The global burden of disease, 1990–2020

The authors discuss the Global Burden of Disease Study and its role in setting priorities for improving international public health into the next century*.

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RELIABLE INFORMATION ON the nature and extent of the causes of disease, and how such patterns are changing, is of essential importance for public health, with uses ranging from priority setting in the health sector to the evaluation of interventions. Yet, as the twentieth century draws to a close, statistics on who dies of what are not available for large populations in many parts of the developing world, and even where they are available, they often suffer from problems in accuracy and comparability. Data on the incidence and prevalence of major diseases and injuries are even more difficult to assemble. Nonetheless, there are several sources of information on the health status of populations throughout the world, varying from complete vital registration to small-scale community research projects on a specific disease such as malaria. The challenge for public health has been to weave these disparate data sets of variable reliability and completeness into a global assessment of health conditions and the causes of disease and injury to guide public policy into the next century.

The Global Burden of Disease (GBD) Study[1–8], initiated in 1992, is a collaborative effort between the Harvard School of Public Health, the World Health Organization (WHO) and the World Bank that seeks to meet this challenge. Volumes I and II of the GBD series were published in 1996 (ref. 1) and Volume III, which uses the Study data sets to assess the health dimensions of sex and reproduction, was published in October this year[2]. The GBD Study has three specific aims:

1. To systematically incorporate information on non-fatal outcomes into the assessment of health status (using a time-based measure of healthy years of life lost due either to premature mortality or to years lived with a disability, weighted by the severity of that disability)

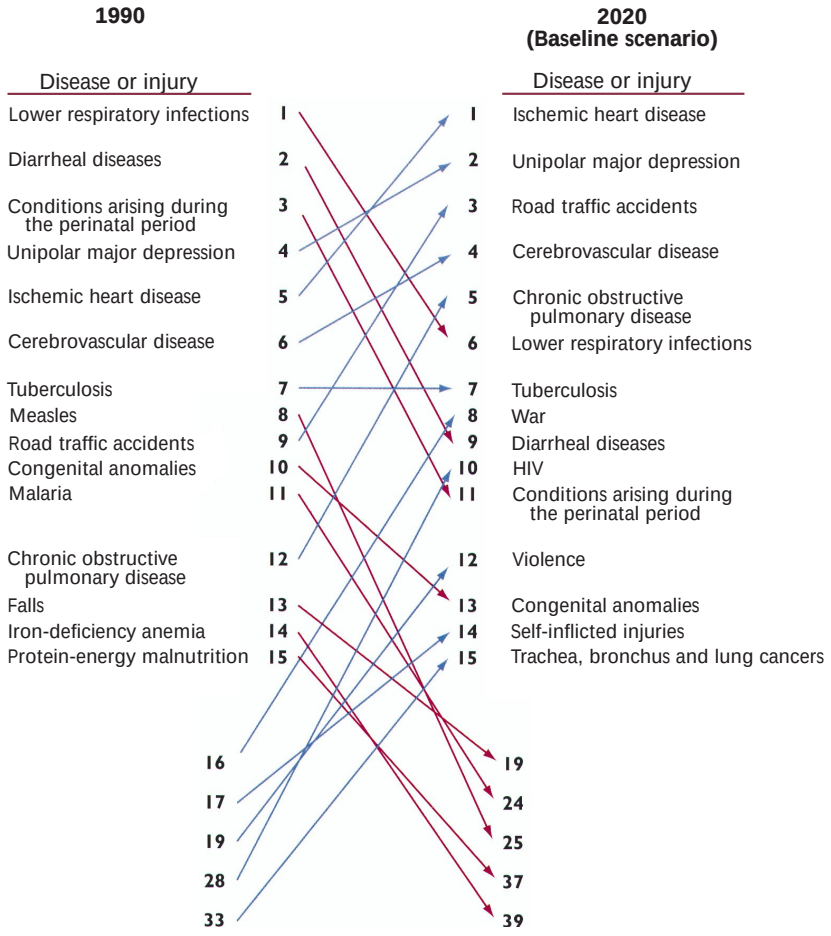
2. To ensure that all estimates and projections were derived on the basis of objective epidemiological and demographic methods, which were not influenced by advocates

3. To measure the burden of disease using a metric that could also be used to assess the cost-effectiveness of interventions. The metric chosen was Disability-Adjusted Life Years, or DALYs (ref.3).

As volumes I and II report, approximately 50 million people are estimated to have died in 1990; 75 percent of them in developing regions of the world[1]. About one in three deaths worldwide still occur from communicable, maternal, perinatal or nutritional causes (labelled as Group I causes in the Study), virtually all of them in the developing world. The 'unfinished agenda' to reduce premature mortality from such causes, mostly associated with poverty, remains a priority for public health policy, particularly because most of these Group I deaths occur among infants and young children. Yet even in 1990, non-communicable diseases (Group II) caused more deaths in the developing world than did Group I causes. The extent of this 'epidemiological transition' varied from region to region, being more pronounced in China and Latin America than in India and sub-Saharan Africa. Almost all deaths (86 percent) in developed countries now occur from non-communicable diseases, although the contribution from injuries (7–8 percent) is substantial, as it is in the developing world (10–11 percent).

Ischemic heart disease is the leading cause of death in developed countries (2.7 million deaths in 1990), followed by stroke (1.4 million) and lung cancer (0.5 million). Only one Group I cause (lower respiratory infections) ranks in the top ten causes in these countries. On the other hand, lower respi-

Change in the rank order of disease burden for 15 leading causes worldwide, 1990–2020 (as measured by DALYS)



*Based in part on the Leverhulme lecture presented by Alan Lopez to the Liverpool School of Tropical Medicine.

ratory infections caused 10 percent of deaths in developing regions in 1990. Group I causes dominated the list of leading public health problems in developing countries, with diarrheal diseases (2.9 million), perinatal conditions (2.4 million), tuberculosis (1.9 million), measles (1.1 million) and malaria (0.9 million) all ranking among the top ten causes of death. Yet, perhaps somewhat surprisingly, ischemic heart disease and stroke were the second and third leading causes of death in developing regions in 1990, causing an estimated 3.6 and 3.0 million deaths, respectively. Road traffic accidents (0.8 million deaths) were also among the leading causes in developing countries, as they were (eighth rank, 0.2 million deaths) in rich countries.

The regional pattern of age-specific risks of death highlights the extent of inequality in survival prospects in the world today. Thus in sub-Saharan Africa, a newborn infant has a 20–25 percent chance of dying before reaching adulthood (age 15), compared with 1–2 percent in the industrialized world. Almost all of this excess risk is due to Group I causes. These inequalities persist into adulthood as well. A 15-year-old male in sub-Saharan Africa has an almost 40 percent chance of dying before age 60 (based on 1990 death rates), compared with a 14 percent risk for men in countries with established market economies. This comparison emphasizes the extraordinary reversal in survival that characterized public health conditions in Russia and neighboring countries in the early 1990s. Indeed, men living in the former socialist countries of Europe, on average, have a 28 percent chance of dying between 15 and 60 years of age, double that of industrialized countries and higher than the risk estimated for any developing region with the single exception of sub-Saharan Africa. This remarkable excess risk of death is not apparent for women in these countries, and is largely attributable to high death rates from non-communicable diseases and injuries.

One of the strengths of the GBD Study is that it focuses attention on conditions that are the chief causes of disability (see Table). These are generally very different from leading causes of death and have been mostly ignored in debates about public health priorities. The massive but largely unrecognized burden of mental illness is obvious, with neuropsychiatric disorders filling five of the top ten causes of disability. Alcohol use was the leading cause of disability in men in developed countries and, somewhat surprisingly, the fourth largest cause of disablement among men in developing regions. The importance of alcohol use as a global public health problem is obscured by limiting attention to mortality alone, because the cardioprotective effects in some (mainly developed) populations probably prevent as many deaths as alcohol use causes, albeit at much older ages[9].

Table The leading causes of disability worldwide, 1990

(As measured by years of life lived with a disability, YLD)	Total YLDs (millions)	Percent of total
All causes	472.7	
1. Unipolar major depression	50.8	10.7
2. Iron-deficiency anemia	22.0	4.7
3. Falls	22.0	4.6
4. Alcohol use	15.8	3.3
5. Chronic obstructive pulmonary disease	14.7	3.1
6. Bipolar disorder	14.1	3.0
7. Congenital anomalies	13.5	2.9
8. Osteoarthritis	13.3	2.8
9. Schizophrenia	12.1	2.6
10. Obsessive-compulsive disorders	10.2	2.2

How are these patterns of death and disability likely to change as we enter the twenty first century? The GBD study also included an attempt to project death and DALYs based on a relatively simple model of how 'distal' determinants of health, such as education and wealth, affect the trajectory of specific conditions, with the inclusion of a smoking intensity variable to reflect the emergence of chronic disease epidemics and time as a variable to incorporate the effects of technological advances such as immunization and gains in knowledge. Three scenarios were developed, called 'optimistic,' 'pessimistic' and 'baseline', reflecting different assumptions about the predicted values of these variables. According to the 'baseline' assumptions, average life expectancy is predicted to increase from 73 years in 1990 to 78 years in 2020 for males in industrialized countries, and from 81 years to 88 years for females. Similar, if not larger gains are projected for all other regions with the single exception of the former socialist countries of Europe for which male life expectancy in 2020 is projected to be identical to that in 1990 (refs. 10, 11).

In terms of the leading causes of disease burden, several changes in ranking are foreseen (see Fig.). With development, the leading contributors to disease burden from Group I (lower respiratory diseases, diarrheal diseases and perinatal conditions) are projected to decline in relative importance, as are measles, malaria and nutritional disorders. By 2020, based on current trends, ischemic heart disease will be the leading cause of disease burden worldwide, followed by depression, road traffic accidents, stroke and chronic obstructive lung disease. HIV, which in 1990 was estimated to be the thirty-third leading cause of DALYs worldwide, will be among the top ten leading causes by 2020. Reproductive health risks accounted for 2–4 percent of all deaths in 1990 (contributing 5–15 percent of the overall disease burden) and are predicted to remain unchanged into the year 2000, presenting a formidable public health challenge[2].

Tobacco use is projected to vastly increase as a source of disease burden over the next few decades. Tobacco is a cause of several diseases, some of them of major public health importance, and currently kills about 3.5 million people each year[11]. Most of those who will die from tobacco are smokers today, and if they cannot be convinced to quit in large numbers, tobacco will cause between eight and nine million deaths in 2020 (and about 120 million DALYs), making it by far the largest cause of disease burden worldwide. Moreover, much of this massive increase in death and disability will occur in the developing world, where one in two men regularly smoke cigarettes.

The impact of the GBD Study

We feel that a number of features of and findings from the study have brought new perspectives on public health and encouraged debate. These include:

1) Greater attention by the international public health community to the importance of non-communicable diseases and mental health in all regions of the world

2) Widespread recognition of the importance of disability as a major source of disease and injury worldwide. The methods used in the Study to quantify disability continue to be improved (for example, the choice of disability weights is being re-examined through a European Disability Weights Project led by the Department of Public Health at Erasmus University, Rotterdam) and have stimulated ethical debate about measurement issues for non-fatal health outcomes

3) Better appreciation of the importance of major risk factors for human health through the comparative analysis of diseases and injuries provided by the Study. For

example, exposure to tobacco, alcohol and unsafe sex is estimated to have caused about the same amount of disease burden (2–3 percent each) as measles, malaria or tuberculosis. Before the study, this comparative assessment of diseases with risk factors was not available

4) Widespread application of GBD methods to estimate the national burden of disease; not only has this served to guide decisions in the health sector, but these studies have also resulted in methodological advances.

Future directions

Whereas the GBD Study has had some influence on thinking in the health sector, much remains to be done. From the point of view of methodological improvements, work has begun on developing better projection methods that more formally incorporate statistical uncertainty into the projections and make use of newer data sets. With a view to repeating the Study for the year 2000, an intensive effort has begun to collect cause of death data sets, which are being compiled using innovative surveillance techniques to reduce the still substantial uncertainty about global mortality patterns.

The WHO has begun the process of institutionalizing burden of disease methods through the creation of the new Global Programme on Evidence for Health Policy, within which the substantive agenda around improving and promoting these methods is being carried out. At the same time, WHO continues to support the dissemination of the methods and findings of the Study, with the publication of Volume III of the GBD series last month and Volumes IV and V expected to be published in early 1999.

1. Murray, C.J.L. & Lopez, A.D. (eds) The Global Burden of Disease. A comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. (GBD Series Vol. I. Harvard School of Public Health on behalf of the World Health Organization and the World Bank, Cambridge, Massachusetts, 1996).
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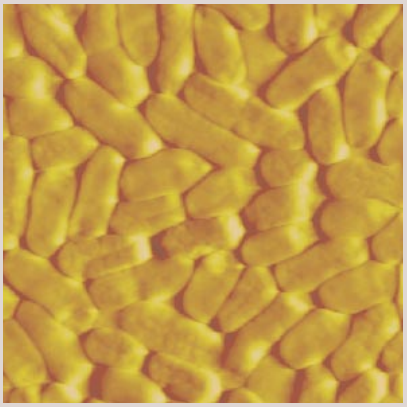
United they withstand

BACTERIA ARE ADEPT at adhering to surfaces. Worse still, adherent bacteria can unite to form biofilms that are refractory to antibiotic treatment. Particularly problematic are the biofilms formed by *Escherichia coli* and *Staphylococcus aureus* in foreign materials, such as catheters and joint prostheses, that have been introduced into patients. The first step in biofilm formation is the energetically favorable interactions between bacteria and an artificial surface, which bring the bacteria into sufficiently close proximity to enable them to form strong interactions. A recent paper by Razatos and colleagues (*Proc. Natl. Acad. Sci. USA* **95**, 11059–11064, 1998) establishes that atomic force microscopy can be used to investigate, in a quantitative manner, the long-range interactions between bacteria and different artificial surfaces.

Using this technology, which enables detection of forces in the piconewton range, the investigators showed that the non-specific interactions between the cantilever tip of the atomic force microscope and bacteria can be measured in terms of tip displacement. For example, a confluent lawn of *E. coli* spread on a thin surface (see photograph) slightly attracts the silicon nitride tip of the microscope. However, certain *E. coli* mutants, which have shorter outer membrane lipopolysaccharides, repel the cantilever tip. In each case, the degree of attraction or repulsion can be quantified and the conditions of the experiment altered—for example, by changing the salt concentration—to assess the contributions of different types of contacts (such as electrostatic or van der Waals interactions). There is a precedent for such energetic studies: atomic force microscopy has already been used to study intricate biological reactions, such as protein–ligand binding and DNA base pairing.

The information that this technique yields ranges from the very detailed—what types of interactions are involved—to the very practical—which materials attract particular strains of bacteria and which do not. Clearly, it may be more useful to study the interactions between bacteria and medically relevant materials, such as polystyrene or polymethylmethacrylate, than to investigate interactions with the silicon nitride tip of the microscrope. It is easy to coat the silicon tip with polystyrene, but other materials are not so amenable. To solve this problem, Razatos and co-workers devised a



protocol for coating the tip of the microscope with a confluent layer of bacteria instead of the test material. Using this approach, they were able to make reproducible measurements of tip displacement with respect to a variety of substrates. Now that these control studies with laboratory strains of *E. coli* have validated the technique, different bacterial species and clinical isolates can be tested with confidence. Moreover, this method should allow researchers to define in detail what governs both attractive and repulsive interactions of bacteria with the wide variety of materials used in medical devices.

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