Heart Disease in Africa

Cardiovascular Disease in the Developing World and Its Cost-Effective Management

Thomas A. Gaziano, MD, MSc

At the beginning of the 20th century, cardiovascular disease (CVD) was responsible for fewer than 10% of all deaths worldwide. Today, that figure is about 30%, with ≈80% of the burden now occurring in developing countries (Figure 1). In 2001, CVD was the No. 1 cause of death worldwide. This article reviews the epidemiological transition that has made CVD the leading cause of death in the world, assesses the status of the transition by region, and shows the regional differences in the burden of CVD. Furthermore, this article reviews the economic burden placed on developing countries by CVD and the very limited resources available for its management. Finally, the cost-effectiveness of various interventions addressing the most relevant causes of CVD morbidity and mortality in sub-Saharan Africa and the other developing regions is reviewed. The focus is primarily on ischemic heart disease (IHD), stroke, and congestive heart failure, which contribute most to the burden of CVD globally. The cost-effectiveness of interventions for rheumatic heart disease is reviewed elsewhere.4,5

The Epidemiological Transition

Over the last 2 centuries, the industrial and technological revolutions and the economic and social transformations associated with them have resulted in a dramatic shift in the cause of death from infectious diseases and malnutrition before 1900 to CVD and cancer currently in most high-income countries. Omran6 divided this epidemiological transition into 3 basic ages: pestilence and famine, receding pandemics, and degenerative and man-made diseases (Table 1). Olshansky and Ault added a fourth stage, delayed degenerative diseases.7

The 4 stages are outlined in Table 1 and were previously reviewed in detail in this journal.8 The age of pestilence and famine is characterized by the predominance of malnutrition and infectious disease and by the infrequency of CVD. The age of receding pandemics is marked by increases in wealth that lead to better availability of food, improved sanitation, and access to vaccines and antibiotics. These changes along with increased lifespan eventually lead to a greater incidence of CVD, particularly hemorrhagic stroke. The age of degenerative man-made diseases is characterized by dramatic lifestyle changes in diet, activity levels, and smoking that set the stage for the emergence of atherosclerosis. The average lifespan increases beyond 50 years, and mortality from CVD in particular and other noncommunicable diseases exceeds mortality from malnutrition and infectious diseases. The predominant form of CVD is coronary heart disease (CHD), but ischemic stroke also emerges as a significant cause of mortality and morbidity. In the age of delayed degenerative diseases, age-adjusted CVD mortality tends to decline because of widespread primary and secondary prevention efforts. Congestive heart failure prevalence increases, however, because of the improved survival of those with IHD.

New trends suggest that the many developed countries could be entering a fifth as-yet-unnamed phase of the epidemiological transition, characterized by an epidemic of obesity and diabetes prevalence. This trend is not unique to developed countries, however. According to the World Health Organization, worldwide, more than 1 billion adults are overweight, and 300 million are clinically obese. Even more disturbing are increases in childhood obesity, which lead to large increases in diabetes and hypertension.

Although countries tend to enter these stages at different times, the progression from one stage to the next tends to proceed in a predictable manner, with both the rate and the nature of cardiovascular diseases changing over the course of the transition. Japan is unique among the high-income countries, where the transition started later but proceeded much more rapidly. In the early part of the 20th century, stroke rates increased dramatically, eventually becoming the highest in the world. CHD rates, however, did not rise as sharply as they did in other industrialized countries and have remained lower. The historically lower heart disease rates may be attributable at least in part to genetic factors, but it is more likely that the average plant-based, low-fat diet with a high fish intake and resultant low LDL cholesterol levels has played a more important role.

Status of the Epidemiological Transition in 2004

The World Bank groups countries on the basis of economic and geographic variation. The low- and middle-income countries (gross national income per capita lower than US $9200) are divided according to geographic region. The 6 developing
regions are East Asia and the Pacific, Europe and Central Asia, Latin America and the Caribbean, Middle East and North Africa, South Asia, and sub-Saharan Africa.

The stage of the transition that each region finds itself in varies widely (Table 1). As a result of the epidemiological transition outlined above, CVD is the leading cause of death in all World Bank developing regions (Figure 2) with the exception of sub-Saharan Africa. Despite large regional variations, sub-Saharan Africa remains largely in the first phase of the epidemiological transition. Although human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) is the leading overall cause of death in this region, CVD is the second-leading killer and is the first among those over the age of 30 years. Hypertension has emerged as a major public health concern and has resulted in stroke being the dominant form of CVD. Rheumatic heart disease and cardiomyopathies are also important causes of CVD mortality and morbidity.

Most other developing regions appear to be following a similar pattern as the developed countries, with an initial rise in stroke and then a predominance of CHD, but the transition has occurred at a more compressed rate than in the high-income countries. Between 1990 and 2020, CHD alone is anticipated to increase by 120% for women and 137% for men in developing countries, compared with age-related increases of between 30% and 60% in developed countries.

East Asia and the Pacific region appear to be straddling the second and third phases. A geographic gradient has emerged, with higher CVD rates in northern China than in southern China. The Europe and Central Asia region is firmly in the peak of the third phase of the transition, with CVD representing 60% of all deaths. Croatia, Belarus, and the Ukraine saw an increase of 40% to 60% in CHD death rates between 1988 and 1998 (Figure 3). The Europe and Central Asia region has a rate of 690 CVD deaths per 100,000, more than double that of the high-income countries. Within the Middle East and North Africa region, the majority of the Middle Eastern Crescent appears to be entering the third phase of the epidemiological transition; increasing economic wealth has been accompanied by a rapid increase in CVD. As a whole, the Latin America and the Caribbean region appears to be in the third phase also, but this region, as defined by the World Bank, includes all of South America, where residents of some countries are still at risk of contracting malaria and dengue fever, and those portions are still in the first transitional phase. Heterogeneity is also apparent throughout the rest of

### Table 1. Stages of the Epidemiological Transition and Its Global Status, by Region

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>Life Expectancy, y</th>
<th>Dominant Form of CVD</th>
<th>Percentage of Deaths Due to CVD</th>
<th>Percentage of the World’s Population in This Stage</th>
<th>Regions Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pestilence and famine</td>
<td>Predominance of malnutrition and infectious diseases</td>
<td>35</td>
<td>RHD, cardiomyopathy due to infection and malnutrition</td>
<td>5–10</td>
<td>11</td>
<td>Sub-Saharan Africa, parts of all regions excluding high-income regions</td>
</tr>
<tr>
<td>Receding pandemics</td>
<td>Improved nutrition and public health leads to increase in chronic diseases, hypertension</td>
<td>50</td>
<td>Rheumatic valvular disease, IHD, hemorrhagic stroke</td>
<td>15–35</td>
<td>38</td>
<td>South Asia, southern East Asia and the Pacific, parts of Latin America and the Caribbean</td>
</tr>
<tr>
<td>Degenerative and man-made diseases</td>
<td>Increased fat and caloric intake, widespread tobacco use, chronic disease deaths exceed mortality from infections and malnutrition</td>
<td>60</td>
<td>IHD, stroke (ischemic and hemorrhagic)</td>
<td>&gt;50</td>
<td>35</td>
<td>Europe and Central Asia, northern East Asia and the Pacific, Latin America and the Caribbean, Middle East and North Africa, and urban parts of most low-income regions (especially India)</td>
</tr>
<tr>
<td>Delayed degenerative diseases</td>
<td>CVD and cancer are leading causes of morbidity and mortality; prevention and treatment avoids death and delays onset; age-adjusted CVD declines</td>
<td>&gt;70</td>
<td>IHD, stroke (ischemic and hemorrhagic), CHF</td>
<td>&lt;50</td>
<td>15</td>
<td>High-income countries, parts of Latin America and the Caribbean</td>
</tr>
</tbody>
</table>

RHD indicates rheumatic heart disease; CHF, congestive heart failure.

![Figure 1. CVD compared with other causes of death.](http://circ.ahajournals.org/DownloadedFrom))))
the developing world, even within countries. Some regions of India, for example, appear to be in the first phase of the transition, whereas others are in the second or even the third phase.

The remaining established market-economy countries are in the fourth phase of the epidemiological transition, the age of delayed degenerative diseases. In these countries, CHD rates tend to be higher than stroke rates. Overall CVD deaths are \( \approx 30\% \) of the total, with a rate of 320 deaths per 100 000 population.

**Social and Economic Impact**

In addition to the great suffering and loss of life associated with CVD, developing countries face great economic challenges associated with the epidemic. The costs are to the healthcare system and to the national economy. In South Africa, for example, 2% to 3% of the country’s gross national income, or roughly 25% of South African healthcare expenditures, was devoted to the direct treatment of CVD.\(^{11}\) An indication of possible future expenditure in developing countries is also provided by current expenditures in developed countries. For example, the United States spent an estimated \$368\ billion in relation to direct and indirect costs of CVD in 2004.\(^{12}\) In 1998, US \$109\ billion, or \( \approx 13\% \) of the healthcare budget, was spent on hypertension.\(^{13}\) In 2004, an estimated \$26\ billion was spent for the care of congestive heart failure patients. Studies are limited but suggest that obesity-related diseases are responsible for 2% to 8% of all healthcare expenditures in developed countries.\(^{14}\)

This is further compounded by the fact that such a high proportion of CVD burden occurs earlier among adults of working age in developing countries. This can lead to a large impact on a developing country’s economic viability. In the recent report *A Race Against Time*,\(^{10}\) the authors evaluated the potential loss due to early CVD. In 5 countries surveyed (Brazil, India, China, South Africa, and Mexico), conservative estimates indicated that at least 21 million years of future productive life are lost because of CVD each year.

Although the disease burden and the societal and healthcare costs of CVD are high, the resources devoted toward

**Figure 2.** Major causes of death in persons of all ages for low- and middle-income regions.

**Figure 3.** Percentage change in IHD death rates in people aged 35 to 74 years, 1988 to 1998, in selected countries. Adapted with permission from the World Health Organization, *The Atlas of Heart Disease and Stroke*.\(^{23}\)
health care are extremely scarce. The gross national income (GNI) per capita of developed countries ($27,000) is nearly 25-fold that of developing countries ($1100). Furthermore, developed countries devote twice as much of their GNI (10%) to health care compared with low- and middle-income countries (6%). This results in about a 40-fold difference between developed and developing countries in funds devoted to health care (Figure 4). 15 Given the limited resources available, only the interventions that can lead to large reductions in the CVD burden at relatively low cost are likely to be sustainable.

Cost-Effectiveness Analysis of Interventions

There are many interventions with strong evidence for significant reductions in morbidity and mortality associated with CVD, but there are few intervention trials that have been performed solely in developing countries. As a result, estimates of cost-effectiveness ratios have been extrapolated16 to the developing world based on changes in key input prices. This process is limited by the fact that both the underlying epidemiology and costs can be quite different across countries and regions. This section reviews results of the interventions based on models that used prices and epidemiological data from the World Bank developing regions as part of the Disease Control Priorities Project (DCPP). 17

The analyses complied with the DCPP “Guidelines for Authors” of July 2003. 18 Only the costs related to the intervention itself and CVD events were included in the model. Costs include personnel salaries, healthcare visits, diagnostic tests, and hospital stays according to the DCPP September 2004 draft of unit costs. 19 Indirect costs such as work loss or family assistance were not included in the analysis. Drug costs are from the International Drug Price Indicator Guide. 20 All costs, unless otherwise specified, are in US dollars. Results are reported in costs per quality-adjusted life-year (QALY) gained. For a detailed explanation of the methods and results for the following analyses, please refer to the DCPP working papers series on cardiovascular disease. 17

Coronary Heart Disease

Acute Myocardial Infarction

Four incremental strategies were evaluated for the treatment of acute myocardial infarction and compared with a strategy of no treatment as a base case. The 4 strategies compared were as follows: aspirin; aspirin and atenolol; aspirin, atenolol, and streptokinase; and aspirin, atenolol, and tissue plasminogen activator (tPA). Doses for aspirin and streptokinase were those used in ISIS (International Study of Infarct Survival)-2. The atenolol regimen was that of ISIS-1, and the tPA dosing was that used in GUSTO-I (Global Utilization of Streptokinase Tissue plasminogen activator for Occluded coronary arteries). All patients given the medications received relative risk reductions in the risk of dying of an acute

TABLE 2. ICERs for Multiple CVD Interventions, by Region

<table>
<thead>
<tr>
<th>Region</th>
<th>Medical Therapy for AMI Compared With Baseline of No Treatment, $/QALY</th>
<th>Medical Therapy and CABG for IHD Compared With Baseline of No Treatment, Hospital Access, $/QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ASA, BB, SK</td>
<td>ASA, BB, TPA</td>
</tr>
<tr>
<td>East Asia and the Pacific</td>
<td>15 672</td>
<td>15 867</td>
</tr>
<tr>
<td>Europe and Central Asia</td>
<td>15 722</td>
<td>15 878</td>
</tr>
<tr>
<td>Latin America and the Caribbean</td>
<td>20 734</td>
<td>15 887</td>
</tr>
<tr>
<td>Middle East and North Africa</td>
<td>17 715</td>
<td>15 893</td>
</tr>
<tr>
<td>South Asia</td>
<td>11 638</td>
<td>15 860</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>9 634</td>
<td>15 862</td>
</tr>
</tbody>
</table>

ASA indicates aspirin; BB, atenolol; SK, streptokinase; ACEI, enalapril; Statin, lovastatin; and MET, metoprolol.
The intervention in the first column of each set of strategies is compared with baseline; each successive intervention for each set of strategies is compared with the intervention immediately to its left.

Source: author’s calculations.
myocardial infarction. Patients receiving the thrombolytics also faced increased risks of major bleeds and hemorrhagic strokes as a complication. Two further sensitivity analyses were done comparing streptokinase for those over and under the age of 75 years and whether or not the patient receive the intervention more than or less than 6 hours from onset of symptoms, because effectiveness diminishes over time.

Incremental cost-effectiveness ratios (ICERs) for each therapy by region are listed in Table 2. The incremental cost per QALY gained for both the aspirin and \( \beta \)-blocker interventions were under $25 for all 6 regions. Costs per QALY gained for streptokinase were between $630 and $730 across the regions. ICERs for TPA were approximately $16,000 per QALY gained compared with streptokinase.

Table 2 also displays the results of the sensitivity analysis for streptokinase. Giving the streptokinase within 6 hours of the onset of symptoms reduces the incremental cost per QALY gained to approximately $400 compared with increasing it to over $1200 per QALY gained if streptokinase is given after 6 hours. Equivalent effects are seen when streptokinase is given to those under 75 years of age ($600/QALY) compared with those over the age of 75 years ($1300/QALY).

**Secondary Prevention**

Four medical therapies—aspirin, \( \beta \)-blockers, statins, and ACE inhibitors—have been the mainstay of treatment for those with CHD in the developed world. To evaluate the best medical intervention, the 15 different possible combinations of the 4 standard medical therapies were examined in an incremental cost-effectiveness analysis. The 4 therapies were aspirin at 75 to 100 mg/d, atenolol at 100 mg/d, enalapril at 10 mg/d, and lovastatin at 40 mg/d. In addition, CABG plus all 4 medications for those with left main disease or with 3-vessel coronary artery disease and reduced left ventricular function was evaluated. Because the above therapies also have significant effects on the incidence of stroke, the impact on QALYs gained and costs for these events were included in the analyses.

In addition to the mortality benefits in the trials of the individual medications or surgery listed above, significant reductions in hospitalizations also occurred in developed countries. The cost savings from these reduced admissions to hospitals make the cost-effectiveness of such interventions quite favorable in developed countries. However, given that hospital facilities may not be available to a majority of patients in many developing regions, separate analyses were undertaken, one that included hospital costs and one that did not. In the first analysis, it was assumed that hospitals would be available such as in urban areas of many middle-income countries, and thus, these savings would be realized in these settings. In the second analysis, hospitals were assumed to not be available, and thus, the intervention primarily focused on the mortality reduction, with little savings in morbidity costs. There is likely some benefit to mortality for the hospitalizations; however, the analyses does not reflect that benefit. Further investigation should be done to quantify the benefit of hospitalization itself.

In the setting in which hospitals were available, a combination of aspirin and atenolol was cost-saving compared with no therapy in all regions (Table 2). The ICERs for the combination of aspirin, atenolol, and enalapril ranged from $660 in the sub-Saharan Africa region to $866 per QALY gained in the Europe and Central Asia region. The combination of all 4 medications ranged from $1700 to 2000 per QALY gained across the regions. CABG compared with the 4-drug combination had ICERs that ranged from $24,000 per QALY gained (South Asia) to $62,000 per QALY gained (Latin America and the Caribbean). Despite having similar benefits on mortality, enalapril and lovastatin had less beneficial effects on the ICER because of the added cost of monitoring renal and liver function, respectively, required of these 2 medications compared with aspirin and atenolol.

When it was assumed that hospitals were not available (Table 2), no combination of therapies was cost-saving compared with no therapy. The combination of aspirin and \( \beta \)-blockers was the next-best strategy, with ICERs ranging from $386 per QALY gained in the South Asia region to $545 per QALY gained in the Latin America and the Caribbean region. The addition of enalapril resulted in ICERs that ranged from $783 per QALY gained to $1111 per QALY gained in sub-Saharan Africa and Latin America and the Caribbean, respectively. The addition of lovastatin increased the ICERs to between $2000 and $2500 per QALY gained.

### TABLE 2. Continued

<table>
<thead>
<tr>
<th>Medical Therapy for IHD Compared With Baseline of No Treatment, Limited Hospital Access, $/QALY</th>
<th>ACE Inhibitors and ( \beta )-Blockers for CHF Compared With Baseline of Diuretics, Hospital Access, $/QALY</th>
<th>ACE Inhibitors and ( \beta )-Blockers for CHF Compared With Baseline of Diuretics, Limited Hospital Access, $/QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA, BB</td>
<td>ASA, BB, ACEI</td>
<td>ASA, BB, Statin</td>
</tr>
<tr>
<td>ASA, BB</td>
<td>ASA, BB, ACEI</td>
<td>ASA, BB, Statin</td>
</tr>
<tr>
<td>461</td>
<td>942</td>
<td>2220</td>
</tr>
<tr>
<td>530</td>
<td>1097</td>
<td>2470</td>
</tr>
<tr>
<td>545</td>
<td>1111</td>
<td>2497</td>
</tr>
<tr>
<td>527</td>
<td>996</td>
<td>2305</td>
</tr>
<tr>
<td>386</td>
<td>828</td>
<td>2034</td>
</tr>
<tr>
<td>389</td>
<td>783</td>
<td>1955</td>
</tr>
</tbody>
</table>

ASA indicates aspirin; BB, atenolol; SK, streptokinase; ACEI, enalapril; Statin, lovastatin; and MET, metoprolol.

The intervention in the first column of each set of strategies is compared with baseline; each successive intervention for each set of strategies is compared with the intervention immediately to its left.

Source: author’s calculations.
TABLE 4. GNI per Capita in 2000

<table>
<thead>
<tr>
<th>Region</th>
<th>GNI per Capita 2000, US$</th>
<th>GNI per Capita (\times 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>East Asia and Pacific</td>
<td>1060</td>
<td>3180</td>
</tr>
<tr>
<td>Europe and Central Asia</td>
<td>2010</td>
<td>6030</td>
</tr>
<tr>
<td>Latin America and Caribbean</td>
<td>3670</td>
<td>11 010</td>
</tr>
<tr>
<td>Middle East and North Africa</td>
<td>2090</td>
<td>6270</td>
</tr>
<tr>
<td>South Asia</td>
<td>440</td>
<td>1320</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>470</td>
<td>1410</td>
</tr>
<tr>
<td>Low-income countries</td>
<td>1230</td>
<td>3690</td>
</tr>
<tr>
<td>High-income countries</td>
<td>27 680</td>
<td>83 040</td>
</tr>
</tbody>
</table>

Source: author’s calculations.

*In addition to aspirin and atenolol.

over the 6 regions. CABG was not evaluated because of the underlying assumption that hospitals were not available.

Congestive Heart Failure

The interventions examined for congestive heart failure were the addition of an ACE inhibitor (enalapril and/or metoprolol) to a baseline of diuretic treatment. As in the CHD interventions, separate analyses were conducted based on the assumption of whether or not hospital facilities would be available. Table 2 lists the results for the model of treatment for congestive heart failure assuming hospitalization. In this intervention, enalapril was cost-saving, and the ICER for metoprolol was in the range of $120 to $220 per QALY gained, depending on the region. When the availability of hospitals was limited (Table 2) the ACE inhibitor strategy was no longer cost-saving, but it only cost approximately $30 per QALY gained, and the \(\beta\)-blocker ICER only increased to approximately $275 per QALY gained. These are likely underestimates of the cost per QALY gained given that there is some loss in the mortality benefit for the hospitalization that is not captured in the model.

Cost-Effectiveness Ratios in Context

Cost-effectiveness ratios differ from region to region on the basis of input prices. But what determines what is cost-effective in an individual country? Certainly, the lower the cost-effectiveness ratio, the better, but what should determine an upper limit? There is no legal standard or regulation for what is cost-effective in the United States, but values between $50 000 and $100 000 per QALY have become an accepted benchmark for policy makers and insurance agencies. But that level is unlikely to be sustainable in developing countries. The World Health Organization’s Commission on Macroeconomics and Health\(^{21}\) recommended choosing interventions that were less than 3 times the GNI per capita. With a GNI per capita of $26 000 in the United States, $78 000 is well within the standard benchmark already in use. Table 4 lists the GNI of the 6 regions multiplied by 3. Most of the strategies reviewed above would be acceptable in all regions, with the exceptions of tPA and CABG. Countries within the sub-Saharan Africa and South Asia regions could evaluate whether statins for secondary prevention fit within their willingness and ability to pay.

Conclusions

A global CVD epidemic is rapidly evolving, with the burden of disease shifting. Twice as many deaths due to CVD now occur in developing countries as in developed countries.\(^{22}\) The vast majority of CVD can be attributed to conventional risk factors. Even in sub-Saharan Africa, high blood pressure, high cholesterol, tobacco and alcohol use, and low vegetable and fruit consumption are already among the top risk factors for disease.\(^{23}\) Because of the lag time associated with CVD risk factors, especially in children, the full effect of exposure to these factors will only be seen in the future. Information from more than 100 countries shows that more 13- to 15-year-olds smoke than ever before, and studies show that obesity levels in children are increasing markedly in countries as diverse as Brazil, China, India, and almost all island states.\(^{10} \)

Population-wide efforts now to reduce risk factors through multiple economic and educational policies and programs will reap savings later in medical and other direct costs, as well as indirectly in improved quality of life and economic productivity. Until that time, many currently available treatments for acute and chronic management of CVD exist and ought to be considered in developing countries where their use is currently limited.

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References


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