Epidemiology and Public Health Policy of Tobacco Use and Cardiovascular Disorders in Low- and Middle-Income Countries

Danish Saleheen, Wei Zhao, Asif Rasheed

Abstract—All forms of tobacco lead to an increased risk of cardiovascular disorders. During the past few decades, the number of people who consume tobacco has increased worldwide because of an overall increase in the global population. It is estimated that close to 80% of the >1.3 billion people who smoke tobacco in the world are in low- and middle-income countries. Smokeless forms of tobacco are also widely consumed in low- and middle-income countries, including chewing and snuffed forms. Lack of targeted and effective strategies to control tobacco consumption contributes to a large burden of cardiovascular disorders in low- and middle-income countries, where cardiovascular disorders have become the leading cause of morbidity and mortality. In this review, we evaluate the epidemiology of tobacco use in low- and middle-income countries and assess the public health policies needed to control tobacco use in such regions for the prevention of cardiovascular disorders and other tobacco-related morbidities and mortality. (Arterioscler Thromb Vasc Biol. 2014;34:1811-1819.)

Key Words: coronary disease ■ low- and middle-income countries ■ smoking ■ stroke ■ tobacco

Tobacco consumption is a causal but a modifiable risk factor for cardiovascular disorders (CVDs).1 Cigarette smoking, the predominant form of tobacco consumption globally,2 is one of the strongest lifestyle behaviors associated with the risk of CVDs.3,4 Although the prevalence of tobacco smoking has declined between 1980 and 2012, the number of people who smoke tobacco worldwide has increased during this time period because of an increase in the global population.5 Hence, the burden of tobacco use remains stubbornly high worldwide.5 This is of particular concern for people in many low- and middle-income countries (LMICs) who have limited social and personal capacity to deal with the burden of wide-ranging tobacco-associated diseases.5 In the year 2000 alone, ≈2.5 million people died because of tobacco consumption in LMICs, which comprised half of all tobacco-related deaths globally.6 It is estimated that by the year 2030 tobacco-related deaths will rise to ≈6.6 million in LMICs if such rapid increases in tobacco consumption are not curtailed effectively. One third of all tobacco-related deaths will be because of CVDs.7 These numbers do not take into account cardiovascular morbidity because of tobacco use in these regions. Effective and targeted public health interventions are hence needed to control effectively the growing increase of tobacco use in LMICs. In this review, we evaluate the use of different forms of tobacco in LMICs and their relevance in CVDs. We further assess the public health policies needed to minimize tobacco use in these regions.
Typical waterpipes combust tobacco (usually with the help of charcoal), and smoke is passed through a bowl of water before being inhaled through a hose. A wide variety of products may be added along with tobacco for combustion, including hashish and other flavoring agents. Despite a common association of waterpipe tobacco consumption with the Eastern Mediterranean region, waterpipe tobacco consumption is also high in certain East Asian countries. In a recent survey, current prevalence of waterpipe tobacco consumption for men was found higher in Vietnam (13%) than in Egypt (6.2%) and Turkey (4.0%). There has also been a recent emergence in the use of waterpipe tobacco consumption among young adults and adolescents in many LMICs and developed countries. Several factors are responsible for the popularity of waterpipe tobacco consumption among the youth, including proliferation of cafes where waterpipes are available to consume tobacco in a communal setting. They are also often consumed by adding different flavors (eg, apple, honey, and strawberry) that are misconceived to have natural or cleansing effects. Waterpipes deliver most of the same toxic compounds that are present in cigarette smoke. Behavioral studies, however, suggest that intake of smoke and exposure to nicotine through waterpipes is several folds higher than cigarettes because waterpipe smoking sessions typically last longer than the duration it takes to consume a cigarette.

### Cigars and Pipes
A cigar traditionally comprises of shredded tobacco in a rolled tobacco leaf that has been dried and fermented. Cigars vary in size ranging from cigarette-shaped little cigars (that often have filters) to large cigars. A cigarillo is also a type of small cigar that is larger than a cigarette but smaller than a regular cigar. Pipe is a devise that comprises of a bowl (for tobacco consumption) attached to thin hollow stem ending in a mouthpiece. Tobacco for smoking in pipes is often blended with flavoring agents.

### Smokeless Tobacco
Smokeless tobacco is a broad term encompassing tobacco products that are used orally or nasally and are not burned for consumption. They are used throughout the world; however, their consumption is variable based on geography. For instance, an estimated 258 million people use smokeless tobacco products in South Asia, in contrast to the United States where an estimated 8.1 million people use such products. Some of the most widely used smokeless tobacco products include betel quid or paan, gutka, zarda, toombak, khaini, and dry snuff (Table 2). These tobacco products may be chewed (eg, betel quid, gutka), sucked (eg, khaini), and placed in the oral cavity (ie, in the space between gums and the cheek) for variable time intervals (eg, naswar, toombak) or snuffed nasally. Many of these products are handmade; whereas some are produced commercially and require complex manufacturing processes. The constituents of smokeless tobacco products range from simply cured tobacco to a wide range of chemical ingredients and additives. Ingredients for these tobacco products may contain plant material (eg, betel leaf, areca nut), alkaline modifiers (eg, inorganic slats, plant/fungi ashes, slaked lime), and other flavoring agents (eg, saffron, eucalyptus). The amount and type of tobacco, addition of plant ingredient and use of alkaline

### Table 1. Some Smoked Forms of Tobacco Prevalent in Low- and Middle-Income Countries

<table>
<thead>
<tr>
<th>Tobacco Type</th>
<th>Brief Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cigarettes</strong></td>
<td>Roll of tobacco wrapped in a paper or a substance not containing tobacco.</td>
</tr>
<tr>
<td>Bidis</td>
<td>Tobacco flakes wrapped in a leaf (usually from tendu plant). Bidis are prevalent in South Asia.</td>
</tr>
<tr>
<td>Kreteks</td>
<td>Made with a blend of tobacco, cloves, and other flavors.</td>
</tr>
<tr>
<td>Chillum</td>
<td>Straight conical pipe (made of clay or other substance) for smoking tobacco. They are prevalent in South Asia, especially in rural settings.</td>
</tr>
<tr>
<td>Hookah</td>
<td>A waterpipe instrument that consists of a water basin. Vaporized or smoked tobacco is passed through the water basin before inhalation.</td>
</tr>
<tr>
<td>Sheesha</td>
<td>A waterpipe similar to Hookah, most commonly used in Middle East. Flavors (eg, apple and honey) are added to enhance the taste.</td>
</tr>
<tr>
<td>Cigars</td>
<td>Roll of dried and fermented tobacco leaves that contain shredded tobacco.</td>
</tr>
<tr>
<td>Pipes</td>
<td>Devise comprising of a bowl (for tobacco consumption) and a thin hollow stem ending in a mouthpiece. Tobacco for smoking in pipes is often blended with flavoring agents.</td>
</tr>
<tr>
<td>Cheroot</td>
<td>A low cost cylindrical cigar with both ends clipped during manufacturing; common in Burma and India.</td>
</tr>
</tbody>
</table>
Table 2. Some Smokeless Forms of Tobacco Prevalent in Low- and Middle-Income Countries

<table>
<thead>
<tr>
<th>Tobacco Type</th>
<th>Brief Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco chewing</td>
<td></td>
</tr>
<tr>
<td>Paan</td>
<td>Wrapped betel leaf containing betel quid made of tobacco, areca nut, slaked lime, and other flavoring agents.</td>
</tr>
<tr>
<td>Gutka</td>
<td>Chewable tobacco that consists of dry tobacco, crushed betel nut, and catechu, slaked lime, and other flavoring agents.</td>
</tr>
<tr>
<td>Mawa</td>
<td>Mixture of thin shavings of tobacco, slaked lime, and areca nut and is widely used in the Indian Gujarat.</td>
</tr>
<tr>
<td>Qiwam or khiwam</td>
<td>A paste containing mixture of tobacco extract, spices, and other additives (eg, musk); used in South Asia.</td>
</tr>
<tr>
<td>Zarda</td>
<td>Ingredient often used in betel quid and contains a mixture of tobacco, lime, spices, vegetable dyes, and areca nut.</td>
</tr>
<tr>
<td>Khaini</td>
<td>Sun-dried tobacco, slaked lime paste, sometimes areca nut is added; commonly used in India (Gujarat and Maharashtra).</td>
</tr>
<tr>
<td>Tobacco sucking</td>
<td></td>
</tr>
<tr>
<td>Naswar or nass</td>
<td>Moist and crushed tobacco. Tobacco is stuffed in the floor of the mouth, under the lower lip, or inside the cheek for extended periods of time.</td>
</tr>
<tr>
<td>Chimó</td>
<td>Crushed tobacco leaves containing sodium bicarbonate, brown sugar, ashes from the Mamón tree (Melicocca bijuga), and other flavoring agents; used in Venezuela Chimó is placed between the lip and cheek and the gum and left there for some time (usually half an hour).</td>
</tr>
<tr>
<td>Toombak</td>
<td>A moist tobacco product used primarily in Sudan that consists of tobacco and sodium bicarbonate. Tobacco leaves used in toombak are harvested and dried followed by fermentation. They are then ground and matured (≤1 y), followed by addition of sodium bicarbonate. Toombak is rolled into a ball (called saffaa), which is slowly sucked by holding it in the oral cavity.</td>
</tr>
<tr>
<td>Tobacco dentifrice</td>
<td></td>
</tr>
<tr>
<td>Masheri or mishri</td>
<td>Roasted tobacco flakes. Applied to gums and teeth as a dentifrice but also kept inside mouth for extended times because of addiction.</td>
</tr>
<tr>
<td>Gul or gudakhu</td>
<td>Paste containing tobacco powder, molasses, and other ingredients; applied to the gums and teeth as a dentifrice.</td>
</tr>
<tr>
<td>Tobacco sniffing</td>
<td></td>
</tr>
<tr>
<td>Dry snuff or tapkeer</td>
<td>Powdered form of tobacco that has been fire cured, fermented, and processed and is nasally sniffed; may also be used orally for sucking. Known as tapkeer in some parts of South Asia.</td>
</tr>
</tbody>
</table>

Addiction Potential of Tobacco
Nicotine in tobacco is highly addictive and is primarily responsible for the maintenance of tobacco consumption.50,51 Addiction to any tobacco product is largely dependent on the amount of nicotine that is absorbed and the speed of nicotine delivery.52,53 The amount and rate of nicotine absorption relate to the pH of the tobacco product, route of administration, and the overall nicotine content of the product. Cigarette smoking provides the fastest mode of systemic delivery of nicotine.54 pH of the tobacco product determines the amount of free or unionized nicotine. Unionized nicotine, compared with its ionized form, is more rapidly absorbable in the blood, causing faster spikes in blood nicotine levels;53 hence, tobacco products with a higher fraction of unionized nicotine have a greater addiction potential than products with a lower fraction of unionized nicotine.52 Different types of tobacco products have different levels of unionized nicotine. Addition of alkaline modifiers in smokeless tobacco products increases the pH of tobacco, converting a greater fraction of nicotine in the unionized form.51,53

Variability in Nicotine, pH, and Other Constituents Among Tobacco Products
The concentration of nicotine, the pH of tobacco, and levels of carcinogens differ across various tobacco species and across different tobacco products.41–43,45,46,47 The type of tobacco and curing of tobacco can influence the nicotine content.46 For instance, tobacco products from many LMICs contain Nicotiana rustica, a tobacco species that has higher nicotine levels than found in tobacco cultivated in the United States.46 An estimated 35% to 40% of tobacco present in smokeless tobacco products in India derive from N. rustica.46,47 In a recent survey conducted by Stanfill et al43 in 9 different countries (many of which are LMICs), nicotine concentrations were observed to vary substantially among different smokeless tobacco products, ranging from 0.05 to 31.0 mg/g (a 620-fold range of variation); products such as Bangladeshi gul powder, Indian zarda, and Sudani toombak were found to have the highest nicotine levels (>27 mg/g product).43 Stanfill et al43 also observed that the pH of various smokeless tobacco products were variable ranging from 5.2 to 10.1, which equated to 0.2% to 99.1% of nicotine being in the free form. Gul powder from Bangladesh and Venezuelan chimó was found to have ≥2-folds higher unionized nicotine levels than all other smokeless tobacco products studied across various countries.43 The results of their survey were also consistent with prior estimates that have suggested that roughly 40% of the moist snuff products consumed in many LMICs have pH values exceeding the highest value observed for any smokeless tobacco product in the United States.48 Some chewable forms of tobacco (eg, pan, gutka, and mawa) manufactured in South Asia have also been found to have high amounts of areca nut, which has been classified as an International Agency for Research group 1 carcinogen.47,48 The concentration of tobacco-specific N-nitrosamine, the most potent classes of carcinogen, has been observed to be several times higher in many smokeless tobacco forms consumed in India, Bangladesh, and Sudan (eg, tambook, gutka, and zarda) than the maximum concentration modifiers, however, vary locally and regionally, resulting in a wide range of smokeless tobacco products.41,43,45 Smokeless tobacco products contain many harmful and toxic constituents, including alkaloids (such as nicotine, cotinine, nornicotine), toxic metals (mercury, lead, chromium, and other trace elements), aldehydes, lactones, radioactive metals, polycyclic aromatic hydrocarbons, and tobacco-specific N-nitrosamines, many of which are also known to have carcinogenic effects.46–49
observed for different smokeless forms of tobacco available in the United States and the Sweden.43

Tobacco Consumption in Men and Women
Patterns and choice of tobacco form consumed by men and women vary across different regions.2,5,55 There is a higher prevalence of tobacco smoking in men than in women globally.2,5 A recent study, that reviewed data on tobacco smoking between 1980 and 2012 from 187 countries, estimated that in the year 2012 age-standardized prevalence rates of daily tobacco smoking in men and women were 31.1% and 6.2%, respectively.5 Across various LMICs, the prevalence of daily smoking in year 2012 was variable in men and women.5 Daily smoking in men ranged from >50% (eg, Armenia, Indonesia, Kiribati, Laos) to <10% (eg, Ghana, Niger, Sudan and Ethiopia). Similarly in women, estimated prevalence of daily smoking in 2012 across various LMICs ranged from >30% (eg, Kiribati and Bulgaria) to 1% or lower (eg, Azerbaijan, Algeria, Gambia, Sri Lanka, and Sudan).5 However, a weak correlation was observed between daily smoking in men and women in the year 2012 across different regions.5 Although prevalence rates of daily tobacco smoking have decreased between 1980 and 2012 globally, during this time period prevalence of tobacco consumption increased in men living in some LMICs, including Cote d’Ivoire, Kazakhstan, Mauritania, and Serbia.5 Similarly for women living in LMICs, an increase in the prevalence of tobacco smoking was observed in Tunisia, Kyrgyzstan, Costa Rica, Tonga, and Bulgaria.5 In the year 2012, the prevalence rate of daily smoking in men living in LMICs increased sharply in the 15 to 19 year age group, reached its peak at the age 45 to 49 years, and continuously dropped after the age of 50 years.5 In contrast, the prevalence of daily smoking in women living in LMICs continuously increased with age in the year 2012.5

In contrast to smoked forms of tobacco products, prevalence of chewable forms of tobacco is higher or similar in men and women across various regions within LMICs.2,5,23 The tendency to use chewable forms of tobacco in combination with smoking forms of tobacco, however, differs between the 2 sex groups. A large majority of women who chew tobacco do not smoke; whereas men who chew tobacco also tend to smoke tobacco.55 The snuffed forms of tobacco are mostly used by men and few women report snuffing tobacco within LMICs.2,5,24,55

Tobacco and CVDs
Tobacco smoking is causally associated with increased risk of CVDs.55–59 The impact of tobacco smoking on the risk of CVDs is similar across various regions globally.55,58 There is a strong dose–response relationship between the amount of cigarettes consumed and risk of CVDs.55,58 It was previously suggested such a dose-related increase in coronary heart disease (CHD) risk persists up to ∼25 cigarettes per day.60–62; more recent analyses of data from 5 contemporary cohorts, however, show a significant increasing trend between cigarettes per day and CHD risk for both men and women for ≤40 cigarettes per day.63 Association between cigarette consumption and CHD risk is stronger in younger participants compared with their older counterparts.55,57,59 This is particularly relevant in LMICs where initiation to smoking addiction begins at childhood. The Global Youth Tobacco Survey, a worldwide collaboration that used a uniform methodology to assess prevalence of smoking among school-going children (13–15 years) in 43 countries, found that among many schools in LMICs, including Chile, Peru, Indonesia, and India, prevalence of ever use of any tobacco product was >30%.64 Similar trends have been observed by other studies in LMICs including Bangladesh, Pakistan, Indonesia, and many countries in Africa.65–69 Many studies have demonstrated that risk of CHD is lower in former smokers than current smokers55,63,70–72; however, compared with nonsmokers, the risk of CHD is higher in former smokers.55,60 In both men and women, risk of CHD has been found to be lower among former smokers than current smokers, and risk of CHD has been shown to decrease progressively with time after smoking cessation.11,12,55

Other forms of smoked tobacco products are also associated with increased CVD risk.55 Data from the INTERHEART study found the risk of smoking bidis alone to be similar to that of current cigarette smoking. The risk of CHD progressively increases with an increasing number of bidis smoked per day.70 Similarly, in the absence of current cigarette or bidi smoking, use of pipes, cigars, or waterpipes is also associated with an increased CHD risk.55

All smokeless forms of tobacco lead to an increased risk of CHD.55 Participants who smoke tobacco and chew tobacco have a higher CHD risk than those who only consume tobacco using either way.55 There are, however, many uncertainties that still persist, including the relative quantitative impact of the various smokeless forms of tobacco on the risk of various CVD subtypes, whether the impact of various smokeless forms of tobacco differ across various clinical groups, the shapes of the association for the amount of smokeless tobacco on risk of CVDs, and the biological mechanisms through which these alternative forms of tobacco lead to CVDs. In addition, as noted above smokeless tobacco products from different regions vary in terms of their nicotine content, pH, ionization fraction, and levels of harmful substances.41–43,45 Larger and detailed studies specific to each region, than currently available, are, therefore, needed. Many ongoing studies in LMICs in the coming years may be able to answer some of the uncertainties outlined above. Among these studies, the Pakistan Risk of Myocardial Infarction Events Study (RACE)74 are two ongoing studies in Pakistan that have already enrolled close to 57000 participants, including 17000 cases with myocardial infarction and 6000 stroke cases, and have recorded detailed lifestyle information (including habits related to different types of tobacco consumption). The Kadoorie biobank is a large prospective study in China that has recorded detailed information on lifestyle factors and is accruing participants for various incident diseases, including CVDs.75 Findings from such studies would help better understand the prevalence of different smokeless forms of tobacco (in men and women, across various age groups and other relevant categories, eg, socioeconomic groups), determinants of smokeless forms of tobacco, their relative quantitative impact on the risk of CVDs, and biological mechanisms that link different smokeless forms of tobacco with increased risk of CVDs. Such data would be particularly important to help devise effective public health strategies to control the growing burden of tobacco use in LMICs.
Secondhand Smoke and Risk of CVDs

Passive exposure to tobacco smoke or secondhand smoke (SHS) increases the risk of both CHD and stroke independent of established CVD risk factors.\textsuperscript{76–78} The impact of SHS on CVD risk is similar in men and women.\textsuperscript{78,79} Several studies have shown a dose–response relationship between exposure to SHS and risk of CHD.\textsuperscript{55,79–81} Compared with nonsmokers not exposed to SHS, nonsmokers exposed to 1 to 19 cigarettes/d and to >20 cigarettes/d have been observed to have relative risks of CHD of 1.23 and 1.31, respectively.\textsuperscript{81} There is also strong evidence linking SHS with secondary CVD events.\textsuperscript{82,83} In patients with acute coronary syndrome (ACS), exposure to SHS has been found to increase risk of repeat cardiac events by \(\approx 61\%\) during the first 30 days in comparison with those patients with ACS who are not exposed to SHS.\textsuperscript{82} There is also a dose-related increase in the risk of secondary CVD events in patients with ACS exposed to SHS.\textsuperscript{83}

Studies quantifying cotinine levels, a metabolite of nicotine and a well-established biomarker for measuring exposure to smoking,\textsuperscript{84–86} have, however, suggested that SHS may have a stronger impact on CHD risk than observed through studies using questionnaire based data.\textsuperscript{90,91} In a study conducted in 2105 male nonsmokers, relative risks for CHD in participants with mild (cotinine levels: 0.8–1.4 ng/mL), moderate (cotinine levels: 1.5–2.7 ng/mL), and high (cotinine levels: 2.8–14 ng/mL) exposures to SHS were observed to be 1.45, 1.49, and 1.57, respectively.\textsuperscript{90} Similarly, relative risks for all-cause mortality in patients with ACS exposed to SHS have been shown to increase from 1.66 in those with mild cotinine levels (0.1–0.3 ng/mL) to 3.79 in those with cotinine levels >0.9 ng/mL.\textsuperscript{83} These data suggest that assessment of SHS through objective methods is less prone to biases compared with data obtained through self-report only, thereby encouraging the use of biomarkers in quantifying the risk of SHS on CVD and other tobacco related diseases. Cotinine levels (blood, saliva, or urine), however, have an average half-life of 16 hours and are not able to reflect exposure to chronic smoking.\textsuperscript{91} The average half-life of cotinine levels in the toe nail or urinary 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol on the other contrary is \(\approx 3\) weeks;\textsuperscript{91} however, the relationship of such biomarkers that are reflective of chronic exposure to smoking with CVD status remains poorly understood.\textsuperscript{91,92} More detailed studies on biomarkers that are reflective of both acute and chronic SHS are needed to quantify the impact of SHS on the risk of CVDs.

Tobacco Control Policies in LMICs

There is an urgent need to implement wide-ranging approaches for reducing the growing epidemic of tobacco use in LMICs.\textsuperscript{89,93–95} Local governments, nongovernmental organizations, and private sectors need to act together to implement strategies that will introduce (1) smoke-free legislations; (2) tobacco taxation policies; (3) bans on direct and indirect ways of tobacco promotion; (4) limiting the influence of the tobacco industry on tobacco control policies; and (5) implementation of UN treaties, agreements, and recommendations such as the World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC)\textsuperscript{94} and the MPOWER.\textsuperscript{93} Adopting a multifaceted strategy at all levels of the society will be needed to deal with the growing epidemic of tobacco in LMICs.

In many developed countries, implementation of smoke-free legislations has resulted in rapid reductions in prevalence of smokers and hospitalizations.\textsuperscript{76–78} For instance in New York City, a comprehensive ban on smoking in all public spaces was implemented in 2002, which resulted in a 15% reduction in the prevalence of adult smoking.\textsuperscript{100} Similar smoke-free legislations covering all sections of the society need to be aggressively pursued in LMICs that will ensure establishing public areas, work places, and restaurants that are tobacco-free, thereby reducing the social acceptability of tobacco use and encouraging current tobacco users to quit. In parallel, tobacco excise taxes need to be increased. Implementing tobacco taxation policy has been shown one of the most effective ways of reducing prevalence of smoking, especially among children and adolescents.\textsuperscript{100} A 10% increase in pricing has been shown to reduce cigarette consumption by 3% to 5%.\textsuperscript{101} Although many regions within LMICs have implemented a partial ban on tobacco sponsorship, such partial restrictions have not been proven effective in reducing the burden of tobacco in these regions, necessitating the need for aggressively banning all indirect or alternative forms of tobacco marketing.\textsuperscript{93} Exposure to tobacco marketing has been associated with a doubling of the probability of initiation of smoking in youth.\textsuperscript{102,103} Health warning labels should be placed on tobacco products. Sustained mass media campaigns with graphic depictions of the health consequences of smoking should be implemented; such efforts incorporated in tobacco control programs have been shown to reduce tobacco use in developed countries.\textsuperscript{102,103}

Tobacco Industry—the Vector of the Tobacco Epidemic

Tobacco control policies cannot be effectively implemented without targeting the tobacco industry which is the vector of tobacco epidemic. The tobacco industry has been implementing several strategies to promote and create a demand of tobacco use in LMICs. Weak tobacco control policies and low awareness about the wide-ranging hazardous effects of tobacco use in LMICs have allowed and resulted into the global expansion of various multinational tobacco companies.\textsuperscript{90,104–106} The tobacco industry has used direct investment in many LMICs (eg, Philippines, Indonesia, Cambodia) where it was perceived and often welcomed as a source of economic development.\textsuperscript{107–109} In many LMICs where such direct economic access was restricted because of bans imposed by the government (eg, Malawi and Uganda) or complexity in bureaucracy (eg, China),\textsuperscript{110–112} smuggling was used an alternative route to create demand and set a foothold; it was further used as a leverage for negotiations with the government for tax concessions and licensing permissions. Such economic interventions were coupled with marketing and promotion of tobacco products to create demand in LMICs. Both direct and indirect ways of advertisement have been used by the tobacco industry in many LMICs.\textsuperscript{104,109,113} Products such as mild, light, and low-tar cigarettes have been introduced especially to attract young adults and women.\textsuperscript{107,111,112} Marketing strategies such as associating tobacco use with youth and glamour
have been used to attract young people who have never used tobacco previously. Political lobbying, public relation campaigns, and voluntary self-regulatory advertising codes are some of the ways that the tobacco industry has pursued to produce a favorable environment facilitating growth of tobacco use in LMICs. Manipulation of the scientific evidence and partnering with third party allies have also been adopted by the tobacco industry to oppose implementation of tobacco control policies. For instance, by working with local trade associations (e.g., restaurants and hospitality) which acted as third parties, Accommodation Programs and Courtesy of Choice programs were enforced, allowing creation of smoking and no-smoking sections; thereby opposing laws that could enforce 100% smoke-free environment at work places and public places. Many of the above fraudulent acts have been used by the tobacco industry in developed countries as well. The conviction of major multinational tobacco companies under the United States Racketeer Influenced and Corrupt Organizations Act is a historical verdict which not only holds the tobacco industry liable for fraudulently covering up the health risks associated with smoking and for unlawfully marketing their products to children, but the verdict also highlights the need to change substantially the manner in which tobacco industry is overseen without which the tobacco industry is likely to continue its unlawful activities.

The WHO FCTC and MPOWER: Two Global Public Health Programs for Combating the Tobacco Epidemic

The WHO FCTC, a policy that has been ratified by 177 countries to date (including most LMICs), is an important step toward combatting the epidemic of tobacco internationally. The WHO FCTC pinpointed the factors that are responsible for the spread of the tobacco epidemic globally, including trade liberalization, direct foreign investment, global marketing, transnational tobacco advertising, promotion and sponsorship, and the international movement of counterfeit cigarettes. They made evidence-based recommendations to counter these factors (Table 3). Specific recommendations were also made to reduce the influence of tobacco industry on tobacco control policies, including (1) creating awareness about the interference of the tobacco industry in the implementation of tobacco control policies; (2) limiting interactions with the tobacco industry; (3) rejecting partnerships with the tobacco industry; (4) avoiding conflicts of interest for government representatives; (5) mandating that information shared by the tobacco industry is transparent and accurate; (6) regulating corporate social activities by the tobacco industry; (7) no preferential treatment to the tobacco industry; and (8) treatment of any state-owned tobacco industry in a manner similar to other tobacco industries.

To support further the FCTC, the WHO in 2008 devised a 6-point evidence-based strategy, called MPOWER. The MPOWER strategy includes (1) monitoring tobacco use and prevention policies; (2) protecting people from tobacco smoke by establishing smoke-free public areas; (3) offer help to those who would like to quit tobacco; (4) warn people about the dangers of tobacco, including the smokeless forms that are commonly used by women and being increased used in younger generations; (5) enforcing bans that cover all types of tobacco advertising, promotion, and sponsorship activities; and (6) raising the price of all tobacco-related products through taxation. Such a program has been either fully or partially implemented in many parts of the world and is already proving to be effective. For instance, the MPOWER measures implemented in Turkey resulted in a 13% relative decline in smoking prevalence between 2008 and 2012.

Implementation of tobacco control programs, such as FCTC and MPOWER, is clearly important, and a wider reach of such programs in LMICs should be ensured. One of the key limitations, however, in all such programs is the lack of advocacy for eradication tobacco at its source. Curtailing tobacco cultivation gradually and offering tobacco farmers with incentives (e.g., providing seeds for alternative crops, monitory assistance in the initial few years) should be made part of tobacco eradication policies. Tobacco farmers need to be educated about both acute and chronic effects of tobacco farming and harmful effects of tobacco use in general. It has been reported that ≤55% of the tobacco farmers and their families experienced green tobacco sickness, an acute toxicity syndrome associated with tobacco exposure. A large proportion of the affected are children. In rural settings that currently rely on tobacco farming, community-based initiatives should be placed that can discourage families from cultivating tobacco and offer help to grow alternative crops. Governments can further intervene by making other alternative healthier crops as profitable as tobacco farming. Such wider initiatives that can help in reducing tobacco cultivation along with tobacco control programs that restrict the use of tobacco will ultimately help in creating a tobacco-free society.

Table 3. Main Provisions in the WHO FCTC

<table>
<thead>
<tr>
<th>Provisions</th>
<th>Demand for tobacco through price and tax measures</th>
<th>Tobacco advertising, promotion, and sponsorship</th>
<th>Illicit trade in tobacco products</th>
<th>Sales to and by minors</th>
<th>Measures concerning tobacco dependence and cessation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulation</td>
<td>Packaging and labeling of tobacco products</td>
<td>Regulation of tobacco product disclosures</td>
<td>Regulation of the contents of tobacco products</td>
<td>Protection from exposure to tobacco smoke especially smoking in work and public areas</td>
<td></td>
</tr>
<tr>
<td>Provision and support</td>
<td>Education, communication, training, and public awareness</td>
<td>Support for economically viable alternative activities</td>
<td>Research, surveillance and exchange of information</td>
<td>Legislative actions to prevent the influence and interference of the tobacco industry on public health policy</td>
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</tbody>
</table>

FCTC indicates Framework Convention on Tobacco Control; and WHO, World Health Organization.
Conclusions

Despite availability of overwhelming evidence that all forms of tobacco lead to a higher risk of CVDs, the burden of tobacco consumption remains high in LMICs. Comprehensive and multilevel public health strategies are needed to control the burden of tobacco in LMICs, including smoke-free legislations, tobacco taxation policies, limiting the influence of the tobacco industry on public health policies, bans on direct and indirect ways of tobacco promotion, and implementation of international treaties such as the WHO FCTC and the MPOWER.

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Disclosures

None.

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### Significance

Despite extensive efforts for the past several decades, prevalence of tobacco use remains stubbornly high in low- and middle-income countries. Various forms of smoked and smokeless tobacco products are consumed in low- and middle-income countries. Cardiovascular disorders are a major group of diseases that result because of consumption of any form of smoked or smokeless tobacco. We have reviewed the epidemiology of various forms of tobacco consumption in low- and middle-income countries and their impact on the risk of cardiovascular disorders. We have further summarized the public health strategies that are needed to control the epidemic of tobacco consumption in low- and middle-income countries.
Epidemiology and Public Health Policy of Tobacco Use and Cardiovascular Disorders in Low- and Middle-Income Countries
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