6 Cardiovascular disease

Burden, epidemiology and risk factors

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This is one of two chapters on cardiovascular disease (CVD). Chapter 7 focuses on priority interventions for CVD and monitoring and evaluation.

Definitions

CVD is a term for conditions affecting the heart and blood vessels. The two main sites for CVD are ischaemic heart disease (IHD) and cerebrovascular disease (such as ischaemic or haemorrhagic stroke). Common manifestations of IHD include angina pectoris (chest pain due to insufficient oxygen supply in the coronary arteries), heart attack (also called myocardial infarction, which causes the loss of a part of the heart muscle) and heart failure (impairment of the heart pumping function due to weakened heart muscle). Cerebrovascular disease can result in lasting neurological damage, including hemiplegia and severe brain cognitive alterations. Transient ischaemic attacks (TIAs) are similar to a stroke but last only a few minutes or hours and cause no lasting disability, but a third of persons with a TIA can subsequently develop a full stroke.

Common to IHD and ischaemic stroke is atherosclerosis (an intravascular build-up of cholesterol, calcium, fibrous tissue and platelets) that progressively over many decades results in narrowed and inelastic arteries, which results in decreased blood flow and oxygen supply (hence the word 'ischaemic') and ultimately total vessel block (causing heart attack or stroke). Haemorrhagic stroke is particularly strongly associated with hypertension.

Other cardiovascular diseases include congenital heart disease malformations, heart valves defects (including rheumatic heart disease), cardiomyopathies (diseases of the heart muscle that are not directly related to ischaemia), arterial aneurysm, peripheral arterial disease, deep vein thrombosis and pulmonary embolism.

This chapter focuses on IHD and stroke because they cause around 80% of the global CVD mortality (IHME, 2019), and they share (along with some other CVDs such as peripheral arterial disease) a common set of modifiable risk factors and therefore similar prevention and management strategies. For these reasons, the focus on CVD in the WHO Global NCD Action Plan is on IHD and stroke and their main risk factors.

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Disease burden and trends

The three most important elements of the epidemiology of CVD are: (i) the increasing total CVD burden owing to the increasing and aging populations in the world, i.e. demographic transition; (ii) the decreasing age-standardized CVD mortality rates in most countries because progress is being made in tackling risk factors and improving treatment; and (iii) large differences in age-standardized CVD mortality between countries as a result of markedly different risk factor levels across populations and large differences in implementation of population-wide prevention and control programmes, including effective health care.

Based on data from IHME, there were 523 million people living with a CVD in 2019 of which 197 were IHD and 101 were stroke. CVD accounted for 18.6 million deaths in 2019, while IHD accounted for 9.1 million deaths.[1]

Table 6.1 shows that CVD (including IHD and stroke) in 2019 accounted for 32.8% (18.6 million) of all deaths globally, IHD for 16.2% (9.1 million) and stroke for 11.2% (6.6 million) (data from IHME).

However, there are large differences between countries from different World Bank income categories. The proportion – from all deaths – of CVD deaths for CVD, IHD and stroke were high in 2019 in high-income countries (HICs) but had decreased compared to 1990; were highest in upper-middle-income countries (MICs) in 2019 (an increase from 1990); and were lowest in lower-MICs and low-income countries (LICs), but a twofold increase from 1990. These differences in regions partly reflect changing age distributions of populations.

Although IHD and stroke deaths are more common above the age of 70, they also cause substantial premature mortality. For example, nearly 30% of all deaths worldwide between 50 and 69 years in 2019 were from IHD and stroke.

Decreasing age-standardized mortality

Table 6.1 also shows that the age-standardized mortality rates from CVD, IHD and stroke (which are not influenced by the age distribution of the populations

Table 6.1 Mortality for CVD, IHD and stroke (IHME)

	Global		*HICs*		*Upper-MICs*		*Lower-MICs*		*LICs*	
	1990	*2019*	*1990*	*2019*	*1990*	*2019*	*1990*	*2019*	*1990*	*2019*
Proportion of all deaths (%)										
All CVD	25.9	32.8	42.2	32.5	32.3	40.7	17.4	29.7	9.1	16
IHD	12.2	16.2	24.4	16.4	12.7	18.8	8.5	16	3.2	6.2
Stroke	9.8	11.6	11.8	8.4	14.8	16.6	6.4	9.8	3.9	6.5
Age-standardized mortality rates (per 100,000)										
All CVD	345	240	283	134	401	267	384	313	355	304
IHD	170	118	164	68	163	124	191	169	131	121
Stroke	132	84	79	34	180	107	141	104	149	123

compared) were higher in low- and middle-income countries than in HICs. However, the rates *decreased* over time in all income groups, with a large two-fold decrease in HICs, and a marked decrease in upper-MICs, but only a small decrease in lower-MICs and LICs.

Decreasing CVD mortality is due to a decrease in both incidences (of new cases) and case fatality (among cases) over time.[2] The decreasing incidence reflects a downward shift in several CVD risk factors in the population due to prevention and treatment (e.g. tobacco use, BP and blood cholesterol),[3] while increasing survival reflects improving case management.[4] Large gains in life expectancy at birth observed over the past few decades worldwide largely resulted from the decrease in age-standardized CVD mortality but, in several regions, including Africa, also largely resulted from reductions in maternal and child mortality.[5]

However, the downward trend in age-standardized CVD mortality has been slowing in many countries over recent years, including in HICs, particularly among younger adults, which has been in part attributed to the increasing prevalence of obesity and diabetes.

Variations across countries

Age-standardized CVD rates vary by more than ten-fold between countries, for example <30/100,000 population in 2019 (and still decreasing) in Japan and France compared to >700/100,000 population (but decreasing) in Uzbekistan for IHD, with a similar magnitude of variation for stroke (IHME).

Proportions of IHD/stroke mortality that are attributable to modifiable risk factors (population-attributable fractions)

These fractions express the estimated proportions (or percentages) of the total IHD/stroke burden that could be prevented if a risk factor was eliminated in the *whole* population (i.e. if all individuals in the population had this risk factor at the optimal level range).[6] At a global level, in 2019, these fractions were as follows:[7]

- *Environmental*: particulate matter (e.g. pollution, indoor smoke) 21%; non-optimal temperature 7%.
- *Physiologic/metabolic*: high blood pressure 51%; high blood cholesterol 28%; high blood glucose 23%; kidney dysfunction 11%.
- *Behaviours*: unhealthy diet 41%★; tobacco use 19%; physical inactivity 4%; harmful use of alcohol 1%.

  ★This includes: high sodium (salt) and low whole grains (10% each); low vegetables and fruit (7% and 5% respectively); high red meat, high trans fat, low nuts and seeds low fibre (4% each); low vegetables, alcohol (3% each), low polyunsaturated fats and low omega-3 fatty acids (2% each); processed meat and sugar-sweetened beverages (1% each).

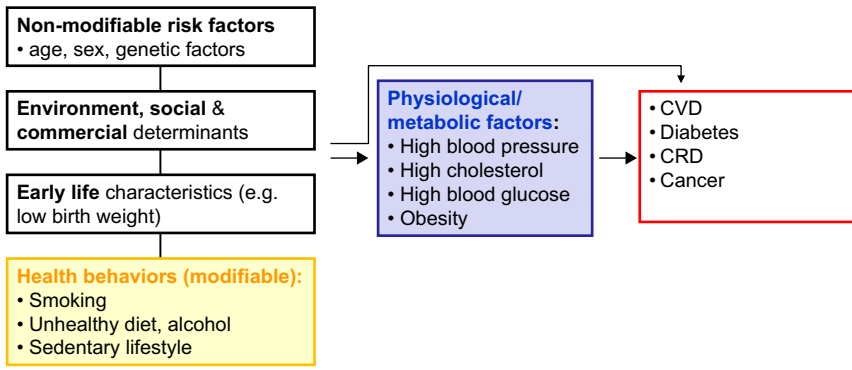

Figure 6.1 The relationship between risk factors and CVD (and other selected NCDs).

These large attributable fractions across a wide range of risk factors emphasize the need to prevent IHD and stroke through a large number of interventions, and these are addressed in the following chapter and other chapters.

Risk factors

The relationships between modifiable and non-modifiable risk factors, as well as broader determinants of health with physiological and metabolic risk factors and with IHD and stroke, are shown in Figure 6.1. Peripheral vascular disease, as well as cancer and chronic respiratory disease, are included to highlight the relationship between these risk factors and NCDs more broadly. The relationship between risk factors and CVD outcomes is graded (i.e. dose-dependent). This explains why the majority of CVD outcomes arise in individuals with moderate rather than high levels of risk factors (i.e. the majority of the population) rather than from those (a minority of the population) at high risk. This underscores the need to reduce risk factors in the whole population, not only among those at the highest risk. Chapter 36 on population and high-risk strategies provides a description of this 'prevention paradox'.

Main modifiable risk factors

The main modifiable CVD risk factors were identified in the late 1940s and 1950s when the CVD epidemic was rapidly progressing in high-income countries. The pioneering Framingham cohort study (started in the late 1940s) showed that both the 10- and 30-year risk of CVD risk was <5% among individuals who were non-smokers, with low BP, low blood cholesterol and no diabetes, but the 10- and 30-year risks were as high as around 40% and 80%, respectively, among individuals with elevated levels of these four risk factors, emphasizing the importance of interventions to reduce exposure to these risk factors.[8]

Other studies have shown that individuals with healthy behaviours, including not smoking, being physically active, with a healthy diet, and being lean (which can be interpreted as having healthy nutrition and regular physical activity), had a very low incidence of heart attacks and stroke (as well as diabetes and cancer),[9] emphasizing the critical role of this small number of healthy behaviours. Consistent with this, many studies have shown large protection for CVD among individuals with low levels of these main risk factors, described by the American Heart Association as 'Life Simple 7', which includes three 'ideal health factors' (BP <120/80 mmHg, total cholesterol <5.2 mmol/L, blood glucose <5.6 mmol/L) and four 'ideal health behaviours' (not smoking, regular physical activity, healthy diet, and body mass index <25 kg/m^2).[10] While there is some evidence that low alcohol consumption (e.g. ≤1 drink per day) may reduce the risk of IHD, anything more is associated with increased risk. Hundreds of clinical trials have shown an approximately 20–30% lower relative risk of CVD when reducing one risk factor with therapy (behavioural or medication), and much more when reducing several risk factors at the same time.[11] A list of main modifiable CVD risk factors, and their potential contribution to the CVD incidence (e.g. as assessed by population-attributable fractions), is described in the previous section; a more detailed description of related interventions appears in other chapters in the book (hypertension, diabetes, fats and cholesterol, tobacco, salt, diet, physical activity, alcohol, etc.).

Age, genetics and other risk factors

Chronological age is by far the most important CVD risk factor, independent of the risk factors above. However, biological or physiological age (how old a person seems) is even more important and is a combination of an individual's chronological age, phenotype (e.g. blood pressure, blood sugar level or extent of vascular atherosclerosis), and genetic makeup and alterations over time (e.g. detrimental chromosomal telomere changes with age).[12]

Genetic makeup plays a significant role in CVD.[13] Single gene alterations are rare but important causes of CVD, e.g. familial hypercholesterolemia that causes heart attack at an early age. In contrast, polygenic alterations (i.e. abnormal single nucleotide polymorphisms) are common (e.g. a prevalence of up to 30% for the presence of one particular isolated abnormal SNP associated with CVD), but the effect on CVD is generally small in the presence of one or a few such alterations but can be substantial when many abnormal SNPs are present. However, while a high polygenic risk score (i.e. a score based on many SNPs associated with CVD) can raise CVD risk by as much as two-fold, the impact is reduced among those with healthy lifestyles and diets.[14] In addition, epigenetic factors associated with CVD (i.e. alterations in gene expression, how the body 'reads' DNA rather than alterations of the genetic code itself) can also increase the risk of CVD. These alterations are, for example, enhanced by exposure to risk factors such as tobacco smoke.[15] The above suggests that polygenic risk scores are likely to play an important

role in personalized CVD prevention and treatment in the future[16] (Chapter 29 on genetics).

Psycho-social factors (e.g. stress, depression) and socio-economic variables such as income, education, employment status, and neighbourhood characteristics are associated with CVD, either directly or indirectly (e.g. depression, stress or other unfavourable psycho-social conditions can lead people to smoke more, have a poorer diet, consume more alcohol, do less physical activity, and seek less frequent care for their health).[17] Low birth weight is associated with an increased risk of several cardiometabolic disorders (e.g. obesity, diabetes, CVD) in adulthood,[18] which has significant public health implications in low-income countries. Further details are provided in Chapter 17 on social determinants of health and chapter 37 on a life-course approach to NCDs.

The role of economic development, globalization and urbanization

The relationship between a society's economic development and the development of CVD is complex. Early in the health transition (Chapter 2), individuals of higher socio-economic status (SES) have the highest levels of risk factors, with the correspondingly greatest incidence of CVD events. Individuals of higher SES are, however, the first to acquire an understanding of CVD risks and they modify their behaviour accordingly (e.g. they reduce tobacco consumption and adopt a healthier diet), resulting in a decrease in CVD incidence. In the meantime, those in the lower socio-economic groups are more exposed to risk factors, with a high incidence of disease.

As a result, the relationship between socio-economic development and CVD risk factors generally follows a bell shape curve, with levels of mean blood cholesterol, blood pressure and (to a lesser extent) body mass index rapidly increasing, plateauing and then decreasing as a country's socio-economic development increases over time.[19] These trends partly reflect a transition from (healthy) unrefined traditional foods, to inexpensive (unhealthy) energy-dense processed foods, until a later stage where a broader variety of foods is available (both healthy and unhealthy). In summary, economic development (and by extension globalization) presents both challenges and opportunities with regard to CVD – ones that need to be tackled respectively through policies that impact CVD and health more broadly.[20] There is also emerging evidence that the argument that urbanization is invariably detrimental to cardiovascular health is not always the case. For example, the prevalence of obesity is now increasing faster in rural rather than urban settings in low- and middle-income countries.[21] These issues are also described further in Chapter 2 on the health transition.

Notes

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