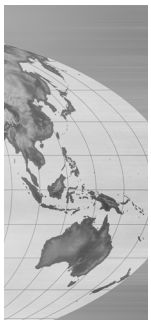
Chapter **1**



Measuring the Global Burden of Disease and Risk Factors, 1990–2001

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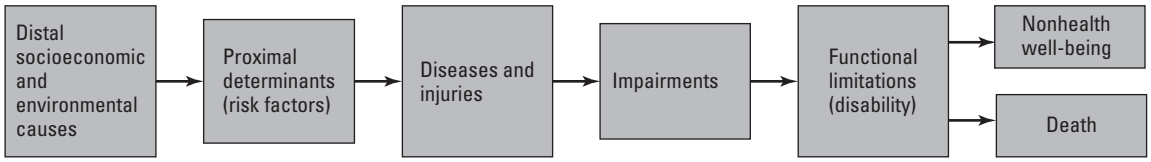
In an era when most societies must cope with increasing demand for health resources, they will inevitably have to make choices about the provision of health services, even if those choices are, by default, to continue current practices. Strategic health planning can accelerate health development and the attainment of health goals or reduce the cost of reaching such goals. Such planning must take into account the needs that the health system must address; that is, policy makers must be aware of the comparative burden of diseases and injuries and the risk factors that cause them, and how this burden is likely to change with the adoption of various policies and interventions. Needs are, of course, not the only factors determining service provision, but should be a critical component of the decision-making and planning processes.

The issue then becomes how to assess the comparative importance of risks to health and their outcomes in different demographic groups of the population. What is needed is a framework for integrating, validating, analyzing, and disseminating the fragmentary, and at times contradictory, information that is available on a population's health, along with some understanding of how that population's health is changing, so that the information is more relevant for health policy and planning purposes. The Global Burden of Disease (GBD) framework is the principal, if not the only, attempt to do so. Features of the GBD framework include the incorporation of data on nonfatal health outcomes into summary measures of population health, the development of methods for assessing the reliability of data and imputing missing data, and the use of a common metric to summarize the disease burden from diagnostic categories of the International Classification of Diseases and the major risk factors that cause those health outcomes. Figure 1.1 presents a simplified version of this framework and indicates the causal chain of events that matter for health outcomes, identifying the key components and determinants of health status that require quantification.

Many countries and health development agencies have adopted the GBD approach as the standard for health accounting and for guiding the determination of health research priorities, for example, Australia (Mathers, Vos, and Stevenson 1999); the state of Andra Pradesh, India (Mahapatra 2002); Mauritius (Vos and others 1995); Mexico (Lozano and others 1995); South Africa (Bradshaw and



Source: Mathers and others 2002.

Note: This presentation is intended as a broad schema: for example, some exposures, such as environmental factors, can be proximate causes of disease, and injuries can lead directly to death.

Figure 1.1 Overview of Burden of Disease Framework

others 2003); Thailand (Bundhamcharoen and others 2002); Turkey (Baskent University 2005); the United States (McKenna and others 2005); and the World Health Organization (WHO 1996).

This chapter begins with a brief history of the work on burden of disease, including a discussion of the nature and origins of the disability-adjusted life year (DALY) as a measure of disease burden. Next it discusses applications of burden of disease analysis to the formulation of health policy. The chapter then summarizes the methods and findings of the 2001 GBD study, reported in more detail in chapters 3 and 4 of this volume. A concluding section takes stock of the work on disease burden since the early 1990s and suggests some key areas for further work.

Following this introductory and summarizing chapter, chapter 2 describes the demographic underpinnings for the epidemiological assessments that follow and provides context by briefly reviewing recent changes (from 1990 to 2001) in key demographic parameters. The chapter also assesses changes in the cause distribution of mortality among children under five between 1990 and 2001 and the difficulties of reliably assessing trends in mortality. Chapters 3 and 4 provide the definitive methods and results of the 2001 GBD study. Chapter 3 reports on deaths and the disease and injury burden by age, sex, and 136 disease and injury categories. Chapter 4 reports on the disease and injury burden resulting from 19 risk factors, specifically for a number of important conditions. Both chapters present results using the World Bank's classification of low- and middle-income countries into six regional groups. Chapter 5 then explores the robustness of the major findings to uncertainties in the data and to alternative assumptions concerning construction of the DALY. Chapter 6 examines the implications of including stillbirths in a global burden of disease assessment. Their inclusion is potentially significant, both because the numbers are large (3.3 million in 2001), and because including stillbirths raises major questions about how to assess the DALY loss associated with deaths near the time of birth.

HISTORY OF BURDEN OF DISEASE STUDIES

In 1992, the World Bank commissioned the initial GBD study to provide a comprehensive assessment of the disease burden in 1990. The study was undertaken for the world as a whole and for 8 regions (Lopez and Murray 1998; Murray and Lopez 1996a,d; Murray, Lopez, and Jamison 1994; World Bank 1993). In order to recommend intervention packages for countries at different stages of development, the estimates were combined with analyses of the cost-effectiveness of interventions in different populations (World Bank 1993; Jamison and Jardel 1994). Whereas earlier attempts to quantify global cause of death patterns (Hakulinen and others 1986; Lopez 1993) were valuable initial contributions to building the evidence base for policy, they were largely restricted to broad cause of death groups, for example, all infections and parasitic diseases combined, and did not address nonfatal health outcomes.

The methods and findings of the 1990 GBD study have been widely published and, as noted earlier, have spawned multiple disease burden exercises (Murray and Lopez 1996c,d; 1997a,b,c). One of the basic principles guiding a burden of disease assessment is that almost all sources of health data are likely to contain useful information provided they are carefully screened for validity and completeness. With appropriate methods, investigator commitment, and expert judgment, obtaining internally consistent estimates of the global descriptive epidemiology of major conditions is possible. To prepare internally consistent estimates of incidence, prevalence, duration, and mortality for almost 500 sequelae of the diseases and injuries under consideration, a mathematical model, DisMod, was developed for the 1990 GBD study to convert partial, often nonspecific, data on disease and injury occurrence into a consistent description of the basic epidemiological parameters in each region by age group (Barendregt and others 2003; Murray and Lopez 1996b).

Many diseases, for example, neuropsychiatric conditions and hearing loss, and injuries may cause considerable ill health but no or few direct deaths. Therefore separate

Box 1.1

Disability-Adjusted Life Years

The DALY is a health gap measure that extends the concept of potential years of life lost due to premature death to include equivalent years of healthy life lost by virtue of individuals being in states of poor health or disability (Murray 1996). One DALY can be thought of as one lost year of healthy life and the burden of disease as a measure of the gap between current health status and an ideal situation where everyone lives into old age free from disease and disability. This conceptualization of DALYs as a measure of health, and not of lost utility, is analogous to the principles of measuring gross domestic product as summarized by Eisner (1989, p. 7): "Our focus . . . is on measures of all economic activity related to welfare [for example, gross domestic product], but not of welfare itself." Information on calculating DALYs, on time discounting, and on age weights is provided in chapter 3.

DALYs for a disease or health condition are calculated as the sum of YLL in the population and YLD for incident cases of the health condition. YLL is calculated from the number of deaths at each age multiplied by a global standard life expectancy for the age at which death occurs. To estimate YLD for a particular cause for a particular time period, the number of incident cases in that period is multiplied by the average duration of the disease and a weight factor that reflects the severity of the disease on a scale from 0 (perfect health) to 1 (dead). The weights used in the 2001 GBD study are listed in detail elsewhere (see annex tables 3A.6 to 3A.8 in chapter 3).

In addition, in calculating DALYs, the GBD study used 3 percent time discounting and non-uniform age weights which give less weight to years lived at young and older ages. For the results reported in this volume and used in the *Disease Control Priorities in Developing Countries,* second edition (DCP2) 3 percent time discounting was applied but not non-uniform age weights. A death in infancy then corresponds to 30 DALYs, and deaths at age 20 to around 28 DALYs. Thus a disease burden of 3,000 DALYs in a population would be the equivalent of around 100 infant deaths or to approximately 5,000 persons aged 50 years living one year with blindness (disability weight 0.6).

measures of survival and of health status among survivors, while useful inputs when formulating health policy, need to be combined in some fashion to provide a single, holistic measure of overall population health. To assess the burden of disease, the 1990 GBD study used a time-based metric that measures both premature mortality (years of life lost because of premature mortality or YLL) and disability (years of healthy life lost as a result of disability or YLD, weighted by the severity of the disability). The sum of the two components, namely, DALYs, provides a measure of the future stream of healthy life (years expected to be lived in full health) lost as a result of the incidence of specific diseases and injuries in 1990 (box 1.1). The effect of fatal cases (of disease or injury) is captured by years of life lost, while YLD captures the future health consequences in terms of sequelae of diseases or injuries of incident cases in 1990 that were not fatal. (For a more complete account of the DALY measure and the philosophy underlying parameter choices, see Murray 1996; Murray, Salomon, and others 2002).

DALYs are not unique to the GBD study. The World Bank used a variant of DALYs in its seminal review of health sector priorities (Jamison and others 1993), and they are derived from earlier work to develop time-based measures that better reflect the public health impact of death or illness at young ages (Dempsey 1947; Ghana Health Assessment Project Team 1981).

Much of the comment on, and criticism of, the GBD study focused on the construction of DALYs (Anand and Hanson 1998; Hyder, Rotllant, and Morrow 1998; Williams 1999), particularly the social choices pertaining to age weights and severity scores for disabilities. Relatively little criticism was directed at the vast uncertainty of the basic descriptive epidemiology for some populations, especially in Sub-Saharan Africa (see chapter 5 in this volume), which is likely to be far more consequential for setting health priorities (Cooper and others 1998).

The results of the 1990 GBD study confirmed what many health workers had suspected for some time, namely, that noncommunicable diseases and injuries were a significant cause of health burden in all regions, and in some rapidly industrializing regions such as East Asia and Pacific, were already by far the leading cause of death and disability. Neuropsychiatric disorders and injuries in particular were major causes of lost years of healthy life as measured by DALYs, and were vastly underappreciated when measured by mortality alone. The original GBD study estimated that noncommunicable diseases, including neuropsychiatric disorders, caused 41 percent of the global burden of disease in 1990, only slightly less than

communicable, maternal, perinatal, and nutritional conditions combined (44 percent), and that 15 percent of the burden was due to injuries. Earlier assessments of global health priorities based on mortality data attributed no deaths to mental health disorders and less than half (7 percent) of that suggested by DALYs to injuries (Lopez 1993).

Estimates of the disease and injury burden caused by exposure to major risk factors are likely to be a much more useful guide to policies and priorities for prevention than a "league table" of the disease and injury burden. In recent decades, researchers have attempted to quantify the effects of specific exposures, for instance, tobacco smoking, on mortality from major diseases such as cancers (Doll and Peto 1981; Parkin and others 1994) or from multiple diseases (Peto and others 1992; United States Department of Health and Human Services 1992), either in individual countries or across groups of countries using comparable methods.

Specific country studies have examined the impact of several leading risk factors (Holman and others 1988; McGinnis and Foege 1993), but prior to the 1990 GBD study, no global assessments of the fatal and nonfatal burden of disease and injury resulting from exposure to multiple major health risks had been attempted. The 1990 study quantified 10 risk factors based on information about causation, prevalence, exposure, and disease and injury outcomes available at the time. The study attributed almost 16 percent of the entire global burden of disease and injury to malnutrition; another 7 percent to poor water and sanitation; and 2 to 3 percent to such risks as unsafe sex, tobacco, alcohol, and occupational exposures (Lopez and Murray 1998; Murray and Lopez 1996a; Murray and Lopez 1997a; Murray, Lopez, and Jamison 1994; World Bank 1993).

APPLICATIONS OF BURDEN OF DISEASE ANALYSIS

Burden of disease analyses are useful for informing health policy in at least five major ways as outlined in this section. Estimates of deaths by cause or years of life lost serve these same purposes, but for some uses, less well.

Assessing Performance

The burden of disease provides an indicator that can be used to judge progress over time within a single country or region or relative performance across countries and regions. In this application, burden of disease may be considered analogous to national income and product accounts, developed by Simon Kuznets and others in the 1930s and culminating in 1939 with a complete national income and product account for the United Kingdom prepared at the request of the treasury. In subsequent decades, national income and product accounts have transformed the empirical underpinnings of economic policy analysis. As one leading scholar put it, "The national income and product accounts for the United States . . . , and kindred accounts in other nations, have been among the major contributions to economic knowledge over the past half century . . . Several generations of economists and practitioners have now been able to tie theoretical constructs of income, output, investment, consumption, and savings to the actual numbers of these remarkable accounts with all their fine detail and soundly meshed interrelations" (Eisner 1989, p. 1).

Generating Forums for Informed Debate of Values and Priorities

In practice, assessing the disease burden involves participation by a broad range of disease specialists, epidemiologists, and often, policy makers. Debating the appropriate values for, say, disability weights or for years of life lost at different ages helps clarify values and objectives for national health policy. Discussing the relationships between diseases and their risk factors in the light of local conditions sharpens consideration of priorities and of programs to address them.

Identifying National Control Priorities

Many countries now identify a relatively short list of interventions whose full implementation becomes an explicit priority for national political and administrative attention. Examples include interventions to control tuberculosis, poliomyelitis, HIV/AIDS, smoking, and specific micronutrient deficiencies. Because political attention and high-level administrative capacity are in relatively fixed and short supply, the benefits from using those resources will be maximized if they are directed toward interventions that are both cost-effective and aimed at problems associated with a high disease burden. National assessments of disease burden are one input into the process of establishing a shortlist of disease control priorities.

Creating Knowledge

Medical schools offer a fixed number of instructional hours, and training programs for other levels and types of health workers are similarly limited. A major instrument for

implementing health policy priorities is to allocate this fixed time resource well. This implies allocating time to training for interventions where the disease burden is high and cost-effective interventions exist.

Information on the disease or risk factor burden is also a vital input for informing resource allocation for research and development. In particular, whenever a fixed effort will have a benefit proportional not only to the size of that effort, but also to the size of the problem being addressed, estimates of the disease burden become essential for formulating and implementing research and development priorities. For example, developing a vaccine for a broad range of viral pneumonias would have perhaps hundreds of times the impact of a vaccine against hantavirus infection.

Allocating Resources across Health Interventions

A key task for priority-setting analyses in health is to create the evidence base to stimulate the reallocation of resources to interventions that, at the margin, will generate the greatest reduction in health loss. When there are major fixed costs in mounting an intervention, as is the case with political and managerial attention for national control priorities, burden estimates are required to improve resource allocation. Similarly, major fixed costs may be associated with the universalization (or major expansion) of an intervention and, if so, the cost-effectiveness of the expansion will depend in part on the size of the burden.

IMPROVING THE COMPARATIVE QUANTIFICATION OF DISEASES, INJURIES, AND RISK FACTORS: THE 2001 GBD STUDY

The 1990 GBD study represented a major advance in the quantification of the impact of diseases, injuries, and risk factors on population health globally and by region. Government and nongovernmental agencies alike have used its results to argue for more strategic allocations of health resources to disease prevention and control programs that are likely to yield the greatest gains in terms of population health. The results have also greatly increased understanding of the basic descriptive epidemiology of diseases and injuries worldwide.

Following publication of the initial results of the GBD study, several national applications of the methods it used have led to substantially more data on the descriptive epidemiology of diseases and injuries becoming available, as well as to improvements in analytical methods and mortality data in a number of countries. By emphasizing substantially more sophisticated approaches than in the past to the interpretation and presentation of population health data to policy makers, national burden of disease studies have stimulated efforts to improve and extend the collection of the health information data that are the basis for such analyses. A good example is the Islamic Republic of Iran where, over the last five years, the government has implemented a system of death registration with medical information on the cause of death that has been extended from four provinces initially to include 26, or almost all of the country's provinces. Another example is the government of Thailand's extensive verbal autopsy study aimed at addressing major coding deficiencies in Thailand's national mortality data (Choprapawon and others 2005).

Critiques of the original study's approach, particularly of the methods used to assess the severity weightings for disabling health states, have led to fundamental changes in the way that investigators incorporate health state valuations, that is, the use of population-based rather than expert opinion as used in the 1990 study, and to substantially better methods for improving the cross-national comparability of survey data on health status (Murray, Tandon, and others 2002; Salomon and Murray 2004). Better methods for modeling the relationship between the level of mortality and the broad cause of death structure in populations that are based on proportions rather than rates have led to greater confidence in cause of death estimates for developing countries (Salomon and Murray 2002). In addition, improved population surveillance for some major diseases such as HIV/AIDS, and the wider availability of data from verbal autopsy methods, particularly in Sub-Saharan Africa, have lessened the dependence on models for cause of death estimates, although substantial uncertainty in the use of such data persists. For more details on these and other methodological advances, see chapter 3 in this volume.

Perhaps the major methodological progress since the 1990 GBD study has been with respect to the quantification of the disease burden from risk factors. The initial study quantified the population health effects of 10 risk factors, but serious concerns exist about the comparability of the methods and estimates used. Different risk factors have different epidemiological traditions, particularly with regard to the definitions of hazardous exposure, the strength of the evidence on causality, and the availability of epidemiological research on exposure and hazard. As a result, comparability across estimates of the disease burden caused by different risk factors has been difficult to establish. In particular, much of classical risk factor research has treated exposures as dichotomous, with individuals either exposed

or not exposed, with exposure defined according to an often arbitrary threshold value, for example, systolic blood pressure of 140 millimeters of mercury as the threshold for hypertension. Recent evidence for such continuous exposures as cholesterol, blood pressure, and body mass index suggests that such arbitrarily defined thresholds are inappropriate, because the hazards for these risks decline continuously across the entire range of measured exposure levels, with no obvious threshold (Eastern Stroke and Coronary Heart Disease Collaborative Research Group 1998; Ezzati and others 2004; Rose 1985; WHO 2002).

For the 2001 GBD study, a new framework for risk factor assessment was defined that examines changes in the disease burden that would be expected under alternative population distributions of exposure to a risk factor or groups of risk factors (Murray and Lopez 1999). Attributable fractions of disease due to a risk factor were then calculated based on a comparison of the disease burden expected under the current estimated distribution of exposure by age, sex, and region with that expected under a counterfactual distribution of exposure. One such counterfactual distribution was defined for each risk factor as the population distribution of exposure that would lead to the lowest levels of disease burden. Thus, for example, in the case of tobacco, this theoretical-minimum-risk counterfactual exposure would be 100 percent of the population being never-smokers, for overweight and obesity it would be a narrow distribution of body mass index centered around an optimal level of 21 kg/m^2 and so on. The distributions of the theoretical-minimum-risk exposure for the risk factors quantified in the World Health Organization's study of comparative risk assessment (the methodological and empirical basis for the 2001 GBD study) were developed by expert groups for each risk factor based on available scientific knowledge of risk factor hazard. The study also used systematic reviews and analyses of extant sources on risk factor exposure and hazard in an iterative process that increased comparability across risk factors (Ezzati and others 2002, 2004). These methods and results are described in more detail in chapter 4 in this volume.

Risk factors may affect disease and injury outcomes through other intermediate factors. For instance, some of the effects of diet and physical activity on cardiovascular diseases are mediated through changes in such intermediate factors as weight, blood pressure, and cholesterol. Risk factors may also affect disease and injury outcomes in combination with one another. For example, people who smoke and have elevated blood pressure and cholesterol have substantially higher probabilities of cardiovascular events. Finally, some risks have common social and behavioral determinants. For instance, members of poor households in rural areas are the most likely to be undernourished, use unsafe water sources, and be exposed to indoor smoke from solid fuels. Because of these epidemiological and social characteristics of risk factor exposure and hazard, policy-relevant analysis should include an assessment of the health benefits of simultaneous reductions in multiple risks. Multicausality also means that a range of interventions can be used for disease prevention, with the specific choices determined by such factors as costs, technology availability, infrastructure, and preferences. A novel aspect of the analysis of risk factors in the 2001 GBD study is the development and application of methods for estimating the disease burden attributable to the combined hazards of multiple risk factors (Ezzati and others 2003).

The basic units of analysis in the 1990 GBD study were the eight World Bank regions defined for the World Bank's (1993) *World Development Report 1993*. Designed to be geographically contiguous, these regions were nonetheless extremely heterogeneous with respect to health development, for example, the region referred to as Other Asia and Islands included countries with such diverse epidemiological profiles as Myanmar and Singapore. This seriously limited the applicability of these regions to comparative epidemiological assessments. Thus the 2001 GBD study followed a more refined approach. Estimates of overall mortality were first developed for World Health Organization member states using different methods for countries at different stages of health development. The choice of methods was largely determined by the availability of data (Lopez and others 2002). Age- and sex-specific death rates for countries were essentially determined using one of three standard approaches: the use of routine life table methods for countries with complete vital registration; the application of standard demographic methods to correct for underregistration of deaths; or the application of model life tables where no vital registration or survey data on adult mortality were available (Lopez and others 2002; Murray and others 2003).

The detailed methodological approaches adopted for estimating cause-specific mortality for countries and the descriptive epidemiology of nonfatal conditions for countries or subregions are described elsewhere (Mathers and others 2002; chapter 3 in this volume). This focus on individual countries as the unit of analysis, as well as the systematic application of standardized approaches for all countries in any given category of data availability, has vastly improved the cross-population comparability of disease and injury quantification.

A final major advance of the 2001 GBD study has been the systematic attempts to quantify some of the uncertainty

in both national and global assessments of the disease burden (see chapter 5 in this volume). This uncertainty must be taken into account when making cross-national comparisons and needs to be carefully communicated to and interpreted by epidemiologists and policy makers alike.

MAJOR FINDINGS OF THE 2001 GBD STUDY

This section, and tables 1.1 and 1.2, summarize the principle findings of the 2001 GBD study. More detailed findings are reported in chapters 3 and 4.

Global and Regional Mortality

Slightly more than 56 million people died in 2001, 10.5 million (or nearly 20 percent) of whom were children younger than five years of age. Almost 4 million children died before 1 month of age, with an additional 3.3 million stillbirths (see chapter 6). Of these child deaths, 99 percent occurred in low- and middle-income countries. Low- and middle-income countries also account for a comparatively large number of deaths at young and middle adult ages: 30 percent of all deaths occur at ages 15 to 59, compared with 15 percent in high-income countries. The causes of death at these ages, as well as in childhood, are thus important for assessing public health priorities.

Worldwide, one death in every three is from what the GBD study terms Group I causes (communicable diseases, maternal and perinatal conditions, and nutritional deficiencies) (see table 1.1). This proportion remains almost unchanged from 1990, with one major difference. Whereas HIV/AIDS accounted for only 2 percent of Group I deaths in 1990, it accounted for 14 percent in 2001. Excluding HIV/AIDS, Group I deaths fell from one-third of total deaths in 1990 to less than one-fifth in 2001. Virtually all Group I deaths are in low- and middle-income countries.

In low- and middle-countries, Group II causes (noncommunicable diseases) are now responsible for more than 50 percent of deaths in adults ages 15 to 59 in all regions except South Asia and Sub-Saharan Africa, where Group I causes, including HIV/AIDS, remain responsible for one-third and two-thirds of deaths, respectively. Outside these two regions, developing countries are now facing a triple burden of disease from communicable diseases, noncommunicable diseases, and injuries (Group III causes). Among low- and middle-income countries as a group, the three leading causes of death in 2001 included ischemic heart disease and cerebrovascular disease, which together accounted for almost one-fifth of all deaths. In other words, the epidemiological transition from infectious to chronic noncommunicable diseases in this group of countries is already well established and is of major relevance to health planning.

Leading Causes of Disability

The 1990 GBD study brought the previously largely ignored burden of nonfatal illnesses, particularly neuropsychiatric disorders, to the attention of health policy makers. The findings of the 2001 GBD study, based on updated data and analyses, confirm that disability and states of less than full health caused by diseases and injuries play a central role in determining the overall health status of populations in all regions of the world. Neuropsychiatric conditions, vision disorders, hearing loss, and alcohol use disorders dominate the overall burden of nonfatal disabling conditions.

In all regions, neuropsychiatric conditions are the most important causes of disability, accounting for more than 37 percent of YLD among adults aged 15 years and older worldwide. The disabling burden of neuropsychiatric conditions is almost the same for males and females, but the major contributing causes are different. While depression is the leading cause of disability for both males and females, the burden of depression is 50 percent higher for females than males, and females also have higher burdens from anxiety disorders, migraine, and senile dementia. In contrast, the male burden for alcohol and drug use disorders is nearly six times higher than that for females and accounts for a quarter of the male neuropsychiatric burden.

More than 85 percent of disease burden from nonfatal health outcomes occurs in low- and middle-income countries, and South Asia and Sub-Saharan Africa account for 40 percent of all YLD. Even though the prevalence of disabling conditions such as dementia and musculoskeletal disease is higher in countries with long life expectancies, this is offset by lower contributions to disability from conditions such as cardiovascular disease, chronic respiratory diseases, and long-term sequelae of communicable diseases and nutritional deficiencies. In other words, people living in developing countries not only face shorter life expectancies than those in developed countries, but also live a higher proportion of their lives in poor health.

Burden of Disease and Injuries

The results of the 2001 GBD study reinforce some of the conclusions of the 1990 GBD study about the importance of including nonfatal outcomes in a comprehensive assessment

Table 1.1 Deaths and Burden of Disease by Cause—Low- and Middle-Income Countries, High-Income Countries, and World, 2001

	Low- and middle-income		High-income		World	
	Deaths	**DALYs(3,0)[a]**	**Deaths**	**DALYs(3,0)[a]**	**Deaths**	**DALYs(3,0)[a]**
All causes						
Total number (thousands)	**48,351**	**1,386,709**	**7,891**	**149,161**	**56,242**	**1,535 871**
Rate per 1,000 population	**9.3**	**265.7**	**8.5**	**160.6**	**9.1**	**249.8**
Age-standardized rate per 1,000[b]	**11.4**	**281.7**	**5.0**	**128.2**	**10.0**	**256.5**
Selected cause groups:			*Number in thousands (percent)*			
I. COMMUNICABLE DISEASES, MATERNAL AND PERINATAL CONDITIONS AND NUTRITIONAL DEFICIENCIES	**17,613 (36.4)**	**552,376 (39.8)**	**552 (7.0)**	**8,561 (5.7)**	**18,166 (32.3)**	**560,937 (36.5)**
Tuberculosis	1,590 (3.3)	35,874 (2.6)	16 (0.2)	219 (0.1)	1,606 (2.9)	36,093 (2.3)
HIV/AIDS	2,552 (5.3)	70,796 (5.1)	22 (0.3)	665 (0.4)	2,574 (4.6)	71,461 (4.7)
Diarrheal diseases	1,777 (3.7)	58,697 (4.2)	6 (<.1)	444 (0.3)	1,783 (3.2)	59,141 (3.9)
Measles	762 (1.6)	23,091 (1.7)	1 (<.1)	23 (<.1)	763 (1.4)	23,113 (1.5)
Malaria	1,207 (2.5)	39,961 (2.9)	0 (0.0)	9 (<.1)	1,208 (2.1)	39,970 (2.6)
Lower respiratory infections	3,408 (7.0)	83,606 (6.0)	345 (4.4)	2,314 (1.6)	3,753 (6.7)	85,920 (5.6)
Perinatal conditions	2,489 (5.1)	89,068 (6.4)	32 (0.4)	1,408 (0.9)	2,522 (4.5)	90,477 (5.9)
Protein-energy malnutrition	241 (0.5)	15,449 (1.1)	9 (0.1)	130 (<.1)	250 (0.4)	15,578 (1.0)
II. NONCOMMUNICABLE CONDITIONS	**26,023 (53.8)**	**678,483 (48.9)**	**6,868 (87.0)**	**129,356 (86.7)**	**32,891 (58.5)**	**807,839 (52.6)**
Stomach cancers	696 (1.4)	9,616 (0.7)	146 (1.9)	1,628 (1.1)	842 (1.5)	11,244 (0.7)
Colon and rectum cancers	357 (0.7)	5,060 (0.4)	257 (3.3)	3,175 (2.1)	614 (1.1)	8,236 (0.5)
Liver cancer	505 (1.0)	7,945 (0.6)	102 (1.3)	1,223 (0.8)	607 (1.1)	9,169 (0.6)
Trachea, bronchus, and lung cancers	771 (1.6)	10,701 (0.8)	456 (5.8)	5,397 (3.6)	1,227 (2.2)	16,099 (1.0)
Diabetes mellitus	757 (1.6)	15,804 (1.1)	202 (2.6)	4,192 (2.8)	960 (1.7)	19,997 (1.3)
Unipolar depressive disorders	10 (<.1)	43,427 (3.1)	3 (<.1)	8,408 (5.6)	13 (<.1)	51,835 (3.4)
Alcohol use disorders	62 (0.1)	11,007 (0.8)	23 (0.3)	4,171 (2.8)	84 (0.2)	15,178 (1.0)
Cataracts	0 (0.0)	28,150 (2.0)	0 (0.0)	493 (0.3)	0 (0.0)	28,643 (1.9)
Vision disorders, age-related	0 (0.0)	15,364 (1.1)	0 (0.0)	1,525 (1.0)	0 (0.0)	16,889 (1.1)
Hearing loss, adult onset	0 (0.0)	24,607 (1.8)	0 (0.0)	5,387 (3.6)	0 (0.0)	29,994 (2.0)
Hypertensive heart disease	760 (1.6)	9,969 (0.7)	129 (1.6)	1,209 (0.8)	889 (1.6)	11,178 (0.7)
Ischemic heart disease	5,699 (11.8)	71,882 (5.2)	1,364 (17.3)	12,390 (8.3)	7,063 (12.6)	84,273 (5.5)
Cerebrovascular disease	4,608 (9.5)	62,669 (4.5)	781 (9.9)	9,354 (6.3)	5,390 (9.6)	72,024 (4.7)
Chronic obstructive pulmonary disease	2,378 (4.9)	33,453 (2.4)	297 (3.8)	5,282 (3.5)	2,676 (4.8)	38,736 (2.5)
Cirrhosis of the liver	654 (1.4)	13,633 (1.0)	118 (1.5)	2,146 (1.4)	771 (1.4)	15,778 (1.0)
Nephritis and nephrosis	552 (1.1)	9,076 (0.7)	111 (1.4)	929 (0.6)	663 (1.2)	10,005 (0.7)
Osteoarthritis	2 (<.1)	13,666 (1.0)	3 (<.1)	3,786 (2.5)	5 (<.1)	17,452 (1.1)
Congenital anomalies	477 (1.0)	23,533 (1.7)	30 (0.4)	1,420 (1.0)	507 (0.9)	24,952 (1.6)
Alzheimer and other dementias	173 (0.4)	9,640 (0.7)	207 (2.6)	7,468 (5.0)	380 (0.7)	17,108 (1.1)
III. INJURIES	**4,715 (9.8)**	**155,850 (11.2)**	**471 (6.0)**	**11,244 (7.5)**	**5,186 (9.2)**	**167,094 (10.9)**
Road traffic accidents	1,069 (2.2)	32,017 (2.3)	121 (1.5)	3,045 (2.0)	1,189 (2.1)	35,063 (2.3)
Falls	316 (0.7)	13,582 (1.0)	71 (0.9)	1,459 (1.0)	387 (0.7)	15,041 (1.0)
Self-inflicted injuries	749 (1.5)	17,674 (1.3)	126 (1.6)	2,581 (1.7)	875 (1.6)	20,255 (1.3)
Violence	532 (1.1)	18,132 (1.3)	24 (0.3)	765 (0.5)	556 (1.0)	18,897 (1.2)

Source: Chapter 3.

Notes: Numbers in parentheses indicate percentage of column total.

Broad group totals in bold are additive but should not be summed with all other conditions listed in table.

a. DALYs (3,0) refer to the version of the DALY based on a 3% annual discount rate and uniform age weights.

b. Age-standardized using the WHO World Standard Population.

c. Includes only causes responsible for more than 1% of global deaths or DALYs in 2001.

of global population health. They also confirm the growing importance of noncommunicable diseases in low- and middle-income countries and highlight important changes in population health in some regions since 1990.

HIV/AIDS is now the fourth leading cause of the burden of disease globally and the leading cause in Sub-Saharan Africa, where it is followed by malaria in second place. Seven other Group I causes also appear in the top 10 causes for this

region. The epidemiological transition in low- and middle-income countries has resulted in a 20 percent reduction in the per capita disease burden due to Group I causes since 1990. Without the HIV/AIDS epidemic and the associated lack of decline in the burden of tuberculosis, this reduction would have been closer to 30 percent.

The per capita disease burden in Europe and Central Asia has increased by nearly 40 percent since 1990, and population health in this region is now worse than all other regions except South Asia and Sub-Saharan Africa. This reflects the sharp increase in adult male mortality and disability in the 1990s, leading to the highest male-female differential in the disease burden in the world. A significant factor in this increase is probably the high level of harmful alcohol consumption among men, which has led to high rates of accidents, violence, and cardiovascular disease. From 1991 to 1994, the risk of premature adult (15 to 59 years) death increased by 50 percent for Russian males. It improved somewhat between 1994 and 1998, but subsequently increased.

The burden of noncommunicable diseases is increasing, accounting for nearly half the total global burden of disease, a 10 percent increase from estimated levels in 1990. Almost 50 percent of the adult disease burden in low- and middle income countries is now attributable to noncommunicable diseases. The implementation of effective interventions for Group I diseases, coupled with population aging and the spread of risks for noncommunicable disease in many low- and middle-income countries, are the likely causes of this shift. Ischemic heart disease and stroke dominate the burden of disease in Europe and Central Asia and together account for more than a quarter of the total disease burden. In contrast, in Latin America and the Caribbean these diseases account for 8 percent of the disease burden, but this region also has high levels of diabetes and endocrine disorders compared with other regions. Violence is the fourth leading cause of the disease and injury burden in Latin America and the Caribbean. Violence does not appear among the top 10 causes of burden in any other region, but is nonetheless significant.

Injuries primarily affect young adults and often result in severe, disabling sequelae. All forms of injury accounted for 16 percent of the adult burden in 2001. In parts of Europe and Central Asia, Latin America and the Caribbean, and the Middle East and North Africa, more than 30 percent of the entire disease and injury burden among male adults aged 15 to 44 is attributable to injuries. Road traffic accidents, violence, and self-inflicted injuries are all among the top 10 leading causes of burden in these regions. The former Soviet Union and other high-mortality (among adults) countries of Eastern Europe have rates of injury death and disability among males that are similar to those in Sub-Saharan Africa.

Burden of Disease Attributable to Risk Factors

As described earlier, a major advance of the 2001 GBD study has been in creating a unified framework for quantifying the burden of disease and injury attributable to major risk factors and in applying this framework to exposure and hazard data for selected major risk factors based on comprehensive and systematic reviews of published literature and other sources. Notwithstanding the inherent uncertainties in assessing the population-level health effects of risk factors, the quantification of the burden of disease attributable to the individual and joint hazards of selected risks suggests that the leading causes of mortality and disease burden include risk factors for Group I conditions (for example, undernutrition; indoor smoke from household use of solid fuels; poor water, sanitation, and hygiene; and unsafe sex), whose burden is primarily concentrated in South Asia and Sub-Saharan Africa, and risk factors for Group II conditions (especially, smoking, alcohol, high blood pressure and cholesterol, and overweight and obesity), which are widespread globally (see table 1.2). In low- and middle-income countries, the leading causes of disease burden included risk factors prevalent among the poor and associated with Group I conditions (for example, childhood underweight [8.7 percent of the disease burden in these regions]; unsafe water, sanitation, and hygiene [3.7 percent]; and indoor smoke from household use of solid fuels [3.0 percent]), unsafe sex (5.8 percent), and risk factors for noncommunicable diseases (for example, high blood pressure [5.6 percent], smoking [3.9 percent], and alcohol use [3.6 percent]). Across high-income countries, risk factors associated with Group II and Group III conditions were the leading causes of loss of healthy life (smoking [12.7 percent], high blood pressure [9.3 percent], overweight and obesity [7.2 percent], high cholesterol [6.3 percent], and alcohol use [4.4 percent]).

An estimated 45 percent of global mortality and 36 percent of the global burden of disease were attributable to the joint hazards of the 19 selected global risk factors. The joint hazards were even larger in regions where a relatively small number of diseases and their risk factors were responsible for large losses of life (HIV/AIDS and risk factors for child mortality in Sub-Saharan Africa; cardiovascular risks, including smoking and alcohol use in Europe and Central Asia). Globally, large fractions of major diseases such as diarrhea, lower respiratory infections, HIV/AIDS, lung cancer,

Table 1.2 Deaths and Burden of Disease Attributable to Risk Factors—Low- and Middle-Income Countries, High-Income Countries, and World, 2001

	Low- and middle-income		High-income		World	
	Deaths	**DALYs(3,0)[a]**	**Deaths**	**DALYs(3,0)[a]**	**Deaths**	**DALYs(3,0)[a]**
Total number (thousands)	**48,351**	**1,386 709**	**7,891**	**149,161**	**56,242**	**1,535 871**
Rate per 1,000 population	**9.3**	**265.7**	**8.5**	**160.6**	**9.1**	**249.8**
Age-standardized rate per 1,000[b]	**11.4**	**281.7**	**5.0**	**128.2**	**10.0**	**256.5**
Risk factor			*Number in thousands (percent)*			
Childhood and maternal undernutrition						
Childhood underweight	3,630 (7.5)	120,579 (8.7)	0 (0.0)	67 (<0.1)	3,630 (6.5)	120,647 (7.9)
Iron-deficiency anemia	613 (1.3)	23,933 (1.7)	8 (0.1)	789 (0.5)	621 (1.1)	24,722 (1.6)
Vitamin A deficiency	800 (1.7)	24,686 (1.8)	0 (0.0)	0 (0.0)	800 (1.4)	24,686 (1.6)
Zinc deficiency	849 (1.8)	27,631 (2.0)	0 (0.0)	5 (<0.1)	849 (1.5)	27,636 (1.8)
Other nutrition-related risk factors and physical activity						
High blood pressure	6,223 (12.9)	78,063 (5.6)	1,392 (17.6)	13,887 (9.3)	7,615 (13.5)	91,950 (6.0)
High cholesterol	3,038 (6.3)	42,815 (3.1)	842 (10.7)	9,431 (6.3)	3,880 (6.9)	52,246 (3.4)
Overweight and obesity	1,747 (3.6)	31,515 (2.3)	614 (7.8)	10,733 (7.2)	2,361 (4.2)	42,248 (2.8)
Low fruit and vegetable intake	2,308 (4.8)	32,836 (2.4)	333 (4.2)	3,982 (2.7)	2,641 (4.7)	36,819 (2.4)
Physical inactivity	1,559 (3.2)	22,679 (1.6)	376 (4.8)	4,732 (3.2)	1,935 (3.4)	27,411 (1.8)
Addictive substances						
Smoking	3,340 (6.9)	54,019 (3.9)	1,462 (18.5)	18,900 (12.7)	4,802 (8.5)	72,919 (4.7)
Alcohol use	1,869 (3.9)	49,449 (3.6)	24 (0.3)	6,580 (4.4)	1,893 (3.4)	56,029 (3.6)
Illicit drug use	189 (0.4)	7,890 (0.6)	37 (0.5)	2,024 (1.4)	226 (0.4)	9,914 (0.6)
Sexual and reproductive health						
Unsafe sex	2,819 (5.8)	80,270 (5.8)	32 (0.4)	909 (0.6)	2,851 (5.1)	81,179 (5.3)
Non-use and use of ineffective methods of contraception	162 (0.3)	7,411 (0.5)	0 (0.0)	23 (<0.1)	162 (0.3)	7,434 (0.5)
Environmental risks						
Unsafe water, sanitation, and hygiene	1,563 (3.2)	51,622 (3.7)	4 (<0.1)	289 (0.2)	1,567 (2.8)	51,911 (3.4)
Urban air pollution	735 (1.5)	8,707 (0.6)	76 (1.0)	664 (0.4)	811 (1.4)	9,371 (0.6)
Indoor smoke from household use of solid fuels	1,791 (3.7)	41,731 (3.0)	0 (0.0)	2 (<0.1)	1,791 (3.2)	41,734 (2.7)
Other selected risks						
Contaminated injections in health care setting	407 (0.8)	8,974 (0.6)	4 (<0.1)	76 (<0.1)	412 (0.7)	9,050 (0.6)
Child sexual abuse	65 (0.1)	5,381 (0.4)	6 (<0.1)	699 (0.5)	71 (0.1)	6,079 (0.4)
All selected risk factors together	22,014 (45.6)	500,066 (36.1)	3,473 (44.0)	51,092 (34.3)	25,488 (45.3)	551,158 (35.9)

Source: Chapter 4. Note that mortality and disease burden attributable to individual risk factors cannot be added due to multi-causality. See Chapter 4 for details.
a. (some footnote as Table 1.1)
b. Age-standardized using the WHO World Standard Population

chronic obstructive pulmonary disease, ischemic heart disease, and stroke were attributable to the joint effects of the risk factors considered in this volume. The joint hazards of these 19 risks for a number of other important diseases and injuries, such as perinatal and maternal conditions, selected other cancers, and intentional and unintentional injuries, which have more diverse risk factors, were smaller, but non-negligible. The relatively small number of risk factors that account for a large fraction of the disease burden underscores the need for policies, programs, and scientific research to take advantage of interventions for multiple major risks to health (Ezzati and others 2003).

CONCLUSIONS

The substantial scientific and policy interest in the methods and findings of the 1990 GBD study, the widespread application of the methods by countries at all levels of health development, and the adoption of the framework as the preferred method for health accounting by international health agencies such as the World Health Organization attest to the critical need for objective and systematic assessments of the disease burden for priority setting in health. The vast and comprehensive effort to quantify the disease burden worldwide dramatically changed views about the

importance of some conditions, particularly psychiatric disorders, and drew global public health attention to the unrecognized burden of injuries. The methodological developments over the past decade, a more systematic approach to collecting key data and research findings on the health of populations, and the results of numerous national and subnational burden of disease studies have dramatically improved the methodological armamentarium and the empirical base for disease burden assessment, in particular, the comparability of the estimated contributions of diseases, injuries, and risk factors to this burden.

As reported in this volume, the 2001 GBD study provides a comprehensive update of the comparative importance of diseases, injuries, and risk factors for global health. The study incorporates a range of new data sources to develop internally consistent estimates of incidence, prevalence, severity and duration, and mortality for 136 major causes by sex and by eight age groups. Estimates of deaths by cause, age, and sex were carried out separately for 226 countries and territories, drawing on a total of 770 country-years of death registration data, 535 additional sources of information on levels of child and adult mortality, and more than 2,600 data sets providing information on specific causes of death in regions not well covered by death registration systems. Together with the more than 8,500 data sources (epidemiological studies, disease registers, notifications systems, and so on) used to estimate incidence, prevalence, and YLD by cause, the 2001 GBD study has incorporated information from more than 10,000 datasets relating to population health and mortality (see chapter 3). This represents one of the largest syntheses of global information on population health carried out to date.

Much of the research on the burden of disease undertaken over the past decade or so has relied on the methodological and empirical efforts that defined the 1990 GBD study as a major advance in global public health statistics. Progress in updating the epidemiological basis for assessing the disease burden from the various diseases and injuries of interest has been uneven, although improvements in the data and methods available for assessing global and regional mortality by cause have been substantial, and some advances have been made in the data for, and epidemiological understanding of some major causes of ill health such as HIV/AIDS and diabetes mellitus. Nevertheless, making more reliable estimates of global, regional, and national disease burdens still faces many methodological and empirical challenges. The substantive agenda, mapped out over a decade ago (Murray, Lopez and Jamison, 1994) remains equally valid today and needs to be addressed more systematically if the burden of disease framework is to gain greater acceptance as *the* international tool for health accounting.

Assessing and documenting in detail the state of the world's health at the beginning of the millennium is a useful undertaking. This volume will provide scholars today and in the future with a definitive historical record of the leading causes of the burden of disease for major regions of the world at the start of the 21st century. An account of global health at the beginning of the 20th century, or earlier, would no doubt have been of more than just historical interest, but given the methods of scientific interchange and the state of scientific and methodological knowledge at the time, this was impossible.

In presenting the comprehensive findings of the 2001 GBD study, this volume is, in many respects, a culmination of the effort launched in 1990 and represents the end of the beginning of global disease burden assessments. The widespread use of disease burden concepts by national and international bodies since the first results were published and the heightened interest in improving the basic descriptive epidemiology of diseases, injuries, and risk factors by both countries and agencies has laid the foundations for future population health assessments. As programs and policies to improve health worldwide become more widespread, so too will the need for more comprehensible, credible, and comparable assessments to periodically monitor world health and the success, or otherwise, of measures to promote health and reduce the burden of disease. New initiatives, and perhaps new global institutions, are required to measure the burden of disease worldwide and how it is changing, more reliably than hitherto. This book provides the baseline against which such progress with global health development will be measured.

REFERENCES

Anand, S., and K. Hanson. 1998. "DALYs: Efficiency Versus Equity." *World Development* 26 (2): 307–10.

Barendregt, J. J., G. J. van Oortmarssen, T. Vos, and C. J. L. Murray. 2003. "A Generic Model for the Assessment of Disease Epidemiology: The Computational Basis of DisMod II." *Population Health Metrics* 1 (1): e4.

Baskent University. 2005. *Burden of Disease Final Report*. Ankara, Turkey: Baskent University and the School of Public Health, Refik Saydam Hygiene Center, Ministry of Health.

Bradshaw, D., P. Groenewald, R. Laubscher, N. Nannan, B. Nojilana, R. Norman, D. Pieterse, M. Schneider, D. E. Bourne, I. M. Timaeus, R. Dorrington, and L. Johnson. 2003. *Initial Burden of Disease Estimates for South Africa, 2000.* Cape Town: South African Medical Research Council. http://www.mrc.ac.za/bod/bod.htm.

Bundhamcharoen, K., Y. Teerawatananon, T. Vos, and S. Begg. 2002. *Burden of Disease and Injuries in Thailand: Priority Setting for Policy*. Bangkok: Ministry of Public Health.

Choprapawon, C., Y. Porapakkham, O. Sablon, R. Panjajaru and B. Jhantharatat. 2005. "Thailand's National Death Registration Reform: Verifying the Causes of Death between July 1997 and December 1999." *Asia-Pacific Journal of Public Health* 17 (2): 110–116.

Cooper, R. S., B. Osotimehin, J. S. Kaufman, and T. Forrester. 1998. "Disease Burden in Sub-Saharan Africa: What Should We Conclude in the Absence of Data?" *Lancet* 351 (9087): 208–10.

Dempsey, M. 1947. "Decline in Tuberculosis: The Death Rate Fails to Tell the Entire Story." *American Review of Tuberculosis* 56 (2): 157–64.

Doll, R., and R. Peto. 1981. *The Causes of Cancer*. Oxford, U.K.: Oxford University Press.

Eastern Stroke and Coronary Heart Disease Collaborative Research Group. 1998. "Blood Pressure, Cholesterol, and Stroke in Eastern Asia." *Lancet* 352 (9143): 1801–7.

Eisner, R. 1989. *The Total Incomes System of Account*. Chicago and London: University of Chicago Press.

Ezzati, M., A. D. Lopez, A. Rodgers, and C. J. L. Murray. 2004. *Comparative Quantification of Health Risks: The Global and Regional Burden of Disease Attributable to Selected Major Risk Factors*. Geneva: World Health Organization.

Ezzati, M., A. D. Lopez, A. Rodgers, S. Vander Hoorn, C. J. L. Murray, and the Comparative Risk Assessment Collaborating Group. 2002. "Selected Major Risk Factors and Global and Regional Burden of Disease." *Lancet* 360 (9343): 1347–60.

Ezzati, M., S. Vander Hoorn, A. Rodgers, A. D. Lopez, C. D. Mathers, C. J. L. Murray, and the Comparative Risk Assessment Collaborating Group. 2003. "Estimates of Global and Regional Potential Health Gains from Reducing Multiple Major Risk Factors." *Lancet* 362 (9380): 271–80.

Ghana Health Assessment Project Team. 1981. "Quantitative Method of Assessing the Health Impact of Different Diseases in Less Developed Countries." *International Journal of Epidemiology* 10 (1): 73–80.

Hakulinen, T., H. Hansluwka, A. D. Lopez, and T. Nakada. 1986. "Global and Regional Mortality Patterns by Cause of Death in 1980." *International Journal of Epidemiology* 15 (2): 226–33.

Holman, C. D. J., B. K. Armstrong, L. N. Arias, C. A. Martin, W. M. Hatton, L. D. Hayward, M. A. Salmon, R. E. Shean, V. P. Waddell. 1990. *The Quantification of Drug Caused Morbidity and Mortality in Australia 1988*. Canberra: Commonwealth Department of Community Services and Health.

Hyder, A. A., G. Rotllant, and R. Morrow. 1998. "Measuring the Burden of Disease: Healthy Life Years." *American Journal of Public Health* 88 (2): 196–202.

Jamison, D. T., and J.-P. Jardel. 1994. "Comparative Health Data and Analyses." In *Global Comparative Assessments in the Health Sector: Disease Burden, Expenditures, and Intervention Packages*, ed. C. J. L. Murray and A. D. Lopez, v–vii. Geneva: World Health Organization.

Jamison, D. T., W. H. Mosely, A. R. Measham, and J. L. Bobadilla, eds. 1993. *Disease Control Priorities in Developing Countries*. New York: Oxford University.

Lopez, A. D. 1993. "Causes of Death in the Industrialized and Developing Countries: Estimates for 1985–1990." In *Disease Control Priorities in Developing Countries,* ed. Dean Jamison, W. Henry Mosely, A. R. Measham, and J. L. Bobadilla, 15–30. New York: Oxford University Press.

Lopez, A. D., and C. J. L. Murray. 1998. "The Global Burden of Disease, 1990–2020." *Nature Medicine* 4 (11): 1241–43.

Lopez, A. D., O. B. Ahmad, M. Guillot, B. D. Ferguson, J. A. Salomon, C. J. L. Murray, and K. Hill. 2002. *World Mortality in 2000: Life Tables for 191 Countries*. Geneva: World Health Organization.

Lozano, R., C. J. L. Murray, J. Frenk, and J. Bobadilla. 1995. "Burden of Disease Assessment and Health System Reform: Results of a Study in Mexico." *Journal for International Development* 7 (3): 555–64.

Mahapatra, P. 2002. *Estimating National Burden of Disease: The Burden of Disease in Andhra Pradesh, 1990s*. Hyderabad, India: Institute of Health Systems.

Mathers, C. D., T. Vos, and C. Stevenson. 1999. *The Burden of Disease and Injury in Australia*. Canberra: Australian Institute of Health and Welfare. http://www.aihw.gov.au/publications/index.cfm/title/5180.

Mathers, C. D., C. Stein, M. Ma Fat, C. Rao, M. Inoue, K. Shibuya, N. Tomijima, C. Bernard, and H. Xu. 2002. *The Global Burden of Disease 2000 Study (version 2): Methods and Results*. Discussion Paper 50. Geneva: Global Program on Evidence for Health Policy, World Health Organization. http://www.who.int/evidence.

McGinnis, J. M., and W. H. Foege. 1993. "Actual Causes of Death in the United States." *Journal of the American Medical Association* 270 (18): 2207–12.

McKenna, M. T., C. M. Michaud, C. J. L. Murray, and J. S. Marks. 2005. "Assessing the Burden of Disease in the United States Using Disability-Adjusted Life Years." *American Journal of Preventive Medicine* 28 (5): 415–23.

Murray, C. J. L. 1996. "Rethinking DALYs." In *The Global Burden of Disease,* ed. C. J. L. Murray and A. D. Lopez, 1–89. Cambridge, MA: Harvard University Press .

Murray, C. J. L., and A. D. Lopez. 1996a. "Evidence-Based Health Policy: Lessons from the Global Burden of Disease Study." *Science* 274 (5288): 740–43.

_____. 1996b. "Global and Regional Descriptive Epidemiology of Disability: Incidence, Prevalence, Health Expectancies, and Years Lived with Disability." In *The Global Burden of Disease,* ed. C. J. L. Murray and A. D. Lopez, 201–46. Cambridge, MA: Harvard University Press.

_____. 1996c. *Global Health Statistics: A Compendium of Incidence, Prevalence, and Mortality Estimates for over 200 Conditions*. Cambridge, MA: Harvard University Press.

_____, eds. 1996d. *The Global Burden of Disease,* vol. 1. Cambridge, MA: Harvard University Press.

_____. 1997a. "Global Mortality, Disability, and the Contribution of Risk Factors: Global Burden of Disease Study." *Lancet* 349 (9063): 1436–42.

_____. 1997b. "Mortality by Cause for Eight Regions of the World: Global Burden of Disease Study." *Lancet* 349 (9061): 1269–76.

_____. 1997c. "Regional Patterns of Disability-Free Life Expectancy and Disability-Adjusted Life Expectancy: Global Burden of Disease Study." *Lancet* 349 (9062): 1347–52.

_____. 1999. "On the Comparable Quantification of Health Risks: Lessons from the Global Burden of Disease Study." *Epidemiology* 10 (5): 594–605.

Murray, C. J. L., A. D. Lopez, and D. T. Jamison. 1994. "The Global Burden of Disease in 1990: Summary Results, Sensitivity Analyses, and Future Directions." *Bulletin of the World Health Organization* 72 (3): 495–508.

Murray, C. J. L., J. A. Salomon, C. D. Mathers, and A. D. Lopez. 2002. *Summary Measures of Population Health: Concepts, Ethics, Measurement, and Applications*. Geneva: World Health Organization.

Murray, C. J. L., A. Tandon, J. A. Salomon, C. D. Mathers, and R. Sadana. 2002. "New Approaches to Enhance Cross-Population Comparability of Survey Results". In *Summary Measures of Population Health: Concepts, Ethics, Measurement, and Applications*, ed. C. J. L. Murray, J. A. Salomon, C. D. Mathers, and A. D. Lopez, 421–32. Geneva: World Health Organization.

Murray, C. J. L., B. D. Ferguson, A. D. Lopez, M. Guillot, J. A. Salomon, and O.B. Ahmad. 2003. "Modified Logit Life Table System: Principles, Empirical Validation, and Application." *Population Studies* 57 (2): 165–82.

Parkin, D. M., P. Pisani, A. D. Lopez, and E. Masuyer. 1994. "At Least One in Seven Cases of Cancer Is Caused by Smoking: Global Estimates for 1985." *International Journal of Cancer* 59 (4): 494–504.

Peto, R., A. D. Lopez, J. Boreham, M. Thun, and C. Heath. 1992. "Mortality from Tobacco in Developed Countries: Indirect Estimates from National Vital Statistics." *Lancet* 339 (8804): 1268–78.

Rose, G. 1985. "Sick Individuals and Sick Populations." *International Journal of Epidemiology* 14 (1): 32–38.

Salomon, J. A., and C. J. L. Murray. 2002. "The Epidemiologic Transition Revisited: Compositional Models for Causes of Death by Age and Sex." *Population and Development Review* 28 (2): 205–28.

_____. 2004. "A Multimethod Approach to Measuring Health State Valuations." *Health Economics* 13: 281–90.

United States Department of Health and Human Services. 1992. *Smoking and Health in the Americas. Report of the Surgeon General, in Collaboration with the Pan-American Health Organization,* Department of Health and Human Services publication (CDC) 92-8419. Washington, DC: Office on Smoking and Health.

Vos, T., M. Tobias, H. Gareeboo, F. Roussety, S. Huttley, and C. J. L. Murray. 1995. *Mauritius Health Sector Reform, National Burden of Disease Study*, *Final Report of Consultancy*. Port Louis, Mauritius: Ministry of Health and Ministry of Economic Planning and Development.

Williams, A. 1999. "Calculating the Global Burden of Disease: Time for a Strategic Appraisal?" *Health Economics* 8 (1): 1–8.

World Bank. 1993. *Investing in Health: World Development Report 1993.* New York: Oxford University Press.

WHO (World Health Organization). 1996. *Investing in Health Research and Development. Report of the Ad Hoc Committee on Health Research Relating to Future Intervention Options.* Geneva: WHO.

_____. 2002. *Reducing Risks: Promoting Healthy Life. World Health Report 2002.* Geneva: WHO.