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Prevention and treatment of chronic diseases in developing countries

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NOTE

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PREFACE

In November 2009, the Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat convened an *Expert Group Meeting on Health, Mortality and Development* at the United Nations Headquarters in New York. The purpose of the meeting was twofold. First, in preparation for the forty-third session of the Commission on Population and Development, the meeting brought together experts and officials of inter-governmental organizations to discuss the challenges in combating the major causes of death and improving health, including consideration of how to strengthen health systems. Second, building upon earlier United Nations Coordination Meetings on the Estimation of Adult Mortality held in 2006 and 2008, the meeting focused on methodological issues in the estimation of adult mortality and initiated a comparison and review of adult mortality estimates for selected countries as produced by different institutions.

The meeting took place from 10 to 12 November 2009. Its agenda and list of participants can be found at http://www.un.org/esa/population/meetings/EGM-healthmortality/agenda-participantslist.pdf. A selection of the papers prepared by experts participating in the first part of the meeting is being issued under the Expert Paper Series published on the website of the Population Division (www.unpopulation.org).

Despite a common perception that chronic diseases are a problem only in affluent societies, cardiovascular disease had become the leading cause of death in the developing world by 2004. About 28 per cent of deaths in low- and middle-income countries were attributable to cardiovascular diseases. Even in societies where the dominant causes of death were communicable diseases, cardiovascular diseases and other chronic diseases were responsible for a significant number of deaths and their prevalence was growing. The Population Division is grateful to Dr. Thomas Gaziano, Assistant Professor in the Department of Health Policy and Management, Harvard School of Public Health, for having participated in the meeting and prepared this paper on the global burden of chronic diseases, focusing particularly on the challenges of addressing those conditions in low- and middle-income countries.

The *Expert Paper Series* aims at providing access to government officials, the research community, non-governmental organizations, international organizations and the general public to overviews by experts on key demographic issues. The papers included in the series will mainly be those presented at Expert Group Meetings organized by the Population Division on the different areas of its competence, including fertility, mortality, migration, urbanization and population distribution, population estimates and projections, population and development, and population policy. The views and opinions expressed in the papers that are part of the series are those of their authors and do not necessarily reflect those of the United Nations. The papers in the series are released without undergoing formal editing.

For further information concerning this series, please contact the office of Hania Zlotnik, Director, Population Division, Department of Economic and Social Affairs, United Nations, New York, 10017, USA, telephone (212) 963-3179, fax (212) 963-2147.

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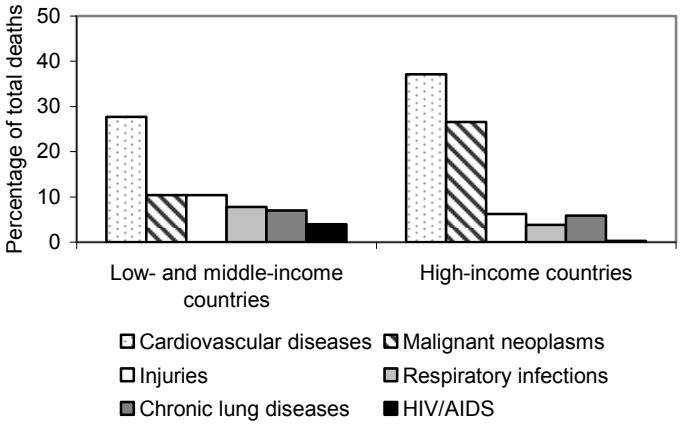
CHRONIC DISEASE BURDEN

It is well known that chronic diseases are responsible for the majority of deaths in high-income countries such as the United States, but these same chronic conditions are a major problem in the developing world and this is only just becoming apparent to the wider public. Chronic diseases by their nature begin insidiously with the progression of risk factors through individuals' interaction with their environments, which then leads to symptomatic disease and, ultimately, to significant suffering and premature death. Adoption of certain behaviours during economic development—such as tobacco consumption, poor dietary habits, and a decline in physical activity—has driven much of this epidemic. Four chronic conditions—cancer, cardiovascular disease (CVD), diabetes, and respiratory diseases—are responsible for just over half of the world's deaths (World Health Organization (WHO), 2008). Together these chronic diseases are responsible for more than six times as many deaths globally as HIV/AIDS, tuberculosis and malaria combined.

A. CURRENT WORLDWIDE VARIATIONS IN CARDIOVASCULAR DISEASE (CVD)

An epidemiological transition much like that which occurred in the United States is occurring in all world regions, but unique regional features have modified aspects of the transition in various parts of the world. In terms of economic development, the world can be divided into two broad categories: 1) high-income countries; and 2) low- and middle-income countries. These two categories can be further subdivided into six distinct economic/geographic regions. More than 80 per cent of the world's population lives in low- and middle-income countries, and it is these countries that are driving the rates of change in the global burden of CVD. Three million CVD deaths occurred in high-income countries in 2004, compared to 14 million in the rest of the world (WHO, 2008).

Figure I. Major causes of death by income group, 2004



Source: World Health Organization, 2008.*The global burden of disease: 2004 update.*

1. High-Income Countries

In 2004, approximately 977 million people lived in the high-income countries, where coronary heart disease (CHD) is the dominant form of CVD, with death rates that tend to be two to five times higher than death rates from stroke (WHO, 2008). Death rates from CVD in Canada, New Zealand, Australia and Western Europe tend to be similar to those in the United States; however, among the countries of Western Europe, the absolute rates vary threefold with a clear north-south gradient. The highest CVD death rates are in the northern countries, such as Finland, Ireland, and Scotland, and the lowest CVD rates are in the Mediterranean countries of France, Spain, and Italy (Thom and others, 2006). Japan is unique among the high-income countries: stroke rates increased dramatically over the last century, but CHD rates did not rise as sharply. This difference may stem in part from genetic factors, but it is more likely that the fish- and plant-based, low-fat diets and resulting low cholesterol levels have played a larger role. Importantly, Japanese dietary habits are undergoing substantial changes, reflected in an increase in cholesterol levels.

2. Low- and Middle-Income Countries

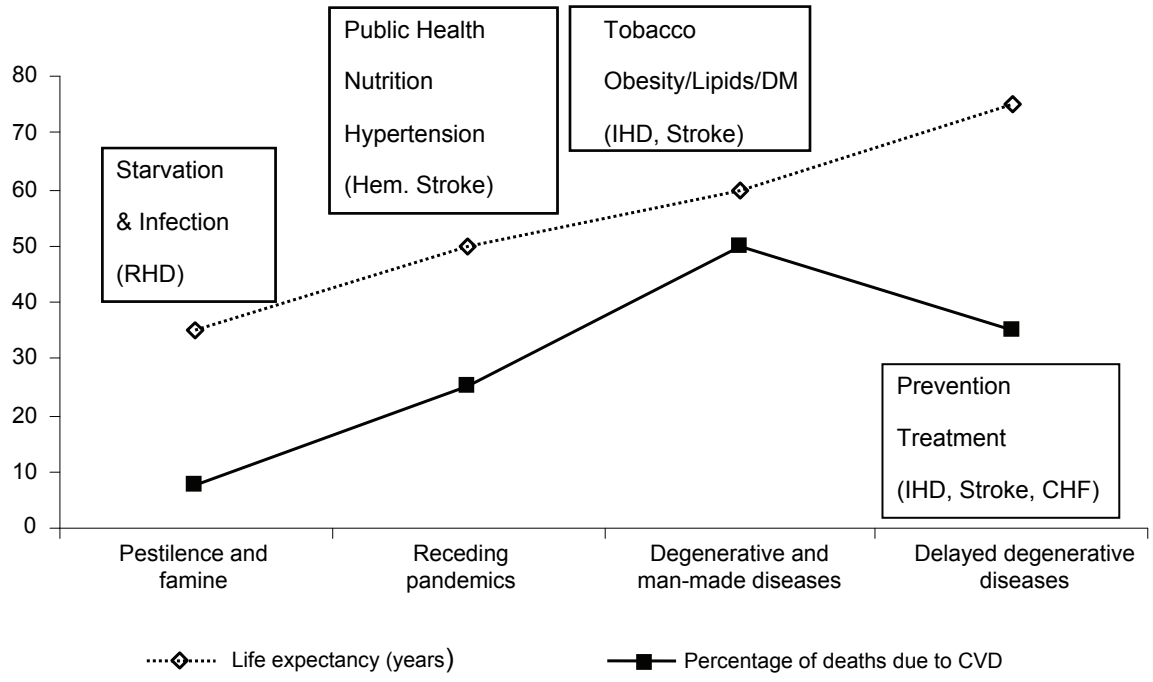
The World Bank groups the low- and middle-income countries (gross national income per capita lower than US $10,065) into six geographic regions: East Asia and the Pacific, (Eastern) Europe and Central Asia, Latin America and the Caribbean, the Middle East and North Africa, South Asia and sub-Saharan Africa. Although communicable diseases continue to be a major cause of death, CVD has emerged as a significant health concern in the low- and middle-income countries. In most of these countries, there is an urban-rural gradient for CHD, stroke, and hypertension, with higher rates in urban centres than in rural areas.

While CVD rates are rising rapidly, there are vast differences among regions and countries, and even within countries themselves. Many factors contribute to the heterogeneity. First, the different regions of the world are at different stages of the epidemiological transition. Second, vast differences in lifestyle and behavioural risk factors exist across regions and countries, as well as within countries. Third, racial and ethnic differences may lead to altered susceptibilities to various forms of CVD. In addition, it should be noted that for most low- and middle-income countries, accurate country-wide data on cause-specific mortality are not available, as death certificate completion is not routine and many countries do not have a centralized registry for deaths.

The overall increase in the global burden of chronic disease and the distinct patterns in various regions can be explained by the epidemiologic transition. Movement through its four stages has resulted in a dramatic shift in the major causes of death over the past two centuries, from infectious diseases and malnutrition in the first stage to CVD and cancer, which are the predominant causes of death in most high-income countries today. The four stages—pestilence and famine, receding pandemics, degenerative and man-made diseases, and delayed degenerative diseases—are outlined briefly in figure II (Omran, 1971; Olshansky and Ault, 1986). Most developed countries find themselves in the fourth phase of the epidemiological transition with age-adjusted declines in CVD and, to a lesser extent, cancers; but many countries may be moving to a yet-unnamed fifth phase, characterized by extremes of obesity and diabetes mellitus. Most developing regions appear to be following a similar pattern to that observed previously in developed countries, but the transition in developing countries has occurred at a more rapid rate, less systematically than in developed countries, and with greater proportions of the economically

disadvantaged affected at an earlier stage. Figure II describes the CVD transition, but the pattern for other chronic diseases is similar.

Figure II. The epidemiological transition for CVD



The East Asia and Pacific region, with a population of nearly two billion people, appears to be straddling the second and third phases of the epidemiological transition, with China and Indonesia's populations driving most of the regional trend. Overall, CVD is a major cause of death in China, but like Japan, stroke (particularly hemorrhagic stroke) causes more deaths than CHD in a ratio of about three to one (Thom and others, 2006). However, age-adjusted CHD mortality increased 40 per cent from 1984 to 1999 (Chritchley and others, 2004), suggesting further epidemiologic transition. China also appears to have a geographic gradient like that of Western Europe, with higher CVD rates in northern China than in southern China. Other countries in this region, such as Viet Nam and Cambodia, are just emerging from the pestilence and famine stage of the transition.

The Eastern Europe and Central Asia region is firmly in the peak of the third phase of the epidemiological transition, with the highest proportion of deaths due to CVD in the world (57 per cent) (WHO, 2008). More troubling is that nearly 35 per cent of deaths from CHD in this region occur among working-age adults, three times the percentage in the United States. There is, however, also regional variability within Eastern Europe and Central Asia. In the Russian Federation, increasing rates of CVD have contributed to falling life expectancy, particularly for men, whose life expectancy has dropped from 64 years in 1985-1990 to 58 years in 2000-2005 (United Nations, 2009). In contrast, over the same period in Poland, both men and women experienced gains in life expectancy of about four years. Slovenia, Hungary, the Czech Republic, and Slovakia have experienced similar improvements in survival (United Nations, 2009).

In general, Latin America appears to be in the third phase of the epidemiological transition, although as in other low- and middle-income regions, there is vast regional heterogeneity, with some areas in the second phase of the transition and others in the fourth phase. Today approximately 29 per cent of all deaths in this region are attributable to CVD, with stroke accounting for 29 per cent of CVD deaths (WHO, 2008). Like Eastern Europe, some Latin American countries have continued to see an overall increase in age-adjusted CHD mortality of 3 per cent to 10 per cent between 1970 and 2002 (Costa Rica, Mexico and Venezuela), while others appear to have reduced rates by as much as 2 per cent per year over the same time period (Argentina, Brazil, Chile and Colombia).

The Middle East and North Africa region appears to be entering the third phase of the epidemiological transition, with increasing life expectancy overall and CVD death rates just below those of developed nations. CHD is responsible for 17 per cent of all deaths in the region, while stroke accounts for 7 per cent (WHO, 2008). The traditional high-fibre diet, low in fat and cholesterol, has changed rapidly. Over the past few decades, daily fat consumption has increased in most of these countries, ranging from a 13.6 per cent increase in Sudan to a 143.3 per cent increase in Saudi Arabia. Over 75 per cent of Egyptians are overweight or obese and the rate is 67 per cent in Iraq and Jordan. Physical inactivity (less than 10 minutes per day) is nearly 60 per cent in Syria and Iraq.

Most people in South Asia live in India, a country that is experiencing an alarming increase in heart disease. CVD accounted for 32 per cent of all deaths in 2000, and an estimated 2 million deaths will occur due to CHD by 2010 representing a 30 per cent increase over the preceding decade. The transition appears to be occurring in a pattern similar to that of developed countries, with CHD becoming the dominant form of CVD. In 1960, CHD represented 4 per cent of all CVD deaths in India, whereas in 1990 the proportion was greater than 50 per cent. Given that stroke tends to be the dominant form of CVD early in the epidemiological transition, this finding is somewhat unexpected and may reflect inaccuracies in cause-specific mortality estimates or a possible underlying genetic component. It has been suggested that Indians have exaggerated insulin insensitivity, which may differentially increase rates of CHD over stroke with the adoption of Western-style diet and lifestyle. The South Asia region has the highest overall prevalence of diabetes of the low-income regions with rates as high as 14 per cent in urban centres. In certain rural areas the prevalence of CVD and its risk factors are approaching urban rates.

Sub-Saharan Africa remains largely in the first phase of the epidemiological transition, with the proportion of deaths due to CVD less than half of that in developed regions. Life expectancy has decreased in many sub-Saharan African countries since the early 1990s, largely because of HIV/AIDS and other chronic diseases; life expectancies are the lowest in the world. Still, CVD accounts for 46 per cent of non-communicable deaths and is the leading cause of death among adults over the age of 35 (WHO, 2008). As more HIV/AIDS patients receive anti-retroviral treatment, management of CVD risk factors such as dyslipidemia in this population is requiring more attention. Hypertension also remains a major public health concern, and has resulted in stroke being the dominant form of CVD. Rheumatic heart disease remains an important cause of CVD mortality and morbidity as well.

B. Potential gains

While trends in some risk factors, such as obesity, are worsening, the developed regions have seen an overall reduction in age-adjusted rates of death from chronic diseases—in particular ischemic heart disease and, to a lesser extent, stroke and cancers. Much of these gains can be attributed to changes in the levels of the various risk factors associated with chronic disease. In

the high-income countries, an estimated one half to three quarters of the reduction in the risk of death from ischemic heart disease is due to the reduction of risk factors through primary care or public health interventions. Some of the reduction in risk factors is attributable to lifestyle interventions and some is related to improved treatment with pharmaceuticals. The remaining one quarter to one half can be attributed to secondary measures, either related to changes in risk factors, specific acute or curative treatments, or improvements in the management of chronic diseases.

Most of the advances in reducing the burden of chronic disease in high-income countries came through the identification of risk factors and technological advances, particularly in pharmaceuticals (table 1). The elucidation of risk factors was critical in several ways. First, it alerted the public to certain behavioural and environmental factors that were harmful, such as cigarette smoking, consumption of saturated and trans-fats, and physical inactivity. Second, it led to the development of screening programmes for certain conditions such as hypertension, colon and cervical cancers, and diabetes. Many of the interventions to reduce risk could then be put into place. Some were based on population awareness that encouraged individuals to change their behaviours. Others were facilitated by technological advances such as new cholesterol-lowering medications, advanced lab facilities to evaluate cervical smear results or glucose, or the use of colonoscopy. Today, a combination of four to six generically available medications can reduce CVD by 50 per cent to 80 per cent over 20 years (Gaziano, Opie and Weinstein, 2006; Wald and Law, 2003).

TABLE 1. PERCENTAGE OF DECLINE IN CHD MORTALITY BETWEEN 1980 AND 1990 EXPLAINED BY PRIMARY PREVENTION AND IMPROVEMENTS IN TREATMENT OF PATIENTS WITH CHD

Improvements	*Percentage explained by*		
	Primary prevention[a]	*Treatment of patients with CHD*[b]	*Combined*
Risk factors			
Diastolic blood pressure	7	7	14[c]
Lipoprotein levels	16	18	33[c]
High-density lipoprotein cholesterol	5	5	10[c]
Low-density lipoprotein cholesterol	11	14	24[c]
Smoking	3	4	6[c]
Total risk factors	**25**[c]	**29**[c]	**50**[c]
Other improvements in treatment			
Case fatality rates for acute MI	…	15	15
Medical/surgical treatment of CAD[d]	…	29	29
Total other improvements in treatment	**…**	**43**[c]	**43**[c]
Total	**25**[c]	**71**[c]	**92**[c]

Source: Hunink and others (1997), *JAMA*, vol. 277 (7).

NOTE: CHD indicates coronary heart disease; MI, myocardial infarction; CAD, coronary artery disease; and … indicates not applicable.

[a] Primary prevention: the decline in CHD mortality through the decrease in CHD incidence as a result of risk factor reductions in the population without CHD.

[b] Treatment of patients with CHD: the decline in CHD mortality through the decrease in event rates, including chronic CHD mortality, as a result of risk factor reductions or other improvements in treatment in the population with CHD.

[c] Note that the total decline in CHD mortality explained is less than the sum of the parts owing to interaction between the components. This also applies to the sum of the parts of each component, although this is not always apparent owing to rounding of the numbers.

[d] Includes the effect of changes in rates of MI and cardiac arrest in persons with CHD, the number and type of revascularization procedures, and chronic CHD mortality rates not explained by changes in risk factors.

C. SOCIAL AND ECONOMIC IMPACT

There are at least three ways to measure the economic burden associated with coronary heart disease (Suhrcke and others, 2006). The first measure of the financial burden associated with CHD is defined by the costs incurred within the health care system itself and is reported in "cost-of-illness" studies. In these studies, the cost of CHD includes the costs of hospitalizations for angina and myocardial infarction, as well as heart failure attributable to CHD. In addition, one must consider the costs of specific treatments or procedures related to CVD, such as thrombolytics, catheterization, and percutaneous coronary intervention (PCI). Furthermore, the costs associated with outpatient management and secondary prevention, both in terms of office visits and pharmaceutical costs must be included. Nursing home, inpatient and outpatient rehabilitation, and home nursing costs also require consideration.

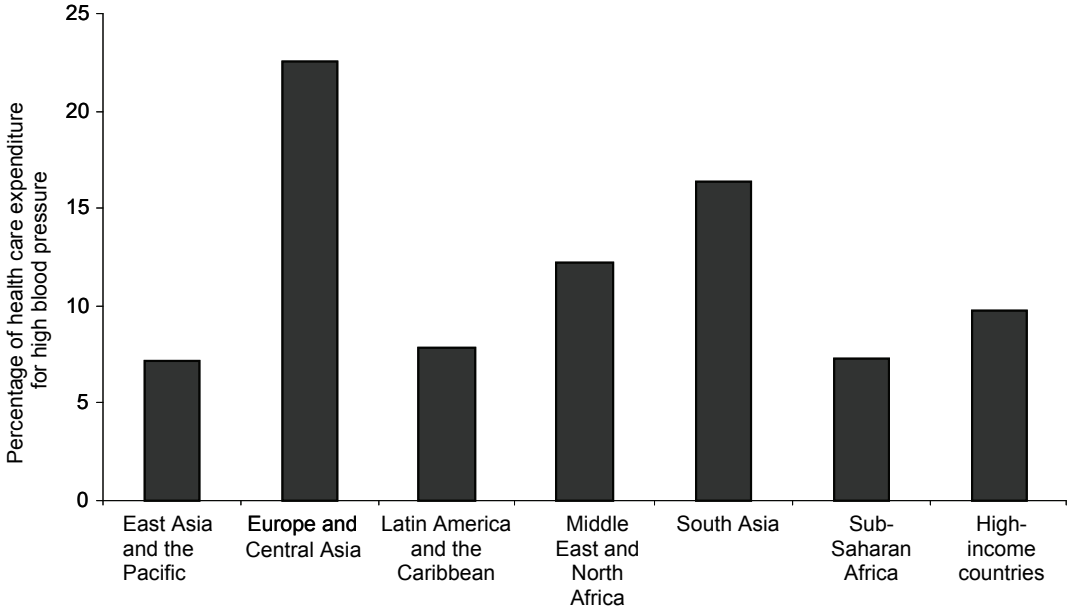
The second economic assessment is based on microeconomic studies that assess the household impact of catastrophic health care events such as myocardial infarction. These studies look at out-of-pocket expenses incurred by the individual or family that might have other downstream economic impacts, such as loss of savings or sale of property to cover medical costs. Given that in many developing countries without an extensive insurance scheme health care costs are borne almost entirely by individuals (Schieber and others, 2007) microeconomic studies to date have not considered coronary heart disease exclusively and instead have looked at chronic diseases more generally. Furthermore, the limited data to date do not confirm the causality between chronic disease and individual or household poverty (Suhrcke and others, 2006). However, expenditures for coronary disease or its addictive risk factors such as tobacco could lead to substantial and even impoverishing costs.

The third method of determining financial burden from coronary heart disease is based on a macroeconomic analysis. These assessments look at lost worker productivity or economic growth that occurs when adults with CHD or their caregivers partially or completely leave the work force as a result of the illness. The data for the impact of chronic diseases on labour supply and productivity are relatively robust. An additional cost not often accounted for is the intangible loss of welfare associated with pain, disability or suffering by the individual. These indirect costs are often accounted for by "willingness-to-pay" analyses, asking generally how much would an individual pay to avert suffering or dying prematurely from coronary heart disease. The gains are not merely improved work performance but also enjoying activities beyond production. Studies in the United States suggest that as much as 1 per cent to 3 per cent of GDP is attributable to CVD, with almost half of that related to coronary heart disease (Thom and others, 2006). In China, annual direct costs of CVD are estimated at more than US$ 40 billion, or roughly 4 per cent of gross national income. In South Africa 2 per cent to 3 per cent of the country's gross national income is devoted to the direct treatment of CVD, which equates to roughly 25 per cent of South African health care expenditures (Pestana and others, 1996). The indirect costs have been estimated to be more than double that of the direct costs. Although few cost-of-illness studies for coronary heart disease have been done in other regions, cost-of-illness studies have reported on the financial burdens attributed to risk factors for coronary heart disease. For example, the direct costs due to diabetes in Latin American and Caribbean countries were estimated at US$ 10 billion. Indirect costs were estimated at over US$ 50 billion in the year 2000 (Barceló and others, 2003). Studies are limited, but suggest that obesity-related diseases are responsible for 2 per cent to 8 per cent of all health care expenditures in developed countries. In India and China the costs of obesity are about 1.1 per cent and 2.1 per cent of GDP, respectively (Popkin and others, 2001).

The costs attributable to non-optimal levels of blood pressure as mediated through stroke and myocardial infarction were evaluated for all regions of the world recently (Gaziano and

others, 2009). Globally, the health care cost of elevated blood pressure was estimated at US$ 370 billion for the year 2001. This amount represented approximately 10 per cent of all health care expenditures for that year globally. Again regional variations do exist, with hypertension being responsible for up to 25 per cent of health care costs in the Eastern European region (figure III). Over a 10-year period, blood pressure-related health care costs could equal US$ 1 trillion globally. Indirect health care costs attributed to blood pressure could be nearly four times as much.

Figure III. Percentage of Health Care Expenditure Attributed to High Blood Pressure



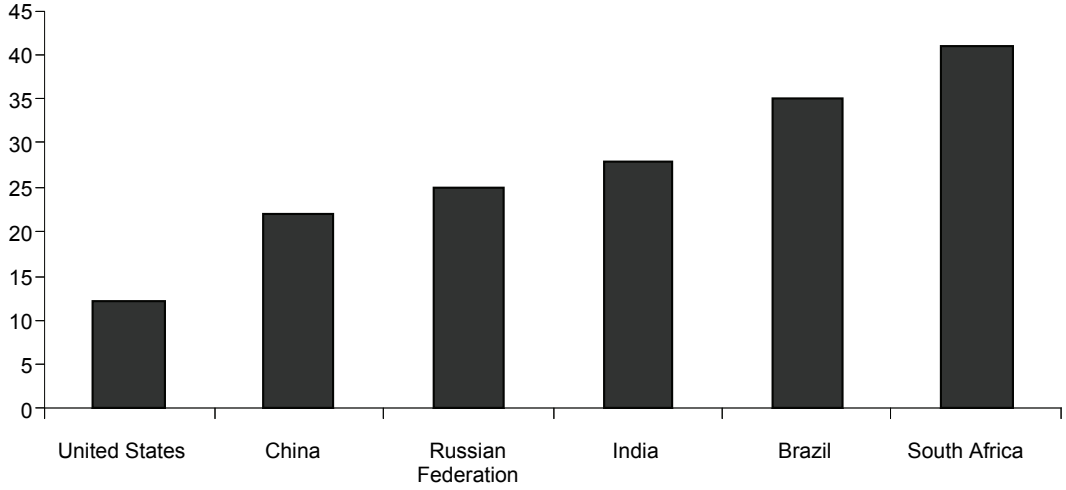
Source: Jamison, D., and others, 2006. *Disease Control Priorities in Developing Countries*. Second edition, New York: Oxford University Press and the World Bank.

The costs of CVD are further compounded by the fact that such a high proportion of the CVD burden occurs earlier among adults of working age in developing countries. Under current projections, CVD will represent 40 per cent of adult deaths between the ages of 35 years and 64 years in developing countries such as South Africa compared to 10 per cent in the United States (Figure IV). India and China will have death rates in the same age group that are two and three times that of most developed countries. Given the large populations in these two rapidly growing economies, this could have profound economic effects over the next 25 years as workers in their prime succumb to cardiovascular disease. This can have a large impact on a developing country's economic viability. The 2004 report *A Race Against* Time (Leeder and others, 2004) evaluated the potential macroeconomic impact due to early CVD in developing countries. In five countries surveyed (Brazil, China, India, Mexico and South Africa), conservative estimates indicated that at least 21 million years of future productive life are lost because of CVD each year, with the potential to slow or reverse economic growth.

Developed and developing countries also differ in the amount of resources devoted to treatment and care for patients with cardiovascular disease. While data are limited, two observations point to the relatively small amount of resources devoted to CVD in developing

countries. First, the mean percentage of gross domestic product (GDP) that developing countries devote to health care is half of the mean devoted to health care in the high-income countries. As a result, low- and middle-income countries spend about US$ 74 per capita on health care in comparison to US$ 2,700 per capita in high-income countries. Second, in the few countries where data exist, there are wide disparities in resources devoted to CVD. For example, there is about a 50-fold difference in per capita CVD-care spending between the United States and South Africa (Pestana and others, 1996; American Heart Association, 2003; World Bank, 2002).

Figure IV. Workforce burden (cumulative percentage of CVD deaths among 35–64-year-olds from 2000–2030)[11]



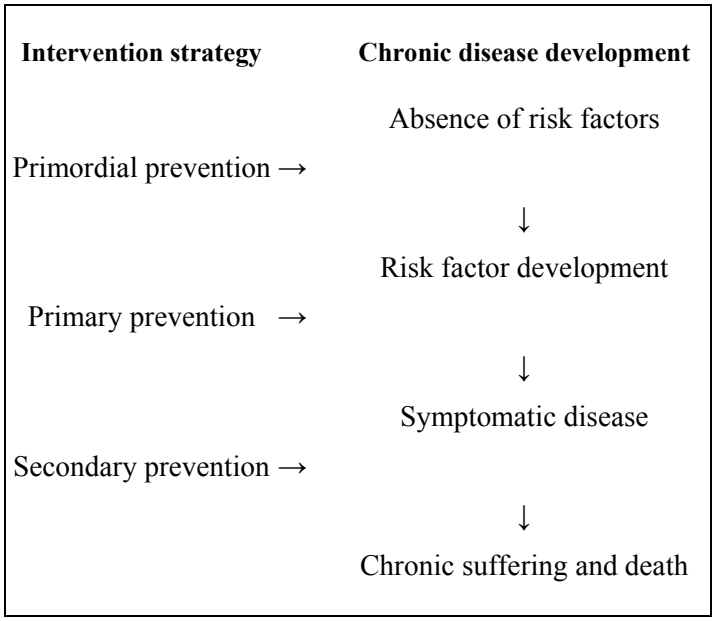
Source: Leeder, S., and others (2004). *A Race Against Time: The Challenge of Cardiovascular Disease in Developing Countries*. New York: Trustees of Columbia University.

D. TIME SPECTRUM

In general, chronic diseases take time to manifest themselves in symptoms, but the risk factors for them begin quite early in life. Some even suggest that some stressors *in utero* may lead to the later development of certain risk factors for chronic diseases (Barker, 1995; Barker and others, 2001; Barker and Law, 1994). Certainly later in life, exposure to tobacco, unhealthy or excessive dietary habits, changes in physical activity, and other environmental exposures can lead to the development of other risk factors, such as hypertension or obesity. In turn, risk factors such as hypertension, dyslipidemia, obesity and diabetes lead to the development of many chronic symptomatic diseases such as cancers, heart attacks, strokes and obstructive lung disease.

Prevention efforts can occur anywhere along the spectrum of chronic disease development (figure V). Primordial prevention efforts are those that are aimed at preventing the development of risk factors. Examples of primordial prevention efforts include tobacco-control programmes to prevent the uptake of smoking, or physical activity or dietary programmes to reduce obesity and diabetes. Primary prevention interventions are those that are aimed at people who have developed risk factors for chronic disease and seek to delay or prevent the symptomatic phase. Secondary prevention is management of the risk factors after disease has occurred, prior to repeat events or to minimize sequelae of the disease.

Figure V. Paths linking intervention strategies to the development of chronic disease



One advantage of primordial interventions is that a large portion of the population benefits from the intervention. The most obvious example of primordial interventions that target wide swaths of the population includes programmes that discourage tobacco use. Other efforts, such as increased physical activity or dietary changes to reduce saturated or trans-fats or salt intake, benefit those who have not already adopted these lifestyle changes. Further, the population-based interventions will prevent the fatal first events that occur particularly with regards to CVD and some difficult-to-detect and aggressive cancers. However, it can take decades to see the full benefits of these risk factor reductions. Moreover, the interventions must be directed at the entire population and often this means that many people who either already have healthy lifestyles or are at low-risk for developing the risk factor do not receive any benefit from the intervention, despite the resources being devoted to them.

At the other end of the spectrum, secondary prevention efforts are often targeted at those with a 10- to 100-fold risk relative to those who do not have a history of symptomatic disease. Interventions at this point can reduce risk of repeated events by as much as 80 per cent. Only those at high-risk for repeated events are treated, limiting the number of people needing the intervention to a small proportion of the population. Benefits from these secondary interventions are realized within months or years rather than decades. However, because the interventions are targeted to certain identified high-risk groups, some preventable fatal events are missed.

It is clear that prevention can occur anywhere along the spectrum of chronic disease development. Perhaps a better way to distinguish between types of interventions is to identify those that are population-based versus individual-based. An effort to reduce tobacco consumption through taxation or an advertising ban would be a population-based strategy, as would be a screening programme to identify high-risk patients. Risk factor management at the request of the patient or the physician's own discretion, regardless of overall risk or screening programme recommendation, would be an example of an individual-based intervention.

E. POPULATION- AND INDIVIDUAL-BASED INTERVENTIONS

Investigators have undertaken a variety of population-based community intervention studies, mostly in developed countries in the 1970s and 1980s. These studies have tended to be multifactorial projects testing whether comprehensive community programmes could produce favourable changes in such risk factors as bodyweight, cholesterol, and blood pressure, and in CVD morbidity and mortality. In general, the intervention studies included a combination of population-wide and individual interventions, including: messages disseminated through local associations, sports clubs, the media, and food associations; healthy food options at restaurants and worksite cafeterias; food labelling at supermarkets; face-to-face communication at meetings and distribution of educational materials; smoking restrictions; and competitions to develop healthy food. With the exception of Finland where the interventions were successful in greatly reducing coronary heart disease mortality, the projects had mixed results (Ebrahim and Smith, 1997), although many demonstrated significant effects with respect to individual components of the interventions. The limitations of many of the projects include the inability to detect small but potentially important changes in risk factors, short duration of intervention and follow-up, and issues with outcome measurement. It has also been suggested that the trials with less favourable results may have lacked adequate community support and public backing (Rodgers and others, 2006; Schooler and others, 1997).

F. INTERVENTION COST-EFFECTIVENESS

Most population-based interventions require public promotion or policy changes at the state level to effect change. However, they can be further divided into two categories. The first category of interventions encompasses those that do not require interaction between individuals and health care providers. They may be cost effective, even if the population effect is small, if the societal cost to achieve a change in one or more risk factors remains low as it is spread across the population. Unfortunately, the data on precise cost estimates for such mass interventions are limited.

The other population category includes screening-based interventions, which require some interaction with individuals and the health care system. These will be cost-effective, even with modest costs, if the approach targets high-risk individuals, and relies on easily identifiable screening tools such as limited lab testing and opportunistic screening initially. Table 2 lists the cost effectiveness estimates of both population- and individual-based interventions from analyses conducted for developing countries. It shows some selected interventions in communicable diseases for comparison. The data reveal that there are both population- and individual-based interventions that are comparable in terms of cost-effectiveness to many communicable disease interventions. However, for some of the interventions there is a considerable range to the ratios, reflecting the different levels of effectiveness or cost that may vary between and within the different developing regions of the world.

TABLE 2. COST-EFFECTIVENESS OF SELECTED HEALTH INTERVENTIONS IN DEVELOPING COUNTRIES

Chronic diseases (population-based)

Strategy	Cost (US$)/DALY (range due to uncertainty)
Tobacco price controls	13 (3–85)
Tobacco non-price interventions	100 (55–761)
Cervical cancer screening (5-year interval)	769
Trans-fat substitution with polyunsaturated fat	1865 (0–7188)
Salt reduction – population level	1320 (9–2761)
Breast cancer mammography	1350
Diabetes (screening)	5000

Chronic diseases (individual-based)

Strategy	Cost/DALY
ACE-inhibitor (congestive heart failure)	Cost saving
Aspirin/beta-blocker (post-myocardial infarction)	Cost saving
ASA/BB (acute myocardial infarction)	11
ACEI/BB (congestive heart failure)	218
Polypill secondary prevention	350
Nicotine replacement	400 (55–761)
Streptokinase (acute myocardial infarction)	634
Primary prevention CVD Polypill (10-year risk > 15 per cent)	900
Diabetes (intensive glycemic control)	3000
tPA (acute myocardial infarction)	15900
CABG (post-myocardial infarction)	27000

Communicable diseases (population- and individual-based)

Strategy	Cost/DALY
Malaria (bed netting)	11
Pentavalent vaccine (haemophilus influenzae type B, tetanus, hepatitis B, diphtheria, pertussis)	85
AIDS (mother-to-child transmission prevention)	120
Tuberculosis (short-course DOTS)	300
Lower respiratory infections (case management)	400
Blood and needle safety (HIV/AIDS)	811
Antiretroviral therapy (HIV/AIDS)	1000
Oral rehydration therapy (diarrheal disease)	3000
Meningitis (Neisseria meningitidis vaccine)	12000

Source: Jamison D, and others (2006). *Disease Control Priorities in Developing Countries*. Second edition, New York: Oxford University Press and The World Bank.

G. TRANSLATION OF TECHNOLOGY

The challenge for low- and middle-income countries is not to come up with new treatments or risk factors, but rather to learn how to implement strategies to adopt existing interventions in a way that makes sense given the prevalence of risk factors as well as the cultural and political context of the individual country. A campaign to reduce saturated fat in the diet can range anywhere from cost saving to US$ 7,000 per disability-adjusted life year averted (DALY) in India (Gaziano and others, 2007). The range in the results depends on the estimated cost to run

such a campaign and the assumed magnitude of change in the cholesterol profiles of those receiving the intervention, both of which may vary from one community to the next.

The same can be said for individual-based interventions. For example, in cancer prevention, quality-controlled cervical smears reduce the risk of cervical cancer. However, if developing countries adopted the system recommended in the United States of annual exams with HPV DNA testing, their costs would be approximately US$ 2 million per quality-adjusted life year (QALY) gained, whereas less frequent exams (such as every 3 years to every 10 years) can reduce the cost to less than US$ 10,000 per QALY or less than $1,000 per QALY in developing countries without noticeable changes in cancer rates. Given that the DALYs reported for the Disease Control Priorities Project listed above did not use age-weighting and relied on regional life expectancies, the cost per DALY averted is essentially equivalent to the cost per QALY gained.

In CVD, a similar example can be found in the use of global risk assessment prior to the use of cholesterol-lowering statin drugs. The importance of global risk assessment in making cost-effective treatment decisions is shown in the following example. Kupersmith and others (1995), showed that treatment with lovastatin for a 50-year-old man with a total cholesterol level of 7 mmol/L (270 mg/dl) and three other CVD risk factors costs US$ 20,000 per life-year saved. In contrast, treatment with the same medication for a 35-year-old woman with the same cholesterol level but no other risk factors costs US$ 2,000,000 per life-year saved. The 100-fold difference in the cost-effectiveness ratios is due to the difference in the global risk attributed to the presence of the additional risk factors, despite the same cholesterol level.

While there is much debate about which strategies are preferable, it is likely that the solution to controlling the burden of chronic diseases will need to include a mixture of interventions that are effective both at the population-level and the individual-level. Population-based interventions—such as educational programmes, advertising, taxation on tobacco, or changes in food labelling—will have the greatest effect in preventing disease over the long term. The advantage of such interventions is that they can reach large populations without great expense.

The challenge for population-based interventions is that, by their nature, they often target proportions of the population that are not at risk and are therefore less effective in some groups. It is a challenge to validate the benefits of the interventions for several reasons. First, the interventions are rarely done in a randomized-trial fashion. This is either due to the difficulties in the design of such studies or because the very nature of a national campaign does not lend itself to a comparison group. Second, the interventions are often about reducing the level of risk factors by a relatively small amount. These small changes may be hard to detect but have potentially large implications if spread across a sizeable population. Lastly, the reduction in particular health outcomes may not be appreciated for a longer time than is feasible to study.

In contrast, the effectiveness of individual-based interventions is relatively easier to assess through the use of randomized clinical trials. These interventions are generally focused on a higher-risk population and thus the rewards of the intervention are generally greater, both in terms of health improvements to the recipients of the intervention and also to the health care system through reductions in repeated consumption of health care resources. The disadvantage of these interventions is that may be more costly and they address only the sickest proportion of the population.

An example of the long-term and short-term results with regards to population-based versus individual-based interventions can be seen in tobacco control. Campaigns that reduce the

numbers of people taking up smoking will see health benefits 20 years to 50 years later through reductions in lung cancer, CVD, and obstructive lung disease, but the overall number of people protected through this measure is quite large. Smoking cessation through nicotine replacement therapies can yield reductions in ischemic heart disease.

H. ESTABLISHED CVD MANAGEMENT

Those at highest risk of CVD mortality are those suffering a myocardial infarction (MI) or stroke; as many as half die before they ever receive medical attention. For those who do make it to a hospital, standard medical therapies were examined in a cost-effectiveness analysis in the Disease Control Priorities Project in Developing Countries (Gaziano and others, 2006), (Gaziano, 2005).

Four incremental strategies were evaluated for the treatment of MI and compared to a strategy of no treatment as a base case for the six World Bank low- and middle-income regions. The four strategies compared were: aspirin; aspirin and atenolol; aspirin, atenolol, and streptokinase; and aspirin, atenolol, and tissue plasminogen activator (t-PA). The incremental cost per QALY gained for both the aspirin and beta-blocker interventions were under US$ 25 for all six regions. Costs per QALY gained for streptokinase were between US$ 630 and US$ 730 across the regions. Incremental cost-effectiveness rations for t-PA were around US$ 16,000/QALY gained, compared with streptokinase. Minor variations occurred between regions due to small differences in follow-up care based on regional costs.

Secondary prevention strategies are equally cost-effective in developing countries. Studies show that a combination of aspirin, an ACE inhibitor, a beta-blocker, and a statin for secondary prevention can lead to acceptable cost-effectiveness ratios in all developing regions (Gaziano, 2005). Use of currently available generic agents even in the absence of the so-called “polypill” could be highly cost-effective, on the order of US$ 300-US$ 400 per person per QALY gained (Gaziano and others, 2006).

I. RISK ASSESSMENT

Primary prevention is paramount for the large number of individuals who are at high risk for CVD. Given the limited resources, finding low-cost prevention strategies is a top priority. Using prediction rules or risk scores to identify those at higher risk in order to target specific behavioural or drug interventions is a well-established primary prevention strategy and has proven to be cost-effective in developing countries (Gaziano and others, 2006; Gaziano and others, 2005). Most have included age, sex, hypertension, smoking status, diabetes mellitus, and lipid values while others have also included family history (Wilson and others, 1998; Assmann, Cullen and Schulte, 2002; Conroy and others, 2003; Ferrario and others, 2005; Conroy and others, 2003). Recently, many investigators have been attempting to see if additional lab-based risk factors can add to predictive discrimination of the risk factors used in the Framingham Heart Study Risk Score. The recent analyses in the Atherosclerosis Risk in Communities (ARIC) Study (Folsom and others, 2006), and the Framingham Offspring Study (Wang and others, 2006; Ware, 2006), suggested that little additional information was gained when other blood-based novel risk factors were added to the traditional risk factors. Although the ReynoldsRisk Score for women, which added family history, hsCRP and haemoglobin A1c levels only had a marginally higher C-statistic (0.808) than the Framingham covariates (0.791), it correctly reclassified many individuals at intermediate risk (Ridker and others, 2007). Some women who were otherwise

thought to have been low risk by the Framingham Risk Score were reclassified as intermediate or high risk according to the Reynolds and thus would have been eligible for more aggressive management. Also, some women who were initially high risk according to Framingham were reclassified as lower risk and thus would not have needed treatment.

More attention is now focused on developing risk scores that would be easier to use in clinical practice without loss of predictive discrimination in resource-poor countries. In high-income countries, a prediction rule that requires a lab test is an inconvenience, but in low-income countries with limited testing facilities, a lab test may be too expensive for widespread screening or preclude screening altogether. In response to this real concern, the WHO recently released risk-prediction charts for the different regions of the world with and without a measure of cholesterol (Lindholm and Mendis, 2007; Mendis and others, 2007). A study based on the United States National Health and Nutrition Examination Survey (NHANES) follow-up cohort demonstrated that a non-lab-based risk tool that uses information obtained in a single encounter (i.e., age, systolic blood pressure, BMI, diabetes status, and smoking status) can predict CVD outcomes as well as one that requires lab testing with C-statistics of 0.79 for men and 0.83 for women that were no different from the Framingham-based risk tool (Gaziano and others, 2008). Further, the results of goodness-of-fit tests suggest that the non-lab-based model is well-calibrated across a wide range of absolute risk levels and without changes in classification of risk.

J. Policy and Community Interventions

Education and public policy interventions that have reduced smoking rates, lowered mean blood pressure levels and improved lipid profiles have contributed to the reduction in CHD rates (Ford and others, 2007). Education and policy efforts directed at tobacco consumption have been a leading cause of the reductions in CVD. In addition, salt and cholesterol reduction has been evaluated by investigators at the World Health Organization to be a cost-effective strategy to reduce stroke and MI in low- and middle-income countries (Asaria and others, 2007). Community interventions have reduced levels of multiple risk factors and, in some cases, CHD mortality.

K. Tobacco

Tobacco control can be conceptualized in terms of strategies that reduce supply of or demand for tobacco. Most public health and clinical strategies to date focus on reducing demand through economic disincentives (taxes), health promotion (media and packaging efforts), restricted access (to advertising and tobacco), or clinical assistance for cessation. The WHO effort to catalyze the creation of a global treaty against tobacco use was a key milestone in tobacco control. In May 2003, the WHO World Health Assembly unanimously adopted the WHO Framework Convention on Tobacco Control (FCTC), the first global tobacco treaty (Balbinotto Neto and Silva, 2008). The FCTC had been ratified by 164 countries as of April 2009, making it one of the most widely embraced treaties in the United Nations. The FCTC has spurred efforts for tobacco control across the globe by providing both rich and poor nations with a common framework of evidence-based legislation and implementation strategies known to reduce tobacco use.

In 2006 Dr. Prabhat Jha and colleagues presented a landmark analysis of tobacco control cost-effectiveness (Jha and others, 2006). They calculated the reductions in future tobacco deaths due to a range of tax, treatment and non-price interventions among smokers alive in 2000. They found that a 33 per cent price increase would result in a reduction of between 19.7 million and

56.8 million (5.4-15.9 per cent of total) deaths in smokers from the developing world who were alive in 2000. Calculations show that nicotine replacement therapy (NRT) could reduce the number of deaths by between 2.9 million and 14.3 million (0.8-4.0 per cent of total) in the 2000 cohort. A range of non-price interventions such as advertising bans, health warnings, and smoke-free laws would reduce deaths by between 5.7 million and 28.6 million (1.6-7.9 per cent of total) in that cohort. These reductions would translate into developing world cost-effectiveness values of between US$ 3 and US$ 42 dollars per QALY saved for tax increases (not including tax revenue), US$ 55 - US$ 761 per QALY for NRT, and US$ 54 to US$ 674 per QALY for non-price measures.

Of critical importance for patients who have had a coronary event, smoking cessation saves lives at a greater rate than any individual medical treatment. Mohiuddin and others, conducted a randomized controlled trial of a behavioural and medication smoking cessation programme for smokers who were hospitalized with a coronary event in the critical-care unit (Mohiuddin and others, 2007). They were able to nearly triple quit rates and decrease all-cause mortality at one year by an absolute risk of 9 per cent (77 per cent reduction in relative risk). This reduction corresponded with a number needed to treat (NNT) of 11 for smoking cessation to prevent one death in the year following a major coronary cardiac event. This NNT for secondary prevention is more favourable than that for statins, beta-blockers or even aspirin (Ong, 2007).

L. Salt and Lipid Reductions

The cost-effectiveness analyses on salt reduction as a result of public education are quite favourable (Jamison and others, 2006). The intervention ranges from being cost-saving to US$ 200 per DALY averted. The results suggest that a campaign for reducing saturated fat and replacing it with polyunsaturated fat is also likely to be cost-effective. In the base case, a 3 per cent decline in cholesterol and a US$ 6 per capita education costs were assumed. This resulted in a cost as low as US$ 1,800 per DALY averted in the South Asia region up to US$ 4,000 per DALY averted in the Middle East and North Africa region. However, if the cost for the education plan were halved, the ratio is approximately US$ 900 per DALY and would be cost-saving if the reduction could be achieved for under US$ 0.50 per capita, which may be possible in areas where media is much less expensive.

M. Community Interventions

Several community intervention studies where risk factors for CHD have fallen have been conducted in developing countries, including those in China, Mauritius, and South Africa (Gaziano, Galea and Reddy, 2007). However, a significant reduction in mortality has not been shown nor has the cost-effectiveness of such interventions been evaluated. The Tianjin, China Project showed reductions in hypertension and obesity. The Mauritius project included, among other interventions, a government-led programme that changed the primary cooking oil from a predominantly saturated fat palm oil to a soybean oil that is high in unsaturated fatty acids. Overall, total cholesterol levels fell 14 per cent during the five-year study period from 1987 to 1992. Changes in other risk factors were mixed with declines in blood pressure and smoking rates and increases in obesity and diabetes. The Coronary Risk Factor Study in South Africa compared a control community to two communities receiving two different levels of intensity of interventions. The interventions included mass media, group-sponsored educational sessions, and blood pressure screening and follow-up with the health sector when appropriated. Both high- and low-intensity interventions showed improvements in blood pressure, smoking rates and HDL to

total cholesterol ratio over the control community, but with little difference between the two intervention communities.

One other significant reduction of CHD came not through a concerted community intervention, but through changes in fiscal policy. In Poland, reductions in subsidies for animal products such as butter and lard led to a switch from saturated to polyunsaturated fats. The increased consumption in polyunsaturated fats was mainly through rapeseed- and soybean-based oils. A decrease in CHD mortality of greater than 25 per cent between 1991 and 2002 could not be explained by increased fruit consumption or declines in smoking, suggesting that the fiscal policies succeeded in reducing risk factors for CHD (Zatonski and Willett, 2005).

SUMMARY

Cardiovascular disease remains a significant global problem. A key challenge for developing economies, unlike developed economies, is the swift pace of economic and social transformation in a post-industrial world with rapid globalization. Although CVD rates have declined in the high-income countries, they are increasing in virtually every other region of the world. From a worldwide perspective, the rate of change in the global burden of CVD is accelerating, reflecting changes in the low- and middle-income economies, which represent more than 80 per cent of the world's population. The consequences of this preventable epidemic will be substantial on many levels—individual mortality and morbidity, family suffering and staggering economic costs, including both the direct costs of diagnosis and treatment and the indirect costs of lost productivity.

Different regions of the world face different stages of the CVD epidemic. Currently, the Eastern European countries and members of the former Soviet Republic are facing enormous burdens with over half of all deaths attributed to cardiovascular disease. Meanwhile, countries in sub-Saharan Africa are just beginning to see increases in these chronic illnesses while still grappling with HIV/AIDS. There is no single global solution to the rising burden of CVD, given the vast differences in social, cultural and economic circumstances. The high-income countries must minimize disparities, reverse unfavorable trends in CVD risk factors and behaviours, and deal with the increasing prevalence of CVD in an ageing population. The most complex challenges confront the low- and middle-income countries.

Reducing disease burden will require changes at the policy level as well as at the individual level. In the long run, allocation of resources to lower-cost strategies will likely be more cost-effective than dedicating resources to high-cost management of CVD. From a societal perspective, efforts to strengthen tobacco control strategies, improve dietary choices, and increase physical activity will be paramount. At the individual level, strategies to assess risk will need to be simplified along with the treatment modalities employed. Furthermore, alternative uses of allied health workers such as community health workers will need to be evaluated given the dearth of human resources in the health sectors of most developing countries. High-income countries must begin to share the burden of research and development into every aspect of prevention and treatment with leading and emerging middle-income countries. Through further expansion of the knowledge base, particularly regarding the economic consequences of various treatment and prevention strategies, it is possible that the efficient transfer of low-cost preventive and therapeutic strategies may alter the natural course of the epidemiological transition in every part of the world and thus reduce the excess global burden of preventable CVD.

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