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TOBACCO & CORONARY HEART DISEASE

- *Tobacco use, including exposure to second-hand smoke, harms the cardiovascular system.*
- *About 1.9 million avoidable deaths from coronary heart disease (CHD) per year (approximately 21% of all CHD deaths globally) are attributable to tobacco use and exposure to second-hand smoke.*
- *The benefits of quitting tobacco are substantial. There are immediate and long-term health benefits after quitting, which commence within hours and last for years. After 15 years of abstinence from tobacco, the excess risk of CHD is reduced to that of a person who has never smoked.*

What is coronary heart disease?

Coronary heart disease (CHD)[1] is a disease in which fatty deposits made up of cholesterol and other cellular materials (collectively called plaque) accumulate inside the coronary arteries on the surface of the heart, leading to narrowing of the arteries. This decreases the flow of oxygen-rich blood to the heart, which can trigger a heart attack and may cause serious heart damage or sudden death **(1)**. This process often evolves slowly over a long period, and many affected individuals only become aware of their condition when they suffer a serious heart attack.

The problem

CHD, like most noncommunicable chronic diseases, is complex and influenced by interrelated personal, social and commercial factors. Unhealthy behaviours, such as tobacco use, alcohol abuse, unhealthy diets and physical inactivity, are major examples of risk factors. These, and the resulting intermediary health conditions, such as obesity and diabetes mellitus, increase the risk of developing CHD.

CHD, the leading cause of death and disability globally, causes the loss of 9.4 million lives and over 203 million disability-adjusted life-years (DALYs) every year **(2, 3)**.

Disabilities caused by CHD include angina and fatigue, which may limit functional capacity and impair quality of life. CHD has also been linked to

1 Also known as ischaemic heart disease, coronary artery disease or atherosclerotic heart disease.

Definitions

Smoked tobacco product: any product made or derived from tobacco through a combustion process. Examples include manufactured cigarettes, roll-your-own tobacco, cigars, shisha (also known as waterpipe), kreteks and bidis.

Smokeless tobacco: any product that consists of cut, ground, powdered or leaf tobacco and that is intended to be placed in the oral or nasal cavity. Examples include snuff, chewing tobacco, gutka, mishri and *snus*.

Second-hand smoke (SHS): the combination of "mainstream" smoke exhaled by the smoker and "side-stream" smoke emitted into the environment from the burning end of a cigarette or from other smoked tobacco products, usually in combination with the smoke exhaled by the smoker. The terms "passive smoking" or "involuntary smoking" are also often used to describe exposure to SHS.

Smoke-free policies: "comprehensive" smoke-free policies completely ban smoking in all indoor public places, with no exceptions for designated smoking rooms.

Electronic nicotine delivery system (ENDS): any battery-operated device that heats a solution, or e-liquid, to generate an aerosolized mixture containing flavoured liquids and nicotine that is inhaled by the user.

Heated tobacco product (HTPs): produce aerosols containing nicotine and toxic chemicals when tobacco is heated or when a device containing tobacco is activated. These aerosols are inhaled by users during a process of sucking or smoking involving a device.

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a decrease in work productivity with subsequent emotional distress (4, 5). In addition, in most low- and middle-income countries, families might experience a significant financial burden and need to compensate for their family member's disability by increasing their work responsibilities (5).

Although not curable, CHD can be managed effectively with medication and relevant medical and surgical procedures and by addressing risk factors, e.g. by quitting tobacco use.

Pathophysiology of tobacco use in coronary heart disease

Tobacco use (both smoking and smokeless) and second-hand smoke (SHS) exposure contribute to heart disease through several mechanisms, including inflammation, vasoconstriction, clot formation and reduced oxygen supply (6–8). As well as directly damaging coronary arteries (6, 7), smoking also raises levels of harmful oxidized low-density lipoprotein and reduces beneficial high-density lipoprotein (which removes excess cholesterol deposited in the arteries), thereby contributing to an increase in fatty deposits (plaque) at the site of the injury in the arteries (6, 7) – a disease known as atherosclerosis. Smokers have higher extracellular lipid content in their plaque, which renders the plaque vulnerable to rupture (9). Endothelial injury and dysfunction promote platelet adhesion and lead to the formation of a blood clot – a process known as thrombosis. Tobacco smoking also induces a hypercoagulable state, increasing the risk of acute thrombosis. Smoking-mediated thrombosis appears to be a major factor in the pathogenesis of acute cardiovascular events (6). The reduction in vital nutrients and oxygen to the heart muscle caused by coronary thrombosis can cause catastrophic heart damage, resulting in major disability or sudden death. Stimulation of the sympathetic nervous system and heart by nicotine increases the demand for myocardial oxygen, causing angina. Tobacco smokers are more likely to experience an acute cardiovascular event at a younger age and earlier in the course of their disease (6).

The heart-related effects of SHS exposure are nearly as great as the effects of smoking itself, and most likely operate through the same biological mechanisms (10). Exposure to SHS for as little as one hour can damage the inner layer of the coronary arteries (11), which increases the risk of heart attack.

Smokeless tobacco products are also harmful to health; they contain over 2000 chemical compounds, including nicotine (6, 12–15). Toxic metals, such as cadmium or nickel (16), and other additives that make smokeless tobacco more palatable, such as liquorice, are reported to have an adverse effect on the cardiovascular system (12). Smokeless tobacco has been shown to lead to elevated blood pressure and chronic hypertension, both of which are major risk factors for CHD (17–19).

Tobacco smoking and coronary heart disease

There is a well-established causal link between tobacco smoking and morbidity and mortality related to CHD. The disease contributes to 9.4 million, or 16.6%, of the 56 million global annual deaths (2). Smoking is responsible for 1.62 million, or 18%, of global deaths from CHD (20), and causes substantial ill health estimated at 40.6 million DALYs lost from CHD (20).

Risk of damage to the cardiovascular system increases with duration of smoking, and with the number and type of smoked tobacco products consumed. The strong dose-response relationship is, however, not linear (6). The risk is substantially increased even at low exposure levels – those who smoke only one cigarette per day incur half the risk of CHD of people who smoke at least 20 cigarettes per day (21). Beyond its status as a major independent risk factor for CHD, smoking tobacco has a synergistic action with other major risk factors for CHD, such as high blood cholesterol, untreated hypertension and diabetes mellitus (22, 23).

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Second-hand smoke and coronary heart disease

An estimated 382 000 people died of CHD attributable to SHS exposure in 2017 (20), representing 4.3% of all deaths from CHD and 31% of all deaths from exposure to SHS (20). SHS exposure was also estimated to be responsible for 8.8 million DALYs lost from CHD in the same year (20).

Various systematic reviews and meta-analyses indicate that adults exposed to SHS, in countries with income levels ranging from high to low, have a 23–30% increased risk of developing CHD (10, 24–28). Cohort studies established in the 1970s and 1980s in multiple countries now demonstrate the adverse effects of childhood SHS exposure on the development of cardiovascular disease, including early-onset atherosclerosis (29–31). One major challenge in these studies is accurately assessing lifetime exposure to SHS. The cumulative lifetime SHS exposure may be significantly higher than reflected over the study period (10), which potentially results in an underestimation of the true risk and impact of SHS exposure on CHD (10).

Smokeless tobacco and coronary heart disease

WHO has estimated that at least 380 million of the world's people use smokeless tobacco products (13 million children aged 13–15 years and 367 million adults aged 15 years and over) (32). Although the largest number of smokeless tobacco users are in South-East Asia, tobacco use is increasingly being documented in other regions of the world (14, 32–34). Research on the health effects of smokeless tobacco is relatively recent compared with that on smoked tobacco, and the results are less consistent. Studies demonstrate an association between smokeless tobacco use and fatal and non-fatal heart disease in Asia. However, such associations are generally not observed in Europe (13, 15, 35–39). A 2006 case-control study (INTERHEART analysis of data from 52 countries) found that, after adjusting for smoking status, smokeless tobacco users in Asia had an increased risk of fatal heart disease (odds ratio (OR) 1.57, 95% confidence interval (CI): 1.24–2.00) (40). Further, a 2016 meta-analysis reported similar findings in Asia (OR 1.40, 95% CI: 1.01–1.95) but noted an absence of effect in Europe (OR 0.91, 95% CI: 0.83–1.01). This was also confirmed by a 2018 study, which demonstrated a clear association between smokeless tobacco use and non-fatal cardiac disease in south-east Asian countries (relative risk (RR) 1.30, 95% CI: 0.39–2.21), especially in Pakistan (RR 1.59, 95% CI:1.34–1.83), but not for users of snus (RR 0.92, 95% CI: 0.81–1.03) (15). These two studies corroborate some pooled analyses (41–43), based on Swedish cohort studies, which found no relationship between current use of Swedish snus and the development of acute myocardial infarction. The reasons for these differences are unclear, and further research is needed to better understand the relationship between smokeless tobacco use and the risk of fatal or non-fatal cardiac disease in different parts of the world.

The growing body of evidence was summarized in a 2015 global report on the burden of disease due to smokeless tobacco use. With data from 113 countries, the report estimates that 204 000 deaths (or 2.4% of all CHD deaths in 2010) may be attributed to smokeless tobacco use. The report also estimates that smokeless tobacco use contributed to 4.7 million DALYs lost due to CHD in 2010 (14).

Novel and emerging nicotine and tobacco products and coronary heart disease

More recently, novel and emerging nicotine and tobacco products have become available in various countries. These include electronic nicotine delivery systems (ENDS) and heated tobacco products (HTPs). ENDS, commonly known as "e-cigarettes", are battery-operated devices that heat a nicotine-containing solution (or e-liquid), propylene glycol and vegetable glycerin (44–46) to generate an aerosol that is inhaled by the user. The aerosol contains ultrafine particles and toxic substances similar to those found in tobacco smoke, but generally at lower levels. HTPs, termed "heat-not-burn" tobacco products by the industry, produce aerosols

containing nicotine and toxic chemicals when tobacco is heated or when a device containing tobacco is activated. These aerosols are inhaled by users during a process of sucking or smoking involving a device. They contain the highly addictive substance nicotine as well as non-tobacco additives, and are often flavoured. The tobacco may be in the form of specially designed cigarettes (e.g. "heat sticks", "Neo sticks") or pods or plugs **(47)**. HTP emissions contain nicotine and chemicals similar to the toxic substances found in cigarette smoke, but also generally at lower levels. Exposure to nicotine and toxic substances not only puts users at risk of health complications, but also endangers bystanders through inhalation of second-hand emissions. A recent study, led by the tobacco industry, claims that ENDS are less harmful than cigarettes **(48, 49)**. Although it is possible that ENDS could be less toxic than smoked conventional cigarettes and tobacco products, they are not harmless and bring risks associated with their use and with second-hand exposure **(50, 51)**. ENDS are associated with increased risk of cardiovascular disease **(52, 53)**. The toxic substances contained in these products can lead to impaired endothelial function, narrowing of arteries, increased heart rate and raised blood pressure **(46, 54, 55)**. The aerosols produced by ENDS contain toxic chemicals harmful to both users and non-users, and therefore come with health risks of their own **(51, 56)**. In combination with smoking, which is the common practice among the majority of ENDS users, the adverse health effects of two or more products are combined **(57)**. There is an urgent need for scientifically robust research to determine the long-term health effects of both direct and second-hand exposure to emissions of these products.

Impact of selected tobacco control interventions on coronary heart disease

Tobacco control measures have been shown to substantially benefit heart health. Increases in tobacco taxation, for example, have been directly linked with a reduction in tobacco consumption, thereby leading to better heart health **(58)**. Anti-tobacco media campaigns and graphic health warnings have also brought a better understanding of the dangers of tobacco use for heart health. Although these interventions have been successful in reducing tobacco consumption, tobacco remains a highly addictive substance, and many people need help to quit. Governments can assist by enforcing legislation for smoke-free public places and providing support services to help users quit. A large number of people are still unaware of the risks **(59)**, which means that more needs to be done to raise awareness about the harmful effects of tobacco.

Smoking cessation interventions are a cost-effective measure for preventing CHD and reducing both short-term and long-term health expenditure **(60, 61)**. The excess risk of CHD is halved after one year of quitting smoking, and after 15 years of quitting, the risk of heart disease is similar to that of a never-smoker **(62)**. Smoke-free public places also yield health benefits, such as reported reductions in acute coronary events, hospital admissions and deaths following the implementation of smoke-free legislation **(63–69)**.

A 2013 study in India **(70)** concluded that a combination of smoke-free legislation and increased tobacco taxation could avert 25% of heart attacks and stroke over 10 years. A 2013 meta-analysis identified a 13% reduction in the risk of acute myocardial infarction (pooled RR 0.87, 95% CI: 0.84–0.91) following the implementation of comprehensive smoke-free legislation **(65)**. Similarly, a 2014 meta-analysis identified a 12% reduction in hospitalizations for acute coronary events following the enactment of smoke-free legislation (pooled RR 0.88, 95% CI: 0.85–0.90) **(69)**. This study also found that comprehensive smoke-free legislation (complete smoking ban in public places, including bars and restaurants) was associated with a greater reduction in hospitalization for acute coronary events (14%) compared with partial smoking bans (8%) **(69)**. A 2016 Cochrane review found that implementation of smoke-free legislation reduced smoking-related hospital admissions for both smokers and non-smokers **(71)**.

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Population level actions

Tobacco-related heart disease brings substantial costs at both societal and personal level. We recommend the WHO Framework Convention on Tobacco Control (WHO FCTC) **(72)** as the pre-eminent tool for the implementation of evidence-based tobacco control measures. To help countries implement the WHO FCTC, WHO introduced the MPOWER policy package in 2008. MPOWER is a set of six tobacco control and demand-reduction measures, which correspond to one or more articles in the WHO FCTC. WHO tracks the status of the MPOWER measures in the biennial WHO report on the global tobacco epidemic **(73)**. In 2017, the World Health Assembly also endorsed a set of WHO "best buys" **(74)** and other recommended interventions for governments to implement for the prevention and control of noncommunicable diseases. The implementation of effective tobacco control measures would lead to reductions not only in tobacco consumption, but also in morbidity and mortality from heart disease caused by tobacco.

Preventing CHD deaths caused by tobacco requires a comprehensive, multisectoral approach, including the engagement of health systems. By embedding tobacco cessation support in primary health care settings, countries are better positioned to improve the quality of information and levels of support provided for smokers, as well as increasing the reach of their services. Cardiac health-care providers and organizations can support these efforts by modelling tobacco-free living, not using tobacco themselves, and ensuring that all health facilities, academic institutions, conferences, organizations and training facilities are 100% tobacco- and smoke-free **(75)**. They can also support tobacco control in the policy domain by advocating actively for comprehensive implementation of the WHO FCTC. Health-care providers, including general practitioners, nurses, pharmacists and cardiologists, and health organizations should raise awareness about the harm to the cardiovascular system caused by tobacco use and exposure to SHS, as well as the benefits of quitting tobacco.

Individual level action

Smokers should respect smoke-free policies, and everyone should support friends, family members and colleagues who want to quit smoking or tobacco use. In adults who use tobacco, a combination of behavioural interventions plus pharmacotherapy is recommended by health professionals to maximize quit rates **(76)**. Non-smokers should demand smoke-free legislation for all enclosed public places and ensure that they are not exposed to SHS at home, at work or in indoor public places.

Individual level action

- WHO FCTC
http://www.who.int/fctc/en/

- WHO Tobacco Free Initiative (TFI)
http://www.who.int/tobacco

- World Heart Federation
http://www.world-heartfederation.org/

Methods

When preparing the present document, WHO conducted a comprehensive literature search for systematic reviews and other articles investigating the relationship between tobacco use/exposure to SHS and CHD. Inclusion criteria included human study population, heart disease outcome and tobacco use (both smoking and smokeless) or exposure (SHS or environmental tobacco smoke) at any time over the life course. The review was not limited to any particular study design or language; however, the literature review identified very few studies in languages other than English.

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