likely the same in all people, quality of building ventilation and use of air conditioning may differ. Also, levels of indoor air pollution from solid fuel combustion (e.g., indoor cooking or heating fires) are high in some low- and middle-income nations. To evaluate epidemiologic evidence related to SHS and CVD in low- and middle-income nations, we conducted a systematic review of epidemiologic studies of SHS and risk for CVD using MEDLINE (via PubMed) and restricting the search to low- and middle-income country studies that gathered SHS exposure information and reported SHS association with a cardiovascular outcome ascertained using standard diagnostic criteria (Supplemental Methods). Across the 10 included studies, self-reported spousal or total household home SHS exposure was most commonly reported and were most comparable to past reviews [1,2], so those exposure types were compared (Table 2). We found no low- or middle-income studies that used cotinine or other biomarkers to assess SHS exposure.

The eight studies from low- or middle-income nations reporting on IHD were case controlled, and for most, the outcome was nonfatal IHD (because cases were expected to report on SHS exposure history). All main odds ratios were above 1.00, only two estimates included 1.00 in the lower 95% CI bound [15,16], and no lower bound exceeded the upper bound of the Surgeon General report's meta-analysis [1] 95% CI (upper limit of relative risk: 1.36). The INTERHEART (A Study of Risk Factors for First Myocardial Infarction in 52 Countries and Over 27,000 Subjects) was an international case–control study of myocardial infarction in which approximately 80% of participants were from low- and middle-income countries. The increased odds of myocardial infarction associated with spousal active smoking in INTERHEART overall was 1.28 (odds ratio; 95% CI: 1.12–1.47) [38].

Four studies reporting on SHS and stroke in low- or middle-income nations have been published since the Surgeon General's 2006 report [1]. One cohort—the Shanghai Women's Health Study—provided data for both a case-control study [17] and a cohort study [18] (Table 2). A strong positive association between household SHS exposure and total stroke was found in all studies. Of note, follow-up of the Shanghai Women's Health Study cohort found no significant association between workplace exposure and stroke [hazard ratio: 0.73 (95% CI: 0.44–1.02)] [18], though this estimate may have been affected by insufficient follow-up time or exposure misclassification bias.

SMOKE FREE LAWS REDUCE IHD RATES IN NONSMOKERS: EVIDENCE FROM POLICY ''NATURAL EXPERIMENTS''

Without a policy intervention, SHS exposures may track downward if active smoking declines and societal attitudes toward indoor smoking change, but these mechanisms for an SHS decline are slow and by no means guaranteed. Smoke-free laws reduce SHS exposure quickly. Smoke-free laws also reduce active smoking prevalence approximately 15% among active smokers and reduce the number of cigarettes smoked daily [39,40]. After a smoke-free workplace legislation in Finland (1995), California (1998), New York (2002), the Republic of Ireland (2004), Scotland (2004), France (2007–2008), and smaller jurisdictions in Colorado, Montana, Canada, and Italy, SHS exposures were reduced dramatically within 5-year periods in workers surveyed before and after the bans [3,41]. A carbon dioxide measurement study demonstrated the effectiveness of a restaurant, bar, and nightclub smoking ban in reducing SHS levels in Sao Paulo, Brazil [42]. Because of the difficulty of accurately

Table 2. Epidemiologic studies of the association of SHS exposure with CVD in low- or middle-income nations

CVD type and study	Nation	Study type	Observation years		Population		Exposure	Outcome	Effect measure	Effect Size			Controlled for CVD risk factors	Dose-response pattern
			Start	End	Cohort or cases (if case control)	Control subjects				Main	Lower	Upper		
IHD														
He et al. (1989) [46]	China	Case control	Unreported		34 female nonsmokers: hospital-based	68 female nonsmokers: 34 hospital-based, 34 population-based	Spouse smoked	Nonfatal IHD	Odds ratio	1.50	1.28	1.77	Yes†	Yes
He et al. (1994) [37]	China	Case control	1989	1992	59 female never smokers diagnosed with IHD, employed full-time, hospital-based	126 female never smokers, employed full-time, hospital- and community-based	Spousal or workplace exposure	Nonfatal IHD	Odds ratio	2.36	1.01	5.55	Yes‡	Yes
McGhee et al. (2005) [12]	China (Hong Kong)	Case control	1988	1998	584 IHD deaths in persons age ⩾60 years from death registries	763 living contemporaries age ⩾60 years giving information at the same time	Smoker in the household	IHD death	Odds ratio	1.35	1.03	1.76	No	Yes
He et al. (2008) [13]	China	Case control	2001	2002	431 female never smokers aged 60 years or older, population-based	778 female never smokers aged 60 years or older, population-based	Home or workplace	Nonfatal IHD	Odds ratio	1.69	1.31	2.18	Yes§	Yes
Ding et al. (2009) [14]	China (Hong Kong)	Case control	2004	2007	314 female never smokers with IHD, hospital-based	319 female never smokers, hospital-based	Household	Nonfatal IHD	Odds ratio	1.52	1.01	2.27	Yes¶	Yes
Ciruzzi et al. (1998) [36]	Argentina	Case control	1991	1994	336 never smokers with first episode of acute MI, hospital-based, median age 66 years	446 never smokers, hospital-based, median age 65 years	Spouse and children smoked	Nonfatal MI	Odds ratio	1.68	1.20	2.37	Yes‖	Yes
Sulo et al. (2008) [15]	Albania	Case control	2003	2006	169 married never smokers with acute coronary syndrome, aged 35–74 years, hospital-based	323 married never smokers, aged 35–74 years, population-based	Spouse smoked	Nonfatal acute coronary syndrome	Odds ratio	1.60	0.95	2.70	Yes♥	No
Rossi et al. (2010) [16]	Costa Rica	Case control	1994	2004	2,094 cases with first acute MI, 1,543 men and 551 women, hospital-based	2,094 control subjects matched by age, sex, area of residence, population-based	Smoker in the household	Acute nonfatal MI	Odds ratio	1.17	1.00	1.37	No	No
Stroke														
McGhee et al. (2005) [12]	Hong Kong	Case control	1988	1998	597 stroke deaths in persons aged ⩾60 years, from death registries	763 living contemporaries aged ⩾60 years, giving information at the same time	Smoker in the household	Stroke death	Odds ratio	1.49	1.15	1.94	No	Yes
Zhang et al. (2005) [17]	China	Case control	1997	2000	526 female married never smokers reporting stroke history, aged 40–70 years	59,851 female married never smokers without stroke history, aged 40–70 years	Spouse smoked	Nonfatal stroke	Odds ratio	1.41	1.16	1.72	Yes♠	Yes
Wen et al. (2006) [18]	China	Cohort	1997	2004	65,180 female never smokers aged 40–70 years at baseline, population-based	Spouse smoking at baseline	Stroke death	Hazard ratio		1.52	1.08	2.15	No	No
He et al. (2008) [13]	China	Case control	2001	2002	172 female never smokers aged 60 years or older, population-based	1,037 female never smokers aged 60 years or older, population-based	Home or workplace	Nonfatal stroke	Odds ratio	1.65	1.17	2.32	Yes§	Yes

BMI, body mass index; IHD, coronary heart disease; CVD, cardiovascular disease; IHD, ischemic heart disease; MI, myocardial infarction; SHS, secondhand smoke.

† Alcohol consumption; exercise; personal and family history of IHD, hypertension, hyperlipidemia.

‡ Age, hypertension, personality type, total cholesterol, high-density lipoprotein cholesterol.

§ Age, marital status, education, exercise, alcohol consumption, BMI, systolic blood pressure, total cholesterol, triglyceride levels, history of hypertension and diabetes, family history of IHD/stroke.

¶ Age, education, hypertension, diabetes, hypercholesterolemia, gout, history of stroke, family history of IHD, physical inactivity, alcohol intake, estrogen use.

‖ Age, cholesterolemia, diabetes, hypertension, BMI, education, social status, exercise, family history of MI.

♥ Age, sex, exercise, hypertension, diabetes, family history of IHD, BMI, waist-to-hip ratio.

♠ Age, education, occupation, family income, alcohol consumption, exercise, BMI, menopausal status, hormone therapy, oral contraceptive use, history of hypertension, diabetes, use of antihypertensive medication or aspirin.

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measuring SHS exposure, and the ethical conflict involved with randomizing participants to SHS exposure, the population health benefits of smoke-free policies have been estimated primarily based on the "natural experiments" comparing disease rates in the population before and after smoke-free policy implementation. Because SHS affects acute myocardial infarction risk immediately, myocardial infarction rates have been the outcome measure of most smoke-free policy natural experiments. A dramatic example occurred in the relatively isolated city of Helena, Montana, in which acute MI hospitalization rates dropped by approximately 40% during 6 months when a public smoking ban was in effect and returned to prior levels when the law was repealed [43]. Lightwood and Glantz [3] pooled and time-standardized 12 before-and-after studies of 100% smoke-free public places laws and found a relative rate of 0.83 (95% CI: 0.80–0.87) for myocardial infarctions after the bans and evidence that the benefit appeared to grow for up to 36 months.

DISCUSSION

SHS increases risk for CVD and non-CVD deaths and disability and may be responsible for 1% of global mortality, with at least two-thirds of these deaths due to CVD [10]. The WHO GATS and Global Youth Tobacco Survey (GYTS) [44] showed that SHS is common in homes, workplaces, and most public places in a geographically and culturally diverse set of low- and middle-income nations. Active smoking is much more frequent in men than in women in many low- and middle-income nations, and the result is that most SHS exposures occur in female nonsmokers in these countries. We found that SHS-associated CVD risks in the few available low- and middle-income country epidemiologic studies are similar to those observed in studies from higher-income nations. Though not reviewed here, other evidence supports associations between SHS and increased risk for lung cancer and a number of other non-CVDs [1]. Smoke-free laws have been highly effective public health interventions in high-income nations and should also be effective in low- and middle-income nations if enforced effectively. In making the business and policy case for implementation of the Framework Convention for Tobacco Control smoke-free policies, the health and economic development gains from SHS reductions must be weighed along with effects on active smoking.

Data from GATS suggest SHS exposure is ubiquitous in low- and middle-income nations, but inconsistencies among the countries beg several questions that are important to consider in future surveillance that is important for measuring the effectiveness of smoke-free policies. How accurate was self-reported SHS in the GATS surveys? Exposure self-report questionnaires developed in the high-income West may not be appropriately tailored to specific tobacco use patterns and other contributing social behaviors in low- and middle-income countries. Also, self-reporting may be biased by low levels of SHS health risks awareness. In the Chinese GATS, only 38.7% of respondents were aware that SHS causes IHD and 27.2% were aware SHS causes stroke [45]. Given these multiple uncertainties surrounding the GATS SHS estimates, we advocate that future surveillance surveys and cohort studies employ serum, urine, or salivary cotinine as a more sensitive and accurate measure of SHS exposures.

Study questionnaire questions and biomarkers related to other sources of indoor air pollution (e.g., indoor solid fuel combustion fumes) should be added to future studies. The low- and middle-income nation studies reviewed here mostly sampled urban populations, so more studies of the interaction between SHS and indoor cooking fire fumes are needed in rural areas, where solid fuel combustion is more common.

Smoke-free laws are a cornerstone of the WHO Framework Convention on Tobacco Control policy agenda and have been shown to be very effective, both in limited (e.g., workplace) scope [41] or as 100% public space bans [3]. Argentina, Brazil, Mexico, Thailand, Turkey, and Uruguay are among the low- and middle-income nations currently pursuing aggressive smoke-free legislation [22]. Smoke-free laws reduce tobacco harms from SHS in those unintentionally exposed—in low- and middle-income nations, predominantly innocent women and children. Smoke-free policy is not individual primary prevention as an intervention on 1 patient's risk factor, but more akin to an infectious disease public health intervention: as in treatment for the cure of tuberculosis, smoke-free laws are likely to improve the health of the smoker and those around him "contaminated" with SHS. Smoke-free laws are an expression of a government's determination to protect its people's health and change society's

expectations so that public smoking is viewed as socially unacceptable.

CONCLUSIONS

Most past estimates of tobacco's impact on health underestimated its burden due to lack of consideration of the SHS harms to the public's health. Governments have an obligation to protect citizens from preventable environmental toxins like SHS. Governments should not wait for perfect data from low- and middle-income nations, because the evidence is sufficient to justify implementation of smoke-free laws now. Along with smoke-free laws, public education about SHS harms is needed, or there may be resistance to the laws from smokers and nonsmokers alike.

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SUPPLEMENTAL METHODS

Electronic search methods. The search terms were designed to capture all the articles pertaining to both secondhand smoke (SHS) and cardiovascular disease (CVD) published during the specified time period (January 1, 1985, to October 15, 2011) and confined to studies of low- and middle-income nation populations. The relevant medical subject headings (MeSH) term included for SHS is "tobacco smoke pollution," and 11 CVD MeSH terms were included as well. For both subjects, other commonly used terms were included in the search parameters to locate articles with those terms in their title or abstract.

Although the intent was to identify only those articles pertaining to low- or middle-income countries, we were unable to create a set of geographical restrictions that captured all of the relevant articles identified a priori (articles known to the authors from the 2006 U.S. Surgeon General's report and bibliographies of high-income country publications). Instead, we placed no geographical restrictions on the search, which returned 582 potential articles. We then screened titles and abstracts of all of these articles, excluding those that pertained to high-income nation populations only, did not include reliable measures of stroke or coronary heart disease, or were not epidemiological in nature. We retained 11 full text articles that met the inclusion criteria. Because the INTERHEART (A Study of Risk Factors for First Myocardial Infarction in 52 Countries and Over 27,000 Subjects) studied a mix of high-, low-, and middle-income country populations, the SHS-related results from that study were reported separately in the manuscript text. We included an additional article (McGhee et al. [2005]) that our search did not locate due to the manner in which it was entered into PubMed, but that we identified through the references of other articles.

PubMed search terms: (tobacco smoke pollution[mesh] OR "passive smoking"[tiab] OR "secondhand smoke"[tiab] OR "second hand smoke"[tiab] OR "environmental tobacco smoke"[tiab]) AND ("myocardial ischemia"[tiab] OR: myocardial revascularization"[tiab] OR "myocardial reperfusion"[tiab] OR MYOCARDIAL ISCHEMIA/epidemiology[mesh] OR MYOCARDIAL ISCHEMIA/mortality[mesh] OR MYOCARDIAL REVASCULARIZATION [mesh] OR MYOCARDIAL REPERFUSION[mesh] OR "cardiovascular disease"[tiab] OR CARDIOVASCULAR DISEASES/epidemiology[mesh] OR "coronary disease"[mesh] OR stroke[mesh] OR stroke[tiab] OR "peripheral vascular diseases"[mesh] OR "peripheral vascular diseases"[tiab] OR "brain ischemia"[mesh] OR "brain ischemia"[tiab] OR "myocardial infarction"[tiab] OR "coronary heart disease"[tiab] OR "Coronary Artery Disease/epidemiology"[mesh] OR "coronary artery disease"[tiab] OR CARDIOVASCULAR DISEASES/mortality[mesh]) AND ("1985/01/01"[PDAT]: "2011/10/15"[PDAT])

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Supplemental Table 1. Active smoking and SHS exposure prevalence (%) in 14 low- and middle-income nations, the Global Adult Tobacco Survey, 2007–2009 [11]. Smoke-free workplace or public space laws status obtained from the 2011 World Health Organization Tobacco Control Country Profiles report (reporting on laws as of December 31, 2010) [22].

	Active smoking	SHS exposures among those visiting these places					
		Home	Workplace	Restaurants	Public transit	Government buildings	Healthcare facilities
Bangladesh							
Smoke-free laws			No	No	No	No	Yes
Men	44.7	N/A	67.8	53.4	35.9	9.2	7.1
Women	1.5	N/A	30.4	2.2	16.9	1.5	4.4
Brazil							
Smoke-free laws			Yes*	Yes*	Yes*	Yes*	Yes*
Men	21.6	28.9	28.5	†	†	†	†
Women	13.1	27	20.4	†	†	†	†
China							
Smoke-free law‡			No	No	Yes	No	No
Men	52.9	70.5	71.1	91.8	36.4	62.6	41.2
Women	2.4	63.9	53.2	83.3	31.5	50.7	35.2
Egypt							
Smoke-free laws			Yes	No	Yes	Yes	Yes
Men	37.7	82.5	62.4	75.6	80.3	75.8	53.8
Women	0.5	80.5	54	62.1	78.6	66.7	46.4
India							
Smoke-free laws			Yes	No	No	Yes	Yes
Men	24.3	52.2	32.2	19.2	22	10.3	6
Women	2.9	52.5	19.4	2.8	12.6	2.6	4.8
Mexico							
Smoke-free laws§			Yes	Yes	Yes	Yes	Yes
Men	24.8	17.2	23.3	30.9	25.4	17.7	5.2
Women	7.8	17.4	13.9	28.1	23.1	16	3.7
Philippines							
Smoke-free laws			No	No	Yes	Yes	Yes
Men	47.7	58.1	43.3	38.3	61.1	27.9	8
Women	9.0	50.6	28.8	28.6	49.7	23.2	7.3
Poland							
Smoke free laws			No	No	Yes	No	No
Men	36.9	44.9	41.3	53.4	10.7	10.7	4.3
Women	24.4	43.6	24.9	54.3	6.6	9.3	4.8
Russian Federation							
Smoke-free laws			No	No	No	No	No
Men	60.2	36.7	45.7	78.3	24.5	21.2	12.1
Women	21.7	33.0	25.7	78.8	25.1	13.8	9.1

(*continued on next page*)

Supplemental Table 1. continued

	Active smoking	SHS exposures among those visiting these places					
		Home	Workplace	Restaurants	Public transit	Government buildings	Healthcare facilities
Thailand							
Smoke-free laws			Yes	Yes	Yes	Yes	Yes
Men	45.6	43.4[‖]	34.9	†	†	†	†
Women	3.1	35.1[‖]	18.9	†	†	†	†
Turkey							
Smoke-free laws			Yes	Yes	Yes	Yes	Yes
Men	47.9	56.1	41.5	57.7	18.7	13	6.6
Women	15.2	56.5	28.3	52.3	14.1	7.8	5.5
Ukraine							
Smoke-free laws			No	No	Yes	Yes	Yes
Men	50	25.4	44	65.7	17.9	12.9	9.2
Women	11.2	21.9	22.9	62.3	17.2	8.2	5.3
Uruguay							
Smoke-free laws			Yes	Yes	Yes	Yes	Yes
Men	30.7	32.0[‖]	21.4	N/A	N/A	N/A	N/A
Women	19.8	26.7[‖]	11.8	N/A	N/A	N/A	N/A
Vietnam							
Smoke-free laws			Yes	No	Yes	Yes	Yes
Men	47.4	77.2	68.7	90.9	38.8	45.4	29.9
Women	1.4	69.2	41.4	75.2	29.6	28.4	19.6

[*] Brazil does not have a national smoke-free policy, but does have complete smoke-free legislation in seven jurisdictions that govern almost 40% of the national population: Amazonas, Paraiba, Parana, Rio de Janeiro, Rondonia, Roraima, and Sao Paolo.

[†] Brazil and Thailand reported public place SHS exposures using total adult population as the denominator (unlike the other countries in this table that used population visiting the selected public place in the prior 30 days as the denominator). See Supplemental Table 3 for the Brazil and Thailand data using total population as the denominator.

[‡] The exception for China is that the Hong Kong Administrative Region was comprehensive smoke-free laws.

[§] Mexico City and Tabasco have comprehensive smoke-free laws (covering 4% of Mexico's population).

[‖] Thailand and Uruguay do not use the same monthly threshold for measuring exposure in the home as the other countries do. Thailand includes exposure that occurs less than monthly, and Uruguay reports exposure that occurs at least weekly.

N/A = not available; SHS = secondhand smoke.

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Supplemental Table 2. SHS exposure prevalence (%) stratified into all surveyed and nonsmokers (never + past smokers) in 14 low- and middle-income nations, the Global Adult Tobacco Survey, 2007–2009.

	SHS Exposure					
	Home	Workplace	Restaurant	Public transit	Government buildings	Healthcare facilities
Bangladesh						
All	N/A	63	27.6	26.3	5.4	5.8
Nonsmokers	N/A	75.7	55.4	35.9	9.2	5.8
Brazil						
All	27.9	24.4	*	*	*	*
Nonsmokers		22.8	*	*	*	*
China						
All	67.3	63.3	88.5	34.1	58.4	37.9
Nonsmokers	N/A	N/A	N/A	N/A	N/A	N/A
Egypt						
All	81.5	60.7	72.7	79.6	72.8	49.2
Nonsmokers	78.4	58.5	69.1	80	71.3	47.9
India						
All	52.3	29.9	11.3	17.5	6.6	5.4
Nonsmokers	48	26.1	N/A	N/A	N/A	N/A
Mexico						
All	17.3	19.7	29.6	24.2	17	4.3
Nonsmokers	14.1	17.7	30.5	23.8	17.4	4.1
Philippines						
All	54.4	36.9	33.6	55.3	25.5	7.6
Nonsmokers	44.8	30.8	31.1	53.7	25.1	7.7
Poland						
All	44.2	33.6	53.9	8.4	10	4.6
Nonsmokers	28	26.8	50.9	7.4	9.9	4.2
Russian Federation						
All	34.7	34.9	78.6	24.9	17	10.2
Nonsmokers	21.5	26.9	72.4	23.9	14.9	8.6
Thailand						
All	*39.1*	27.2	*	*	*	*
Nonsmokers	32.4	23.6	*	*	*	*
Turkey						
All	56.3	38.5	55.9	16.5	11.3	6
Nonsmokers	47.5	31.6	50.2	15.7	11.1	5.7
Ukraine						
All	23.5	34	64.1	17.5	10.2	6.6
Nonsmokers	14.6	26.6	60.8	16.9	9.4	5.7
Uruguay						
All	*29.2*	16.5	N/A	N/A	N/A	N/A
Nonsmokers			N/A	N/A	N/A	N/A

(*continued on next page*)

Supplemental Table 2. continued

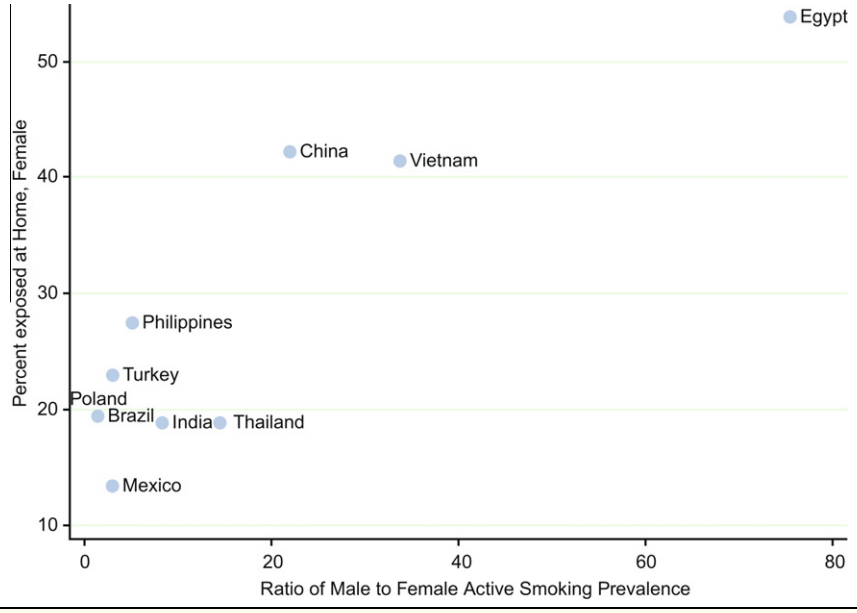
	SHS Exposure					
	Home	Workplace	Restaurant	Public transit	Government buildings	Healthcare facilities
Vietnam						
All	73.1	55.9	84.9	34.4	38.7	23.6
Nonsmokers	67.6	49	80.7	33.3	34.8	21.6

*Brazil and Thailand reported public place SHS exposures using total adult population as the denominator (unlike the other countries in this table who used population visiting the selected public place in the prior 30 days as the denominator). See Supplemental Table 3 for the Brazil and Thailand data using total population as the denominator.
Abbreviations as in Supplemental Table 1.

Supplemental Table 3. SHS exposure prevalence (%) stratified into all surveyed and nonsmokers (never + past smokers) in 14 low- and middle-income nations, the Global Adult Tobacco Survey, 2007–2009.

	SHS exposure of total population					
	Home	Workplace	Restaurants	Public transit	Government buildings	Healthcare facilities
Brazil						
Smoke-free law		No	No	Yes	No	No
Men	28.9	28.5	10.8	4.1	3.7	3.0
Women	27.0	20.4	9.0	4.8	3.5	5.0
All	27.9	24.4	9.9	4.5	3.6	4.0
Nonsmokers		22.8	10.1	4.8	3.7	4.1
Thailand						
Smoke-free law		No	No	Yes	No	No
Men	43.4	34.9	10.8	5.1	4.8	2.0
Women	35.1	18.9	7.2	7.5	3.1	2.1
All	39.1	27.2	9.0	6.3	3.9	2.0
Nonsmokers	32.4	23.6	8.8	6.9	3.8	2.2

SHS = secondhand smoke.



Supplemental Fig. 1. Ratio of male/female active smoking and work place secondhand smoke exposure in women in countries reporting exposures in female nonsmokers, the Global Adult Tobacco Survey, 2007–2009.