

Chapter 2

Relationships among Major Risk Factors and the Burden of Cardiovascular Diseases, Diabetes, and Chronic Lung Disease

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INTRODUCTION

Cardiovascular, respiratory, and related disorders (CVRDs) are a subset of noncommunicable diseases (NCDs) that are an important and increasing cause of morbidity and mortality in low- and middle-income countries (LMICs). CVRDs share common risk factors such as smoking, poor diet, and physical inactivity. They also share common interventions at the clinical, public health, and policy levels. Public health professionals and decision makers share a widespread notion that CVRDs are diseases of the affluent (WHO 2010b). Yet recent cross-national studies have demonstrated that the burden of CVRDs falls disproportionately on lower-income countries and disadvantaged groups within countries. Prevention and control of CVRDs, then, have important equity implications. Addressing CVRDs also fits in with the Sustainable Development Goals that focus on reducing poverty and improving health, particularly through mechanisms (such as universal health coverage) that can address the rise in CVRD risk factors and the potential impoverishing effects of chronic illness.

The concept that current or past exposure to specific factors increases the risk of future ischemic heart disease (IHD) was first established in the Framingham Heart

study in the United States (Kannel and others 1961), but it has been validated extensively in LMICs (O'Donnell and others 2010; Yusuf and others 2004). These risk factors are now well established globally, not only for IHD (Pearson and others 2003; Perk and others 2013; Yusuf and others 2001; Yusuf and others 2004), but also for stroke (Colditz and others 1988; Markus 2011; O'Donnell and others 2010), other cardiovascular diseases (CVDs) (Greenland and others 2010; Khatibzadeh and others 2013; Mosca and others 2004; Smith and others 2011), diabetes (Caballero 2003; Singh and others 2010; Weber and others 2012; Zimmet and others 1999), chronic lung disease (Madison, Zelman, and Mittman 1980; Palta and others 1991; Salvi and Barnes 2009; Strobe and Stempel 1984), and other chronic NCDs (Allender and others 2011; Ezzati and Riboli 2013; Hallal and others 2012). Exposure to these risk factors may occur early in life, including in utero, and continue throughout life or may be limited to only certain phases of the life span. These risk factors may be strongly influenced by socioeconomic and environmental determinants, policy and legislative interventions, lifestyle and behavioral choices, and familial and genetic predisposition. Among modifiable risk factors, reducing the level of individual or population

risk or discontinuing the exposure leads to corresponding reductions in the magnitude of disease burden and preventable deaths. In-depth knowledge of these relationships as well as the distribution of risk factors in the population provides a sound basis for developing prevention strategies at the individual and population levels.

This chapter describes recent trends in mortality and morbidity from CVRDs in LMICs and the specific conditions (including IHD, structural heart disease, heart failure, stroke, peripheral arterial disease, diabetes, kidney disease, and chronic lung disease) and risk factors covered in this volume. It then reviews the evidence regarding the complex interrelationships between specific risk factors, their early- and late-life determinants, and their corresponding influence on CVRD risk later in life. Finally, it presents steps for addressing CVRD risk factors and for reducing preventable deaths within a socioecological framework.

TRENDS IN CVRD MORTALITY AND MORBIDITY

Of the 55.9 million deaths globally in 2012, 37.9 million were from NCDs, including 23.9 million deaths from CVRDs. A plurality of deaths (17.5 million) were from CVDs, with respiratory diseases (4.0 million) being the second-most frequent cause of death; diabetes mellitus and kidney diseases followed, with 1.5 million and 864,000 deaths, respectively. NCDs not covered in this volume—including mental and neurological disorders

and cancers—constituted 37 percent of total NCD deaths. Table 2.1 presents total deaths by cause and country income group.

Because of a convergence of population size and the epidemiological transition, the vast majority of CVRD deaths occur in LMICs, including 74 percent of cardiovascular deaths, 83 percent of diabetes deaths, 84 percent of respiratory disease deaths, and 76 percent of kidney disease deaths. Figure 2.1 illustrates the proportion of total deaths caused by each group: in low-income countries, 21 percent of deaths were from CVRDs, compared with 30 percent and 54 percent of deaths, respectively, in lower-middle-income and upper-middle-income countries.

Most CVRD deaths occur in LMICs because of disparities in age-specific mortality rates and demographic changes. First, age-specific mortality rates from CVRDs are substantially higher in LMICs than in high-income countries (HICs) (figure 2.2). Although the prevalence of various risk factors is generally lower in LMICs (particularly in low-income countries), case fatality rates are much higher, probably because of the low use of evidence-based prevention and treatment interventions (Yusuf and others 2011; Yusuf and others 2014).

Second, rapid demographic changes are driving the overall increase in observed deaths. Between 2000 and 2012, the total population increased 8 percent in HICs and 17 percent in LMICs. The adult population grew even faster (14 percent and 32 percent, respectively). These trends are probably being driven by persistently high fertility rates in many LMICs as well as lower under-five mortality rates, which together contribute to

Table 2.1 CVRD Deaths, by Cause and Country Income Group, for All Ages and Both Genders, 2012
Thousands, unless otherwise noted

Indicator	Low-income	Lower-middle-income	Upper-middle-income	High-income	World (total)
Population	850,000	2,510,000	2,430,000	1,290,000	7,060,000
Total deaths	7,450	19,900	16,900	11,700	55,900
CVRD deaths	1,540	7,780	9,080	5,530	23,900
CVRD deaths as a percentage of total deaths	21	39	54	47	43
<i>CVRD deaths by cause</i>					
Cardiovascular diseases	999	5,220	6,860	4,440	17,500
Diabetes mellitus	135	549	559	254	1,497
Respiratory diseases	309	1,630	1,460	645	4,040
Kidney diseases	99	378	197	190	864

Source: WHO 2014.

Note: CVRD = cardiovascular, respiratory, and related disorder.

overall population growth and aging. In 1960 less than 5 percent of the global population was older than age 65 years, and 15 percent was younger than age 5 years. By 2015, these proportions had converged and were projected to reverse by 2040. The result of this demographic change is that a larger total number of persons in LMICs are living to older ages and are more exposed to CVRD risk determinants and CVRDs themselves (WHO and U.S. National Institute on Aging 2011).

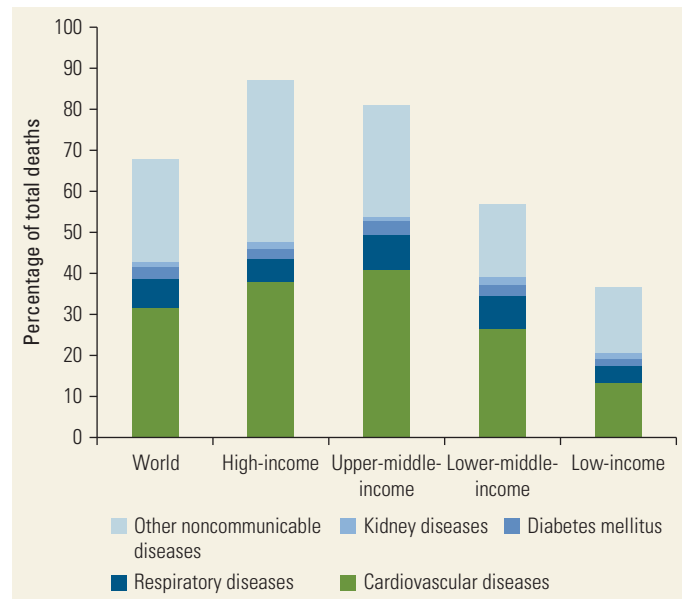
Age-standardized mortality rates are a useful metric for disentangling epidemiological and demographic changes in CVRD mortality. We calculated age-standardized mortality rates for CVRDs using the 2012 global population structure as a reference for region-specific rates in 2000 and 2012. For CVDs, deaths are rising in all regions because of demographic changes; however, age-standardized mortality rates are declining in HICs much faster than in LMICs, probably because of reductions in risk factors and a decline in case fatality rates (table 2.2).

Age-standardized mortality rates in LMICs are rising for diabetes but declining for respiratory and kidney diseases. The substantial decline in respiratory disease rates is probably related to progress in reducing household air pollution, although this reduction has been offset somewhat by the rise in outdoor air pollution, a subject discussed in volume 7 of *DCP3* (Watkins, Dabestani, and others 2017).

CVDs—the predominant cause of CVRD mortality—demonstrate marked and increasingly disparate trends in age-standardized mortality rates. Rates in high- and low-income countries were similar in 2000, but much more rapid progress had been made in HICs by 2012. Lower-middle-income and upper-middle-income countries had higher rates than HICs in 2000, and their rates have continued to decline modestly, as they have in low-income countries (figure 2.3). Again, this growing inequality in cardiovascular health requires further exploration but, in general, reflects rapid epidemiological change in LMICs and the absence of a health system response to address cardiovascular mortality. Unfortunately, if current trends continue, LMICs are unlikely to meet the Sustainable Development Goal target of achieving a one-third reduction in premature mortality from NCDs.¹

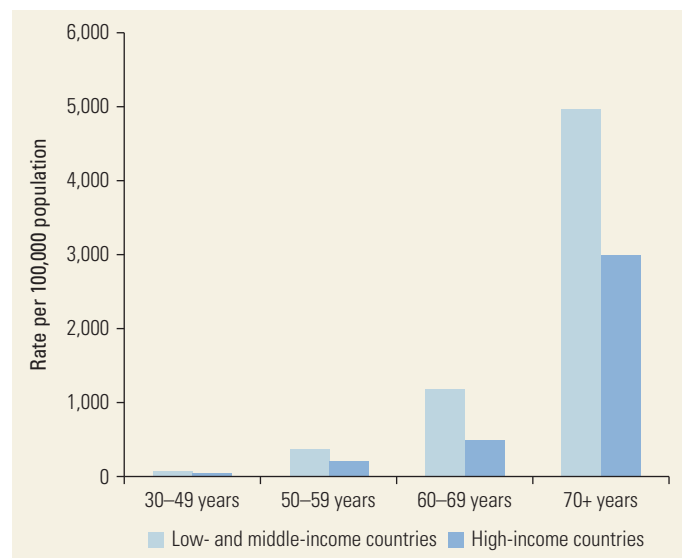
Finally, the summary metric of disability-adjusted life-years (DALYs) provides insight into the relative impact of CVRD morbidity and mortality. Generally, premature mortality (years of life lost) is the major contributor to total DALYs from CVRDs, but morbidity (years lived with disability) is a particularly important aspect of diabetes and respiratory and kidney diseases. CVDs are responsible for 74 percent of deaths, but

Figure 2.1 Proportion of Total Deaths Caused by Cardiovascular, Respiratory, and Related Disorders and Other Noncommunicable Diseases, by Country Income Group, for All Ages and Both Genders, 2012



Source: WHO 2014.

Figure 2.2 Age-Specific Mortality Rates from Cardiovascular, Respiratory, and Related Disorders, by Country Income Group, for Both Genders, 2012



Source: WHO 2014.

only 64 percent of DALYs. Diabetes is responsible for 6 percent of deaths, but 10 percent of DALYs; respiratory diseases are responsible for 17 percent of deaths, but 22 percent of DALYs; and kidney diseases are responsible for 4 percent of deaths, but 5 percent of DALYs.

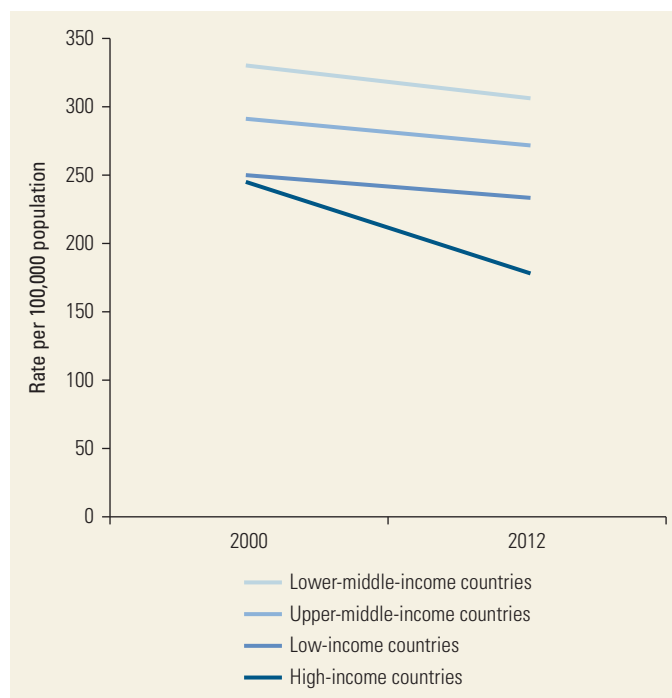
Table 2.2 Percentage Changes in Total Deaths and Age-Standardized Mortality Rates from Cardiovascular, Respiratory, and Related Disorders, by Country Income Group, for Both Genders, 2000–12

Percentage change

Cause of death	Percentage Change in Total Deaths		Percentage Change in Age-Standardized Mortality Rates	
	Low- and middle-income	High-income	Low- and middle-income	High-income
Cardiovascular diseases	30	-8	-6	-27
Diabetes mellitus	54	7	11	-15
Respiratory diseases	1	15	-28	-10
Kidney diseases	21	41	-9	9

Source: WHO 2014.

Figure 2.3 Age-Standardized Mortality Rates from Cardiovascular Disease, by Country Income Group, for Both Genders, 2000–12



Source: WHO 2014.

SPECIFIC CVRDS

Ischemic Heart Disease

IHD is caused by gradual narrowing of the blood vessels that supply the heart muscles as a result of the buildup of fatty plaques. This narrowing reduces the supply of blood and starves the heart muscles of oxygen, culminating in heart attack. The underlying causes of IHD are predominantly of lifestyle origin, including tobacco use, unhealthy diet, low consumption of fruits and green leafy vegetables, physical inactivity, and harmful use of alcohol.

IHD is a leading cause of death and disability worldwide, accounting for 13 percent of all deaths in 2012. IHD rates vary across populations. The onset of IHD is found to be at least a decade earlier among South Asian populations than among Western populations (McKeigue and others 1993). IHD-related mortality rates are also higher among South Asians. Indeed, in the past few years, IHD rates have been declining in many HICs but rising in LMICs as result of increasing longevity, urbanization, and lifestyle changes.

Stroke

Stroke continues to be a leading cause of death in Africa and major parts of South-East Asia. The causative reasons for stroke in these regions include ethnicity as well as the high prevalence of hypertension among Africans and the high consumption of salt (a precursor of hypertension) among South-East Asians. Stroke can be fatal, but it is more frequently debilitating and has been described as worse than death in some communities. However, stroke is eminently preventable: the single most important modifiable factor for preventing stroke is hypertension. A third of stroke events are attributable to hypertension alone, and hypertension is the entry point for all stroke prevention interventions.

Other Cardiovascular Diseases

Peripheral vascular disease is an important cause of morbidity that shares many risk factors and treatments with IHD and stroke. Hypertensive heart disease, which leads to heart failure without overt ischemia, is particularly relevant in African countries early in the epidemiological transition. Congenital heart disease affects about 1 percent of the world's population, and its frequency is similar in LMICs. It is discussed along with two other structural heart diseases that are endemic in LMICs (rheumatic

heart disease and Chagas disease) in chapter 11 of this volume (Watkins, Hasan, and others 2017). Although all of these conditions are relatively neglected compared with IHD and stroke, they accounted for 18 percent of all cardiovascular deaths in LMICs in 2012 (figure 2.4).

Diabetes

Diabetes and metabolic syndrome have emerged as a major problem in many parts of the world, especially LMICs. China and India are home to a large number of people with diabetes. These two countries have an estimated 69 million and 109 million diabetics, respectively, numbers that are projected to increase to 123 million and 150 million, respectively, by 2040 (IDF 2015). Diabetes, in the long term, results in both microvascular and macrovascular complications. Microvascular complications include retinopathy, nephropathy, and neuropathy, and are highly disabling. Macrovascular complications include IHD, ischemic stroke, and amputations as a result of foot infections. Many individuals with diabetes die from IHD or stroke, with the cause of death often being registered as IHD or stroke, not diabetes; therefore, existing estimates likely underestimate the true impact of diabetes on population health.

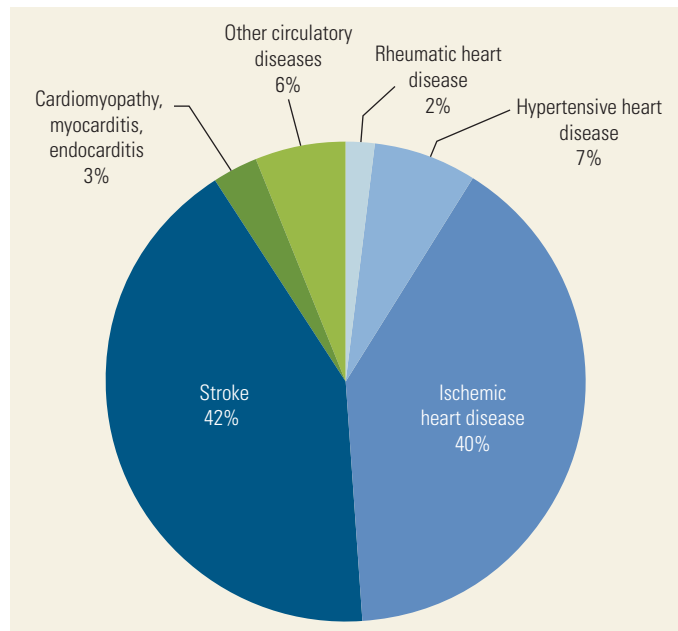
Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide. Tobacco smoking is established as a major risk factor, but emerging evidence suggests that other risk factors are also important, especially in LMICs. An estimated 25 percent to 45 percent of patients with COPD have never smoked, so the burden of nonsmoking COPD is much higher than previously believed. Half of the world's population—about 3 billion people—are exposed to smoke from biomass fuel, compared with 1.01 billion people who smoke tobacco, suggesting that exposure to biomass smoke might be the biggest risk factor for COPD globally. At the same time, age-standardized mortality rates from air pollution are declining in areas where indoor biomass fuels are being replaced with cleaner fuels. Other factors associated with COPD are occupational exposure to dusts and gases, history of pulmonary tuberculosis, chronic asthma, respiratory tract infections during childhood, outdoor air pollution, and poor socioeconomic status.

Asthma

Asthma, a disease of the airways, occurs in people of all ages. Globally, 334 million people have asthma, and the

Figure 2.4 Specific Causes of Cardiovascular Death in Low- and Middle-Income Countries, 2012



Source: WHO 2014.

burden of disability is as high as 222 million DALYs; the most affected people are in LMICs (Global Asthma Network 2014; Institute of Health Metrics and Evaluation 2013). Asthma burden is found to have an age-specific gradient. Children ages 10–14 years and elderly persons ages 75–79 years have higher rates of asthma (Global Asthma Network 2014). Asthma symptoms became more common in children in many LMICs between 1993 and 2003; globally, 14 percent of children experience asthma symptoms (Global Asthma Network 2014). Factors responsible for increasing asthma rates are not fully understood, but environmental and lifestyle changes play the key roles.

RELATIONSHIPS BETWEEN RISK EXPOSURE AND DISEASE BURDEN

Nonmodifiable Risk Factors

Risk factors for CVD, diabetes, chronic lung disease, and other chronic NCDs are considered nonmodifiable if their values, once established at birth, cannot be modified. Examples of these nonmodifiable risk factors include age, gender, race, ethnicity, birthweight, prematurity at the time of birth, family medical history, and genetic makeup. Although their actual values cannot be changed, their physiological implications and overall impact on morbidity and mortality can be modified,

especially when knowledge of these risk factors appropriately informs strategies for screening for, evaluating, preventing, treating, and controlling NCDs and their modifiable risk factors.

In addition to their individual roles as nonmodifiable risk factors, they have important interactions. Notable examples are the interactions between age, gender, and race or between genes and the environment. These interactions could be taken into account in the prevention and control of disease and risk factors (Ahmad and others 2013; Giolo and others 2010; Hui and others 2013; Lin and others 2009; Schumacher, Hunt, and Williams 1990).

Age is the most important nonmodifiable risk factor for CVRDs. Advancing age is the most powerful independent predictor of death and disability because it effectively integrates the cumulative impact of all modifiable and nonmodifiable risk factor exposures over time. Advancing age is a key factor in the global rise in CVRD mortality (Lozano and others 2012). As a result, interventions designed to address modifiable risk factors early in life and through youth and middle age have the greatest potential to reduce preventable death and disability from CVRDs (WHO 2005). Nonetheless, effective primary and secondary prevention and control of modifiable risk factors in older adults remain important, because these risk factors can still be modified as individuals age, resulting in moderate to large reductions in mortality.

CVDs, diabetes, and chronic lung disease are just as important in women as they are in men. However, at equivalent chronological ages, IHD is two to five times more common in men than in women, depending on the population studied (Jousilahti and others 1999). This gender difference in IHD is particularly prominent before the fifth decade of life; however, the difference reverses and IHD becomes more prominent in women in later decades. More than half of the observed gender-related difference in susceptibility to IHD can be explained by gender-related differences in measured risk factors (Jousilahti and others 1999).

Modifiable Risk Factors

The INTERHEART study showed that high blood pressure, smoking, abnormal lipids, diabetes, abdominal obesity, psychosocial factors, low consumption of fruits and vegetables, physical inactivity, and harmful use of alcohol account for most of the risk of IHD worldwide in both men and women at all ages and in all regions (Yusuf and others 2004). Similarly, the INTERSTROKE study demonstrated that 10 risk factors are associated with 90 percent of the risk of stroke and that targeted interventions that reduce blood pressure and smoking and promote physical activity and a

healthy diet could substantially reduce the burden of stroke (O'Donnell and others 2010). Many studies have replicated these findings, and these risk factors are now routinely measured in cardiovascular epidemiology and are tracked in comparative risk assessments conducted for burden of disease studies (GBD 2013 Risk Factors Collaborators 2015).

The prevalence of modifiable risk factors for CVRDs is increasing in many LMICs, particularly middle-income countries, as Western dietary and lifestyle patterns become global dietary and lifestyle patterns (table 2.3).

Tobacco Use

Tobacco use is an important modifiable risk factor for NCD and total mortality. Tobacco use accounted for more than 6.1 million deaths worldwide in 2013 (GBD 2013 Risk Factors Collaborators 2015). This estimate includes exposure to passive smoking (secondhand smoke), which increases the risk of development and progression of atherosclerosis (Law, Morris, and Wald 1997). Cigarettes are the most common smoked form of tobacco, although several other forms are in use. Bidis, small hand-rolled cigarettes widely used in South Asian countries, have levels of nicotine equal to or higher than those in traditional cigarettes and are associated with higher risk for CVRD and cancers (Gupta and Asma 2008). Nearly 80 percent of the world's 1 billion smokers live in LMICs, and that number is projected to rise during the next decade if trends continue (Bilano and others 2015). Most smokers in LMICs are male, which is in contrast to HICs. Tobacco smokers have 2–3 times higher relative risk of IHD, 1.5 times higher risk of stroke, 1.4 times higher risk of COPD, and 12 times higher risk of lung cancer. These risks have an age gradient, with higher relative risk (5–6 times) in younger age groups, although they are similar for men and women (Parish and others 1995; Peto and others 1994). Most of these risks decline within 10 years of quitting smoking (Rosenberg and others 1985). Furthermore, tobacco smoke interacts with other risk factors, and chewable forms of tobacco are as dangerous as cigarettes, causing a range of cancers.

Dyslipidemia (Abnormal Pattern of Blood Fat Level)

Cholesterol in excess, particularly bad cholesterol (low-density lipoprotein), increases the risk of heart disease, stroke, and other vascular diseases. Cholesterol is the key component in the development of atherosclerosis (accumulation of fatty deposits on the inner lining of arteries). The prevalence of high cholesterol among adults in LMICs ranges from 24.3 percent in low-income countries to 45.6 percent in upper-middle-income countries (table 2.3). High cholesterol is estimated to cause 2.6 million deaths and 30 million DALYs annually.

Table 2.3 Prevalence of Selected Cardiovascular, Respiratory, and Related Disorders Risk Factors, by Country Income Group, Various Years

Percent

Indicator	Low-income	Lower-middle-income	Upper-middle-income	High-income
Current tobacco use, males ages 15+ years (2012)	30.5	32.4	42.7	32.8
Current tobacco use, females ages 15+ years (2012)	3.1	2.9	5.2	17.8
Insufficient physical activity, ages 11–17 years (2010)	84.5	77.9	84.4	79.7
Insufficient physical activity, ages 18+ years (2010)	16.6	16.8	25.4	32.7
Overweight (BMI 25 or higher), ages 18+ years (2014)	21.0	27.4	42.7	56.4
Obese (BMI 30 or higher), ages 18+ years (2014)	4.7	7.6	13.0	23.2
High blood pressure (140/90 mmHg or higher), ages 18+ years (2014)	27.6	25.2	20.3	18.5
High blood cholesterol (5.0 mmol/L or higher), ages 25+ years (2008)	24.3	32.4	45.6	58.5
High fasting blood glucose (7.0 mmol/L or higher or on medication), ages 18+ years (2014)	7.4	8.9	9.3	7.0

Source: WHO, various years.

Note: BMI = body mass index; mmHg = millimeters of mercury, a measure of pressure; mmol/L = millimoles per liter. All prevalence ratios are crude estimates except for high fasting blood glucose, which is age-standardized. The most recent estimates are provided, with year of measurement in parentheses.

High Blood Pressure

Globally, high blood pressure (hypertension) is implicated in about 7.5 million deaths (about 13 percent of all deaths) and 57 million DALYs (WHO 2010b). High blood pressure is often without symptoms, silently damaging the arteries that supply blood to the heart, brain, kidneys, and elsewhere and producing a variety of structural changes. High blood pressure increases the risk of stroke, heart attack, kidney failure, and congestive heart failure. When high blood pressure exists with obesity, smoking, high blood cholesterol, or diabetes, the risk of IHD and stroke increases several fold. The relationship of blood pressure to coronary heart disease is linear, positive, and graded, with no discernible lower threshold. Each difference of 20 millimeters of mercury (mmHg, a measure of pressure) in systolic blood pressure is associated with a twofold increase in the relative risk of coronary heart disease, while a 5 mmHg reduction in systolic blood pressure in the population is associated with a 14 percent overall reduction in mortality attributable to stroke, a 9 percent reduction in mortality attributable to coronary heart disease, and a 7 percent decrease in all-cause mortality (Chobanian and others 2003). The prevalence of hypertension among adults in LMICs ranges from 20.3 percent in upper-middle-income countries to 27.6 percent in low-income countries (table 2.3).

Obesity and Overweight

In 2014, more than 1.9 billion adults were estimated to be overweight; of these, more than 600 million were

obese (WHO 2016a). The prevalence of overweight and obesity among adults ranges from 21.0 and 4.7 percent, respectively, in low-income countries to 42.7 and 13.0 percent, respectively, in upper-middle-income countries (table 2.3). Obesity is often defined as the accumulation of abnormal or excessive fat in adipose tissue to the extent that health may be impaired (WHO 2000b). People who develop excess body fat, especially at the waist, are more likely to develop heart disease and stroke even if they have no other risk factors. This condition is termed *abdominal obesity* or *central obesity*. The presence of abdominal obesity along with high glucose and high blood pressure and low levels of good cholesterol (high-density lipoprotein) leads to an insulin-resistant state called metabolic syndrome. There is strong evidence that weight loss in overweight and obese individuals reduces the risk of diabetes and CVD. Weight loss lowers blood pressure in overweight individuals with and without hypertension (Appel and others 2006), reduces serum triglycerides, and increases high-density lipoprotein (Miller and others 2011). More important, reductions in blood pressure occur even before attaining a desirable body weight (Appel and others 2006).

Physical Inactivity

According to the World Health Organization, globally, one in four adults is not active enough, and the problem of insufficient physical activity increases as country income rises (WHO 2016b). A concerning counter to this trend is the recent rise in insufficient physical activity

among adolescents (table 2.3), a problem that is just as large in low-income countries as in HICs (WHO 2016b). An inactive lifestyle is a risk factor for later overweight and obesity and all of the attendant health consequences. Regular, moderate-to-vigorous physical activity helps prevent CVD over the long term. Specifically, exercise can help control blood pressure, cholesterol, and diabetes as well as lead to weight loss. Even among persons who cannot achieve a normal weight, regular exercise can decrease the number and dosages of drugs to treat these other risk factors, thereby reducing costs and the risk of side effects.

Alcohol

The relationship of alcohol to overall mortality and cardiovascular mortality is thought to be J-shaped. A consistent cardio-protective effect has been observed for moderate consumption of one to two standard drinks per day, but heavy drinkers (including binge drinkers) have higher total mortality than moderate drinkers or abstainers (Srinath Reddy and Katan 2004). Moderate alcohol consumption has also been associated with a lower risk of ischemic stroke in men and women, with exceptions in populations such as South Asians (Sacco and others 1999). In contrast, long-term heavy alcohol consumption increases an individual's risk for all subtypes of stroke (O'Donnell and others 2010). The possible beneficial effects of moderate alcohol consumption must be weighed against the deleterious effects of high intake, including increased risk of hypertension, alcoholic cardiomyopathy, atrial arrhythmias, and hemorrhagic stroke (Klatsky 2015). Alcohol consumption in excess of three drinks per day is associated with a rise in blood pressure and plasma triglyceride levels. Many international guidelines recommend reducing or stopping alcohol consumption for nonpharmacologic therapy of hypertension (Srinath Reddy and Katan 2004).

SOCIAL AND ECOLOGICAL DETERMINANTS OF RISK

During the second half of the twentieth century, health indicators improved in almost all regions of the world. However, striking variations in cause-specific mortality rates, particularly related to NCDs, were observed within and between HICs and LMICs. These differentials suggested that social and ecological determinants of NCD risk were at work across populations.

Studies have found that the rapid rise in CVRD risk in LMICs is shaped largely by globalization and urbanization, which have profound impacts on dietary habits, tobacco consumption, and physical activity. The pathway is further modified by poverty, education, and stress levels. These upstream determinants decisively influence

CVRD risk operating through behavioral factors (for example, tobacco use, diet, physical activity), biological factors (for example, blood pressure, cholesterol, blood glucose levels), psychosocial factors (for example, depression, anxiety, acute and chronic life stressors, lack of social support), and health system factors (for example, access to care, screening, diagnosis, quality of care) (Fuster and Kelly 2010).

The biosocial pathway alone cannot explain the cumulative CVRD risk that operates across the life course of individuals and populations. Socioeconomic conditions throughout the life course shape adult health and disease risk. For example, persons living in adverse childhood social circumstances are more likely to be of low birth weight and to be exposed to poor diet, childhood infections, and passive smoking. These exposures may increase their CVRD risk in adult life, perhaps through chains of risk or pathways over time where one adverse (or protective) experience tends to lead to another adverse (or protective) experience in a cumulative way (WHO 2010a). Thus, physical and social exposures during gestation, childhood, adolescence, young adulthood, and later adult life have long-term effects on the risk of NCDs.

Early-Life Determinants

Considerable work in recent years has explored how chronic disease risk begins in fetal life and continues into old age. Multiple studies have shown that adult onset of CVRDs is determined by risks that accumulate throughout life. Such risks are determined largely by what happens in early life and socioeconomic position throughout the life course. There are two major drivers for CVRD risk in adult life: (1) exposures during critical periods in life and (2) accumulation of risks throughout the life course.

Exposures during critical periods such as in the womb, infancy, and childhood have lasting or lifelong adverse effects on body systems that are not modified by any subsequent exposure. The concept of fetal programming explains how and why critical periods are important in the life of an individual, a subject discussed in detail in chapter 3 of this volume (Kumaran, Osmond, and Fall 2017). Furthermore, poverty and chronic undernutrition of women during pregnancy are associated with low birth weight of babies. Given these findings, the importance of the first 1,000 days of life for health and human development has gained greater recognition. The 1,000 days between conception and a child's second birthday offer a unique window of opportunity to shape a healthier and more prosperous future. The right nutrition during this 1,000-day window can have a profound impact on a child's ability to grow, learn, and rise out of poverty.

Risk during Childhood and Adolescence

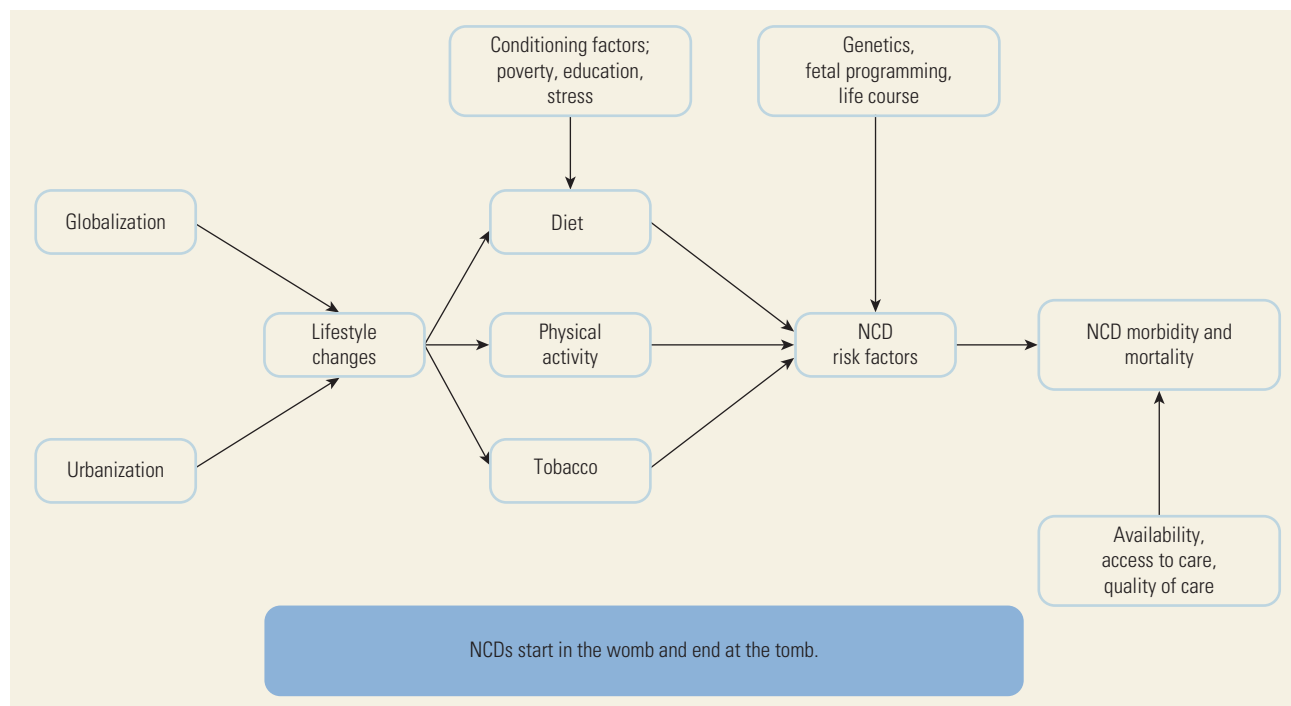
Growing evidence suggests that environmental exposures do more damage to health and potential long-term health during critical periods of growth and development in childhood and adolescence than they would at other times. Children with low birth weight continue to be underweight up to two years, after which growth catches up and they become prone to childhood obesity (Sachdev and others 2005). Higher rates of obesity in these children increase the risk of adult overweight and obesity and CVRDs. Cohort studies have also found that many children with high blood pressure or obesity become adults with high blood pressure or obesity. The stability of these risk factors over time or the predictability of their future levels through measurements early in life is called *tracking* (Singh and others 2008).

In light of these findings, the impact of socioeconomic status is clearly evident in shaping the environment for CVRD risk of populations. Socioeconomic status bears heavily on household income and nutritional status; it can influence nutrition among pregnant women and their fetuses and affect future cognition, intelligence, schooling, and attainment of optimal height and weight and thus risk of CVRD in the next generation. As a result,

households in lower socioeconomic positions face a vicious intergenerational cycle of poor nutrition, ill health, and poverty. Furthermore, children and adolescents from low socioeconomic backgrounds more frequently experiment with risky behaviors such as smoking and alcohol use and continue to maintain such risky behaviors into adulthood. Poor diet, another risk factor for CVRD, has also been documented among such children. Finally, girls who grow poorly become stunted as adults and are more likely to give birth to low-birth-weight babies who are likely to continue the cycle by being stunted in adulthood.

The relatively larger role played by social, economic, and environmental factors in the epidemic of chronic diseases is explained by several theoretical models that highlight the importance of policy-based approaches for protecting the health of populations. A life course perspective in policies and programs helps identify chains of risk that can be broken and times when intervention may be especially effective. Particularly during key life transitions—for example, late adolescence to early adulthood—not just “safety nets” but “springboards” must be provided that can alter life course trajectories and improve the health of subsequent generations (WHO 2000a). Figure 2.5 outlines the relationships

Figure 2.5 Complex Interplay of Determinants and Risk Factors in the Pathway of Noncommunicable Diseases in the Population



Note: NCD = noncommunicable disease.

between specific risk factors, their early- and late-life determinants, and their contributions to NCD risk.

A FRAMEWORK FOR ADDRESSING THE CHALLENGE OF CVRDs

The growing burden of NCDs in the past few decades clearly indicates that the health systems in LMICs need to focus more on preventing and controlling CVRDs, given that these nations face the major brunt of this epidemic. An integrated life course approach to prevention and control will be needed. The life course approach is an integrated continuum that affects all stages of life, including (but not limited to) the following:

- Addressing nutrition during fetal and early life
- Tackling childhood obesity through policy-level interventions such as banning certain advertisements aimed at schoolchildren, particularly in relation to food products
- Vigorously controlling tobacco, particularly to prevent children from experimenting with and getting habituated to smoking
- Effectively implementing the World Health Organization's Framework Convention on Tobacco Control
- Controlling risk factors in persons with single or multiple risk factors for primary prevention
- Managing diseases for secondary prevention
- Rehabilitating people with impairments and disabilities
- Financially protecting people with acute illness
- Focusing on neglected CVRDs.

It is also important to create an environment that is conducive for individuals to adopt and maintain a healthy life through macro-level policies, including agricultural policies promoting the consumption of fruits and vegetables, an enabling environment for physical activity, public transportation, and access to and affordability of essential drugs and diagnostics. This section describes the socioecological model as a basis for designing interventions for CVRD prevention and control.

Reducing Risk

Intervening in the causal pathway of CVRDs is complex. An ideal but comprehensive approach would follow a socioecological model for intervening that enables identification of interactions between an individual and his or her environment. The socioecological

model integrates theories of individual behavior change with an understanding of the role of environmental enhancement in the interactions between an individual and his or her social and physical environments (McLeroy and others 1988). According to this socioecological model, human behaviors are fundamentally determined by five broad categories of factors: intrapersonal factors, interpersonal factors, organizational factors, community factors, and public policy (McLeroy and others 1988).

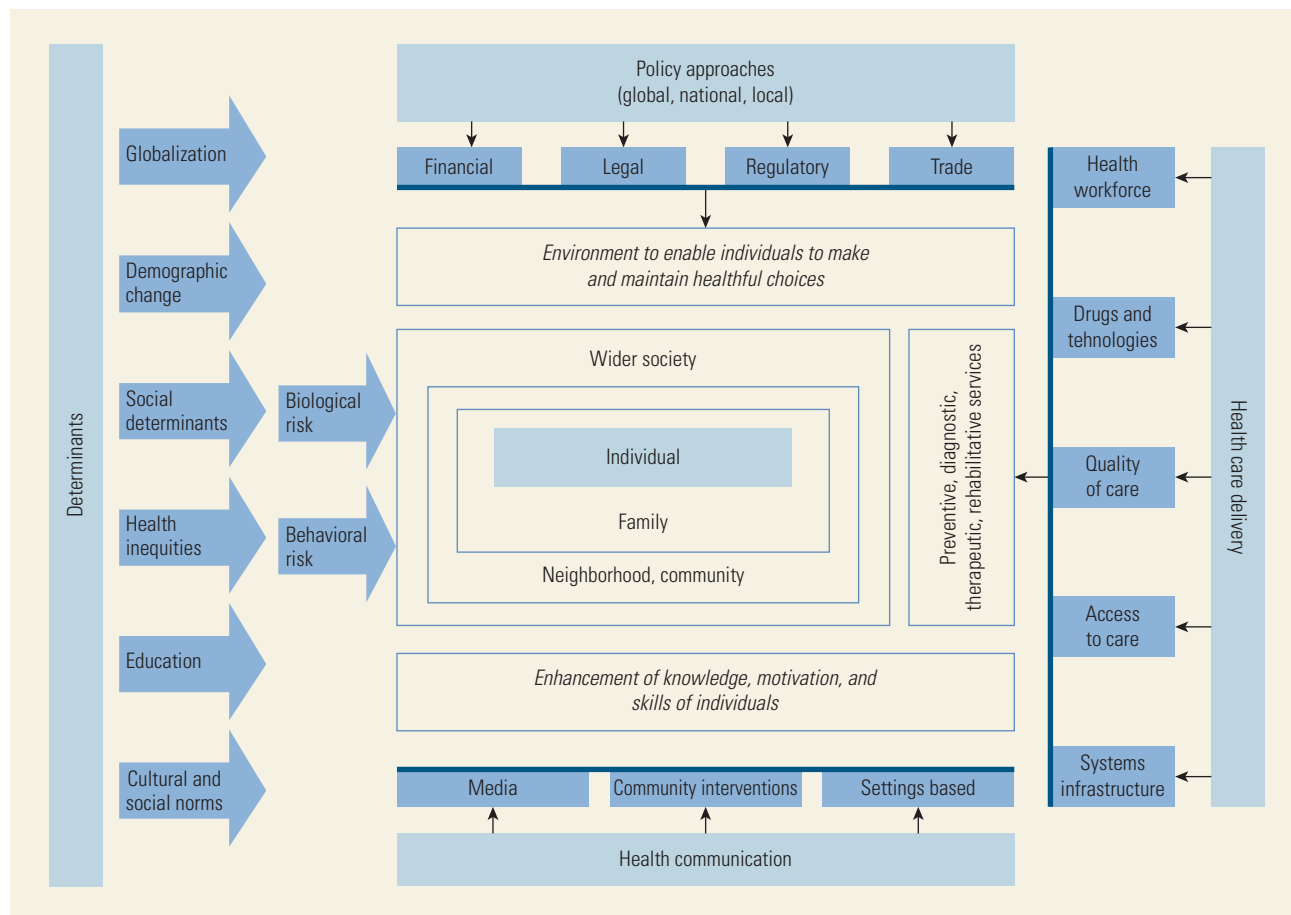
Multiple pathways and factors are involved in the causal pathway of CVRD risk, and a model that focuses exclusively on individuals is likely to fail. Therefore, efforts to improve individuals' health must be directed simultaneously at multiple levels. The ideal approach would be to take advantage of opportunities for intervention at all stages of the life course by preventing the acquisition and augmentation of risk, detecting and reducing risk, managing NCD events, and preventing the progression of disease and recurrence of NCD events (Fuster and Kelly 2010). Relying on these concepts, the Institute of Medicine has provided a framework for NCD interventions (figure 2.6).

An ideal approach would take advantage of multiple strategies that coordinate across multiple sectors with a mix of interventions that take into account context and locale:

- *An individual-level (high-risk) approach* that focuses on clinical identification of individuals in the population at highest risk of CVRD and intensive treatment through behavior change interventions, pharmacological measures, or both
- *A population-level approach* that focuses on shifting the distribution of risk factors in the population by implementing evidence-based policies, laws, and regulations that favorably affect the consumption of healthier foods, the built environment, and tobacco and alcohol use.

A comprehensive approach takes into account the full range of complex determinants of CVRDs to produce synergies among approaches at the individual and population levels. Concurrent modalities could include health promotion campaigns (for example, in communities, schools, and worksites) and reorientation and strengthening of health systems, with greater use of innovative applications of communications technologies, efficient use of medical therapies and technologies, and integrated clinical programs (Fuster and Kelly 2010).

Figure 2.6 Framework for a Comprehensive Strategy to Address Noncommunicable Diseases



Source: Fuster and Kelly 2010.

Addressing Social Determinants to Prevent the Poor from Acquiring Unhealthy Habits

CVRDs and poverty form a vicious cycle. The poor are more vulnerable to CVRDs and are more likely to use tobacco products, to consume energy-dense food, and to consume fewer fruits and vegetables. These risky behaviors arise from social and economic inequalities such as lack of opportunity, lack of education, psychosocial stress, limited choice of consumption patterns, and inadequate access to health care (WHO 2005). They are exacerbated by aggressive marketing of tobacco products and greater access to cheaper energy-dense fried or processed foods, particularly in middle-income countries. As a result, the poor tend to be more obese than the wealthy and at greater risk of dying prematurely from CVRDs (WHO 2005). Ill health has a direct bearing on the livelihoods of poor

individuals and families because the resulting loss of jobs and wages can exacerbate the poverty trap. Policies for inclusive growth and social protection for poor and marginalized groups are essential to protecting and promoting public health.

CONCLUSIONS

CVRDs are an increasing contributor to poor health in LMICs. The epidemic of CVRDs is being driven by population growth and aging in combination with increasing prevalence of risk factors and inadequate clinical management. Health systems in LMICs, which account for most of the CVRD burden globally, are ill equipped to address this challenge and will require additional investments to strengthen access to evidence-based prevention and treatment. At the same time, public policy

could be reoriented with a life course focus so that CVRD prevention and control are not limited to clinical settings but also harness the power of specific policies to improve population health and well-being.

ANNEX

The annex to this chapter is as follows. It is available at <http://www.dcp-3.org/CVRD>.

- Annex 2A. Updated Estimates of the Burden of CVRD in 2015.

NOTES

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US\$1,045 or less
- Middle-income countries (MICs) are subdivided:
 - (a) lower-middle-income = US\$1,046 to US\$4,125
 - (b) upper-middle-income (UMICs) = US\$4,126 to US\$12,745
- High-income countries (HICs) = US\$12,746 or more.

1. Goal 3: Ensure healthy lives and promote well-being for all at all ages, <http://www.un.org/sustainabledevelopment/health/>.

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