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ESSENTIALS To make the best decisions to improve health, policymakers need reliable, up-to-date information on the major challenges facing their country. The Global Burden of Disease study facilitates this by providing comprehensive and scientifically rigorous estimates of the causes of death and illness across the globe. It examines a total of 84 risk factors and the amount of health loss attribut- able to each or combinations of them. Analysis over time reveals a shift from disease burden dominated by communicable, maternal, neonatal, and nutritional causes to a burden increasingly made up of noncommunicable diseases and injuries. By making compari- sons between countries or subnational units like states or coun- ties, the Global Burden of Disease can highlight areas of particular success or challenge, providing opportunities to examine what is working, or what is not. Introduction To improve health by making the best decisions, policymakers need reliable, up-to-date information on the major challenges facing their country. The Global Burden of Disease (GBD) is a large-scale en- terprise dedicated to expanding the quantitative evidence base for health by producing estimates of deaths, prevalence, and incidence by disease for all countries and by identifying the major risks that impinge on population health. The GBD study was created to provide comparable, compre- hensive, and scientifically rigorous estimates of the causes of death and illness across the globe and aims to answer the following ques- tions: What are the world's major health problems? How well is society addressing these problems? Additionally, how do we best dedicate resources to get the maximum impact in improving popu- lation health in the future? In the early 1990s, when the World Bank commissioned the ori- ginal GBD study, researchers were surprised to discover that the an- swers to these questions were elusive. For some parts of the world, data were sparse or nonexistent. In summing disease-specific mor- tality estimates by organizations whose mission was to combat a given disease, GBD researchers found a total that was considerably greater than the number of people, globally, who had actually died in a particular year. The GBD approach not only makes sure that deaths

attributed to different causes sum to the total number of deaths—it goes beyond mortality estimates and looks at causes of disability, or nonfatal con- ditions. Increasingly, around the world, people are living longer and are exposed to disease risks that are more common with increasing age. Examining disabling conditions, such as back pain, dementia, or diabetes is therefore more important than ever. With the diversity of health conditions facing different populations, having compar- able measurements is essential. The GBD approach allows policy- makers to directly compare the public health impact of diseases that often are fatal, such as cancers, and conditions that primarily disable, such as depression or anaemia. Underlying some of these conditions are risk factors including al- cohol and tobacco use, dietary factors, occupational exposures, and air pollution. The GBD 2017 study examined 84 risk factors and the amount of health loss attributable to each or combinations of them. This information can help decision-makers to identify opportunities to promote population health by preventive measures. After the original GBD study, disease burden estimates by world regions were produced on a regular basis in the 2000s by the World Health Organization. In 2007 the Institute for Health Metrics and Evaluation (IHME) was established at the University of Washington in Seattle with funding from the Bill & Melinda Gates Foundation to make these estimates by country and to regularly update esti- mates. IHME published a comprehensive update, the Global Burden of Diseases, Injuries, and Risk Factors Study 2010, in December 2012 in a dedicated issue of The Lancet. Since then, IHME has com- mitted to producing annual updates of these results for the whole time period from 1990s onward and for an increasing number of countries and subnational units such as the provinces of China and the states of India, Mexico, Brazil, and the United States. New risks, diseases, and their disabling outcomes are added based on policy interest. For instance, the GBD 2017 includes new estimates for type 1 and type 2 diabetes mellitus, and bullying victimization as a risk factor for depression and anxiety. Governments and funding partners want to maximize the im- pact of their healthcare spending. By pinpointing the leading causes 2.3 The Global Burden of Disease:
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 of health loss, including risk factors for diseases, GBD can guide how health services are planned and how resources are directed to diseases and risks. By making comparisons between countries or subnational units like states or provinces, GBD can highlight areas of particular success or challenge, providing opportunities to examine what is working, or what is not. Methods GBD quantifies health loss from hundreds of diseases, injuries, and risk factors. In order to achieve this, a large effort is made to col- lect all available data on deaths and the epidemiology of more than 300 diseases and injuries in 195 countries and territories, by age and sex, from 1990 to the present. This large-scale effort is coordinated by IHME. Health data for many countries are sparse, and they are often messy. Researchers at IHME with guidance from a global con- sortium of researchers—more than 3300 in over 140 countries—identify every possible source of data for a country or condition and work to gain access to them. Once in hand, the data are often ad- justed to account for known differences in measurements between data sources. The next step is synthesizing the data—taking what is known and making sense of it. Sophisticated statistical model- ling approaches are used to estimate health loss for every disease and country. Every estimate in GBD is estimated 1000 times over to account for the impact of uncertainty from sampling errors, meas- urement errors, and the choice of models. Causes of health loss are classified at a first level into three broad categories in the GBD: communicable, maternal, neonatal, and nutritional diseases; noncommunicable diseases; and injuries. The first of these encompasses diseases like HIV, tuberculosis, malaria, diarrhoea, lower

respiratory infections, iron-deficiency anaemia, and preterm birth complications. Noncommunicable diseases include heart disease, stroke, diabetes, cancer, depression, and asthma. Injuries range from self-harm (suicide) to road in- juries to animal bites. In order to account for death and disease, GBD uses the disability- adjusted life year (DALY). DALYs equal the sum of years of life lost to premature mortality and years lived with disability. To calculate years of life lost, a choice was made to set a norm for long life. This norm was set by looking at the lowest observed mortality rates at any given age in any population greater than five million. Years of life lost are computed as the remaining life expectancy if an indi- vidual had not died but continued to live at low risk of dying. This works out as almost 88 years of remaining 'ideal' life expectancy for an infant that has died, 39 years for someone who died at age 50, and still another 2.2 years for someone dying at age 100. It reflects an assumption that everyone, all over the world, deserves to live a long life in full health. Years lived with disability take into account the prevalence of disability in a population as well as its severity. To make more than 2500 disabling outcomes of diseases and injuries included in the GBD comparable, researchers mapped these into 234 homogenous 'health states' for which they wrote short lay descriptions of the main symptoms and functional limitations such as pain, inability to move, see, or hear, or changes in mood. These lay descriptions were put to over 60 000 respondents in country and internet surveys, each time in a randomly chosen pair, followed by the question 'who is the healthier'. From over half a million of these judgements, dis- ability weights were derived that indicate the relative severity of a health state as a number between 0 and 1. The disability weights in GBD vary from 0.003 for mild vision loss to 0.778 for a person with schizophrenia with fulminant psychosis. As we combine years of life lost (YLLs) and years lived with disability (YLDs) into the DALY measure by simple addition, it means that we equate the health loss experienced by 333 cases of mild vision loss and a little more than one person with schizophrenia in a year to a year of life lost due to a death. Another factor that is considered in creating GBD estimates is that the world's population is growing. An increase in the number of deaths from a particular disease, then, might simply be explained by the fact that there are more people alive who may then contract the disease. One way to account for these changes in population is to calculate rates of each condition, usually expressed as deaths or DALYs per 100 000 people. In some cases, an apparent increase is revealed as a decrease when considered this way. For example, in the Democratic Republic of Congo between 1990 and 2017, the number of deaths from tuberculosis increased by 45% but the rate of tuber- culosis deaths per 100 000 actually decreased by 32% over the same period. While the absolute burden in terms of number of people suf- fering from TB increased, the proportion of people in the population who are suffering actually decreased. The increase in the number of deaths from TB indicates to health service planners that they need to expand tuberculosis treatment resources even though the decline in rates indicates that the existing TB control measures may be having success. Age-standardizing also allows for more accurate comparison across countries and time frames. This technique applies observed age-specific rates of a condition to a standard age distribution and avoids distortion when one population is older or younger than another. Results GBD 2017 generated 38 billion data points. In order to make these results more accessible to researchers, policymakers, students, health workers, journalists, and others, IHME created a group of interactive data visualization tools that allow people to explore health trends for different countries and regions. One of these, GBD Compare, shows numbers and rates of deaths, YLLs, YLDs, and DALYs by dis- eases and risk factors. The main view is a 'tree map', which is basic- ally a square pie chart showing the proportional distribution of the overall burden by underlying causes. Additional views can be added showing a map of the world, time plots, age plots, and ranking lists. Each can interactively be

explored by country, age, sex, year, cause, or risk factor. They can be found at https://vizhub.healthdata.org/ gbd-compare/. Looking at global patterns in causes of death and disability over time reveals a shift from disease burden dominated by communic- able, maternal, neonatal, and nutritional causes (shown in red) to a burden increasingly made up of noncommunicable diseases (blue) and injuries (green, Fig. 2.3.1). This pattern has been partly driven by improvements in healthcare and greater access to vaccines and life-saving medical interventions that contributed to healthcare

 successes, such as the nearly 90% decrease in health loss from mea- sles and tetanus globally between 1990 and 2017. Meanwhile, heart disease, stroke (intracerebral haemorrhage and ischaemic stroke), type 2 diabetes, low back pain, and chronic obstructive pulmonary disease (COPD) climbed in ranking over this period to occupy 6 of the top-10 slots for causes of DALYs (per 100 000). The rise in noncommunicable diseases can be explained by sev- eral factors. Economic development has propelled some countries from low- to middle-income status, often bringing improvements in healthcare, water quality and sanitation, and living conditions. At the same time, as countries gain higher economic status, air pollu- tion may increase, and changes in diet and levels of physical activity typically occur. Factors like these have led to an epidemiologic tran- sition away from communicable, maternal, neonatal, and nutritional disorders and towards a much greater burden of noncommunicable diseases. The exception to this trend has been the HIV/AIDS epi- demic: in 1990, HIV/AIDS caused the 39th-highest rate of deaths (per 100 000) globally. In 2005, at the peak of the epidemic, this rank had jumped to fifth place, and by 2017 it had dropped to 13th due to increased access to antiretroviral treatment. Greater economic development has also led to a demographic transition, meaning that birth and death rates, typically high in low- income countries, decreased as industrialization occurred. This re- sults in population growth, as death rates decrease faster than birth rates, and later, population ageing. Policymakers must plan for the results of these changes by expanding health services and antici- pating the need to care for the changing spectrum of prevalent dis- eases and comorbidities that are more common at older ages. At the regional and country levels, more variation can be seen. High-income countries, including the United States, Australia, Western Europe, and Japan, exhibit a disease burden dominated by noncommunicable diseases. Life expectancy in these countries is typically high: between 78 and 84 years for both sexes combined in 2017 (Fig. 2.3.2), and the leading causes of health loss are all non- communicable diseases: ischaemic heart disease, low back pain, lung cancer, COPD, and Alzheimer’s disease and other dementias are the top five. By contrast, life expectancy in sub-Saharan Africa ranged from 52 to 71 years; this region also has the greatest burden of communicable diseases including malaria, diarrheal diseases, HIV/AIDS, and tuberculosis among the top ten causes of DALYs Leading causes 1990 Leading causes 2017 1 Lower respiratory infections 1 Ischaemic heart disease 2 Diarrhoeal diseases 2 Lower respiratory infections 3 Preterm birth complications 3 COPD 4 Ischaemic heart disease 4 Diarrhoeal diseases 5 Neonatal encephalopathy 5 Preterm birth complications 6 COPD 6 Low back pain 7 Drug-susceptible tuberculosis 7 Intracerebral haemorrhage 8 Measles 8 Diabetes type 2 9 Malaria 9 Neonatal encephalopathy 10 Intracerebral haemorrhage 10 Ischaemic stroke 11 Other neonatal disorders 11 Migraine 12 Low back pain 12 Malaria 13 Protein-energy malnutrition 13 HIV/AIDS other 14 Drowning 14 Lung cancer 15 Ischaemic stroke 15 Drug-susceptible tuberculosis 16 Congenital heart anomalies 16 Falls 17 Self-harm by other means 17 Age-related hearing loss 18 Dietary iron deficiency 18 Major depression 19 Migraine 19 Other neonatal disorders 20 Pedestrian road injuries

20 Self-harm by other means 23 Dietary iron deficiency 22 Falls 27 Pedestrian road injuries 23 Lung cancer 29 Congenital heart anomalies 26 Diabetes type 2 36 Drowning 28 Major depression 38 Protein-energy malnutrition 30 Age-related hearing loss 73 Measles 38 HIV/AIDS other Cause type: Communicable, maternal, neonatal, and nutritional Noncommunicable Injuries Fig. 2.3.1 Top 20 causes of DALYs per 100 000 globally, both sexes, all ages, 1990 and 2017.

46 SECTION 2 Background to medicine <55 55-59 60-64 65-69 70-74 75-79 ≥80 Caribbean LCA DMA ATG TTO GRD VCT TLS MDV BRB SYC MUS COM Persian Gulf W Afr E Med MLT SGP Balkan Peninsula TON WSM FSM KIR FJI VUT SLB MHL Fig. 2.3.2 Life expectancy at birth, both sexes, 2017. (ATG, Antigua and Barbuda; VCT, St Vincent and the Grenadines; BRB, Barbados; COM, the Comoros; DMA, Dominica; E Med, Eastern Mediterranean; FJI, Fiji; FSM, Federated States of Micronesia; GRD, Grenada; KIR, Kirbati; MDV, Maldives; MHL, Marshall Islands; MLT, Malta; MUS, Mauritius; LCA, St Lucia; SGP, Singapore; SLB, Solomon Islands; SYC, Seychelles; TON, Tonga; TTO, Trinidad and Tobago; TLS, Timor Leste; VUT, Vanuatu; W Afr, West Africa; WSM; Western Samoa.)

2.3 The Global Burden of Disease: Measuring the health of populations 47 lost in 2017. Preterm birth complications, protein-energy malnutri- tion, neonatal encephalopathy from birth trauma and asphyxia, and neonatal sepsis were also among the top 10 causes of health loss in sub-Saharan Africa in 2017. Between 1990 and 2017, the absolute number of deaths from most causes increased (Fig. 2.3.3). For example, cardiovascular disease caused 11.9 million deaths in 1990 and 17.8 million in 2017, a 50% increase (Fig. 2.3.3). Looking at the numbers of DALYs, mental dis- orders were responsible for 82 million DALYs in 1990 and 123 mil- lion in 2017, a 50% increase (Fig. 2.3.4). In terms of age-standardized rates, however, deaths from cardiovascular disease dropped by 30% over this period, and DALY rates from mental and substance abuse disorders changed marginally by 1.7%. The explanation for this dif- ference is that cardiovascular deaths mainly occur in older people. Despite a drop in the age-by-age rates of disease, population ageing is causing the number of deaths to increase. In the case of mental disorders, the rates of disease have not changed much over time and the increase in DALY numbers is largely due to the increase in the world population size. China, in the period 1990 to 2017, provides a clear example of the epidemiological transition. In 1990, the top 10 causes of DALYs per 100 000 included two neonatal conditions along with lower re- spiratory infections and diarrheal diseases (Fig. 2.3.5). By 2017, however, all of the top-10 causes were noncommunicable diseases, including ischaemic heart disease, stroke, diabetes, lung cancer, stomach cancer, low back and neck pain, and age-related hearing loss. Injuries follow a less predictable pattern as countries move through the epidemiological transition. In this example of China, the decrease in DALY rates from drowning, by 79%, and suicide by means other than firearms, by 67%, were remarkable. Risk factors have undergone a similar transition globally. In 1990, the top five risks, in terms of rates of DALYs, were child wasting, short gestation, low birth weight, smoking, and high blood pres- sure. Twenty-seven years later, short gestation had dropped to number five, while high blood pressure had taken over the number- one ranking. Smoking, high fasting plasma glucose, and high body mass index came in at numbers two, three, and four, respectively (Fig. 2.3.6). This trend in risk factors reflects the epidemiological transition, where more health loss now results from poor diets and overweight and obesity than inadequate nutrition. Deaths and DALYs related to smoking have increased in countries like Bangladesh and Indonesia but have decreased in most high-income countries. A notable exception to these trends is sub-Saharan Africa, where many countries continue to experience a large burden of com- municable, neonatal, and nutritional conditions. In 1990, these

made up all of the ten highest-ranked diseases in terms of DALYs per 100 000. By 2017, a few prominent changes had occurred: HIV/AIDS shot to number four, and measles dropped from 4th place to 18th, but the leading causes remained the same: lower respiratory infections, malaria, diarrheal diseases, HIV/AIDS, neo- natal encephalopathy, preterm birth complications, tuberculosis, protein-energy malnutrition, and neonatal sepsis. Trends in risk factors diverge from most other regions as well, with childhood wasting at the top of the list, followed by short gestation, low birth weight, unsafe sex, unsafe water, and unsafe sanitation. These find- ings underscore the continuing need for health services focused on communicable diseases and maternal and child health, as well as infrastructure for clean water and sanitation in sub-Saharan Africa (Fig. 2.3.7). 0 10M 20M 30M 40M 50M 60M 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 Year Deaths in millions Cause of death HIV/AIDS and sexually transmitted infections Respiratory infections and tuberculosis Enteric infections Neglected tropical diseases and malaria Other infectious diseases Maternal and neonatal disorders Nutritional deficiencies Neoplasms Cardiovascular diseases Chronic respiratory diseases Digestive diseases Neurological disorders Mental disorders Substance use disorders Diabetes and kidney diseases Skin and subcutaneous diseases Musculoskeletal disorders Other noncommunicable diseases Transport injuries Unintentional injuries Self−harm and interpersonal violence Fig. 2.3.3 Global number of deaths by cause, both sexes, all ages, 1990–2017.

 Epidemiological trends in disease burden are best identified by examining rates of deaths and DALYs; however, the absolute number of people dying and suffering from various conditions also informs healthcare needs. The distribution of medical specialties might need to shift to accommodate changes in population and in the leading causes of death and illness. A decreasing burden of childhood illnesses would mean less need for paediatricians and children’s hospitals over time. Larger numbers of elderly people Leading causes 1990 Leading causes 2017 1 Lower respiratory infections 1 Ischaemic heart disease 2 COPD 2 Intracerebral haemorrhage 3 Intracerebral haemorrhage 3 COPD 4 Preterm birth complications 4 Ischaemic stroke 5 Ischaemic heart disease 5 Lung cancer 6 Drowning 6 Diabetes type 2 7 Neonatal encephalopathy 7 Neck pain 8 Self-harm by other means 8 Age-related hearing loss 9 Diarrhoeal diseases 9 Stomach cancer 10 Ischaemic stroke 10 Low back pain 18 Preterm birth complications 13 Stomach cancer 21 Neonatal encephalopathy 15 Lung cancer 23 Lower respiratory infections 16 Low back pain 26 Self-harm by other means 19 Neck pain 28 Drowning 21 Age-related hearing loss 78 Diarrhoeal diseases 29 Diabetes type 2 Cause type: Communicable, maternal, neonatal, and nutritional Noncommunicable Injuries Fig. 2.3.5 Leading causes of DALYs per 100 000, both sexes, all ages, China, 1990 and 2017. 0 500M 1B 1.5B 2B 2.5B 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 Year DALYs in billions Cause of DALY HIV/AIDS and sexually transmitted infections Respiratory infections and tuberculosis Enteric infections Neglected tropical diseases and malaria Other infectious diseases Maternal and neonatal disorders Nutritional deficiencies Neoplasms Cardiovascular diseases Chronic respiratory diseases Digestive diseases Neurological disorders Mental disorders Substance use disorders Diabetes and kidney diseases Skin and subcutaneous diseases Sense organ diseases Musculoskeletal disorders Other noncommunicable diseases Transport injuries Unintentional injuries Self−harm and interpersonal violence Fig. 2.3.4 Global number of DALYs by cause, both sexes, all ages, 1990–2017.

2.3 The Global Burden of Disease: Measuring the health of populations 49 Occupational injury Low physical activity Lead Vitamin A deficiency Low omega−3 Child underweight Iron deficiency Low vegetables Secondhand smoke Handwashing Unsafe sanitation Drug use Low nuts and seeds Unsafe sex Household air pollution Impaired kidney function Unsafe water Low fruit High sodium Low whole grains Ambient particulate matter Child wasting High LDL Alcohol use Low birth weight Short gestation High body mass index High fasting plasma glucose Smoking High blood pressure 0 500 1k 1.5k 2k 2.5k DALYs per 100 000 Risk factor Cause of DALY HIV/AIDS and sexually transmitted infections Respiratory infections and tuberculosis Enteric infections Other infectious diseases Maternal and neonatal disorders Nutritional deficiencies Neoplasms Cardiovascular diseases Chronic respiratory diseases Digestive diseases Neurological disorders Mental disorders Substance use disorders Diabetes and kidney diseases Sense organ diseases Musculoskeletal disorders Other noncommunicable diseases Transport injuries Unintentional injuries Self−harm and interpersonal violence Fig. 2.3.6 Leading risk factors in terms of DALYs per 100 000, both sexes, all ages, 2017. with noncommunicable diseases will require expansion of specialty care for conditions affecting this population, including neurologists, geriatricians, and elder care facilities. Subnational studies, which are done at the state or province level, provide an even more granular level of detail, revealing greater disparities within countries than between neighbouring countries and allowing decision-makers to implement more targeted inter- ventions. These have been conducted so far in China, Mexico, the United Kingdom, Brazil, India, Russia, Iran, Indonesia, Japan, the United States, Kenya, South Africa, Ethiopia, Sweden, Norway, and New Zealand. China's subnational study uncovered some striking differences between provinces. In Shanghai, the age-standardized death rate for communicable, maternal, neonatal, and nutritional diseases was 15.1 per 100 000 in 2017, similar to rates in high-income countries like Switzerland and Italy, but lower than rates in the United States and Canada. In China's western provinces like Xinjiang, however, the death rate is several times higher than Shanghai's and comparable to death rates in Morocco, Vietnam, and El Salvador. Leading risk factors 1990 Leading risk factors 2017 1 Child wasting 1 Child wasting 2 Unsafe water 2 Short gestation 3 Short gestation 3 Low birth weight 4 Child underweight 4 Unsafe sex 5 Vitamin A deficiency 5 Unsafe water 6 Unsafe sanitation 6 Unsafe sanitation 7 Low birth weight 7 No access to handwashing 8 No access to handwashing 8 Household air pollution 9 Child stunting 9 Child underweight 10 Household air pollution 10 Vitamin A deficiency 14 Child stunting 12 Unsafe sex Risk factor: Behavioural Environmental Fig. 2.3.7 Leading risk factors in terms of DALYs per 100 000, both sexes, all ages, sub-Saharan Africa, 1990 and 2017.

 Conclusion The Global Burden of Disease enterprise provides powerful tools for clinicians and policymakers alike, to identify both large-scale trends and local disparities. Being aware of these factors can help decision- makers plan for future healthcare needs and make changes that will reduce exposure to harmful risk factors. Healthcare providers, staff at health ministries and international health agencies, researchers, and others can also contribute to the ongoing GBD effort as collab- orators. For more information on joining the GBD network, please visit http://www.healthdata.org/gbd/call-for-collaborators. Collaborating with a worldwide network of researchers strengthens both the data-gathering effort and the quantitative analysis by bringing together experts from a variety of disciplines. IHME and its collaborators are expanding the list of diseases, injuries, and risk factors included in GBD and routinely updating the GBD estimates. Continual updates will ensure that the international community has access to high-quality estimates in the timeliest fashion. Through sound measurement, it will provide the foundational evidence that will lead to improved population health. FURTHER READING Foreman KJ, et al. (2018). Forecasting life expectancy, years of life lost, and all-cause and cause-specific

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