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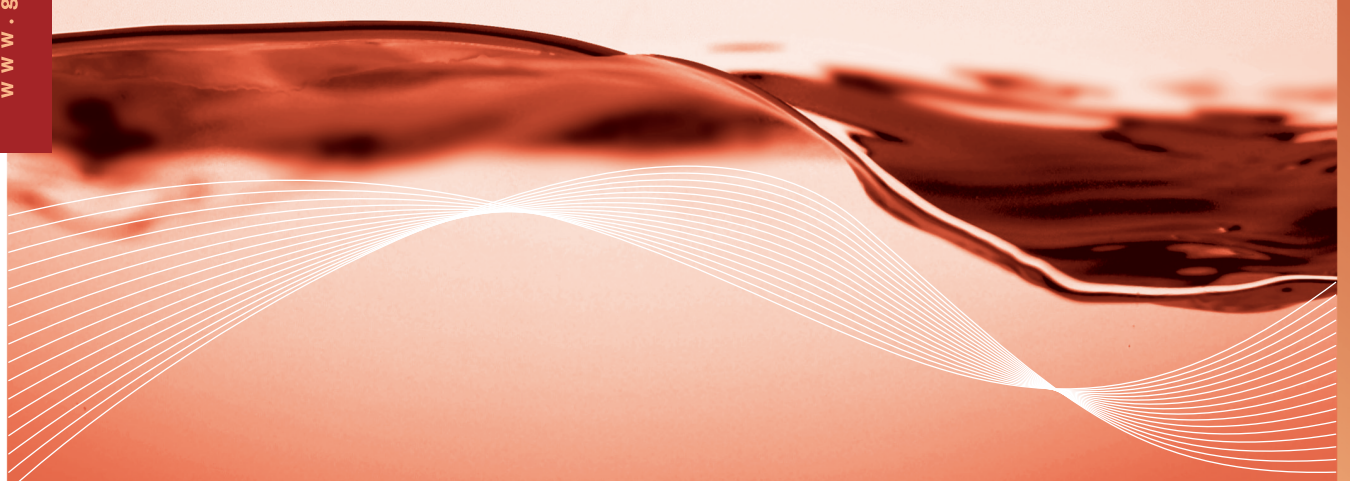
Monitoring Financial Flows for Health Research 2006

The changing landscape of health research for development



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2006

Monitoring Financial Flows for Health Research 2006

The changing landscape of health research for development

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Contents

List of Figures

Chapter 1

Chapter 2

Chapter 3

Chapter 4

List of Tables

Chapter 1

Chapter 2

Chapter 3

Chapter 4

Foreword

The landscape of efforts to improve human health in developing countries has changed dramatically in recent years. There are new actors, new resources and funding channels, and new commitments to meet goals in health and development. Acknowledgement of the importance of health as a human right and as a determinant, outcome and central objective of development has been accompanied by a greater recognition of the vital roles that health research can and must play in achieving this objective.

With the evolving landscape of new funds and initiatives for health come some important questions about health research. Where do the resources come from and how much is being spent? What is being funded? What priorities are being set, and by whom? Are the resources adequate for meeting current and predicted future health challenges as demographic and epidemiological patterns change across the world? As attention shifts from creating and delivering products and services that treat specific diseases and conditions towards learning more about the determinants of health and developing ways to promote and sustain it, are resources for health research becoming available to meet the needs?

The Global Forum for Health Research regularly tracks the world's resources for health research and examines the information gathered in relation to the health challenges faced by developing countries. This year's report surveys the changing scene of global financing for health research and provides new estimates of the resources available and the patterns of ill-health for 2003, as well as projections of these patterns in 2030. It also examines the vital roles that the public sector across all countries must play in supporting health research, creating an enabling environment and strengthening research capacities to meet the present and future challenges.

Pramilla Senanayake
Chair of the Foundation Council
Global Forum for Health Research

Executive summary

The changing scene

The 1990s saw a new awakening of interest in tackling global problems of poverty, development and health that culminated, in 2000, in governments committing to meet the Millennium Development Goals by 2015. The landscape has since become much more densely populated with a variety of actors engaged in efforts to improve health in developing countries.

After a dip in the 1990s, Official Development Assistance (ODA) has significantly increased and many high-income countries have finally set timetables for raising the percentage of their gross national income devoted to ODA to the long-standing target of 0.7%. New funding sources such as the Bill and Melinda Gates Foundation have begun making very substantial contributions to tackling some of the most serious health problems in developing countries – including high levels of infectious diseases and maternal and child mortality. Public-private partnerships, largely funded by philanthropic foundations, have begun creating a pipeline of potential vaccines, drugs, diagnostics and microbicides for infectious diseases of particular importance in developing countries, including HIV/AIDS, tuberculosis (TB) and malaria. To ensure that these products can be bought for use in the poorest countries, new funding channels and initiatives have been developed, including the Global Fund to Fight AIDS, TB and Malaria, the President's Emergency Plan for AIDS Relief and the International Financing Facility for Immunization. Some developing countries have begun to make significant contributions to the process of innovation in health and health technologies, and industry is showing increasing willingness to engage in partnerships to ensure the availability and use of cheap, safe and effective drugs for a range of tropical infectious diseases.

With these developments has come an increasing recognition of the vital roles that health research plays. These roles include uncovering the origins, determinants and biological processes involved in disease and ill health, creating and testing approaches to prevention and treatment, studying and evaluating factors that support or prevent the uptake and effectiveness of interventions, and providing evidence for policy-makers to use in setting and implementing their priorities.

But a number of crucial issues now need to be addressed:

- Will the increases in resources for health research continue, eventually reaching the scale needed to ensure adequate financing for the full range of activities required, including product research and development (R&D) and research at country level to improve services, eliminate health inequities, elucidate the social determinants of health and provide evidence-based pathways to better health for all?
- Within this overall set of goals, will funding allocations take account of the changing epidemiological and demographic profiles of developing

countries, or remain concentrated on a few high-profile diseases and conditions?

- Will countries take up the challenge of building and resourcing national health research systems, to ensure that they create and systematically utilise research capacities as an integral part of their efforts to improve health?
- Will those countries that are rapidly developing their innovation capacities create legal frameworks and practical environments, including state investments where necessary, to ensure that innovation works to benefit the health of needy populations, rather than producing only expensive products for rich markets?
- Will the public sectors of all countries show the individual and collective commitments needed to finance the required spectrum of research for health – research not only into disease states but also into the wider, underlying causes of ill health (e.g. social and other determinants of health that lie outside the health sector) and into developing a deeper understanding of the factors necessary for people to achieve and sustain overall good health and well-being?

What the world spends on health research

The Global Forum for Health Research has carried out a new assessment of how much the world is spending on health research. For 2003 – the most recent year for which comprehensive data are available – the total amount spent on R&D for health was US$ 125.8 billion. This is a substantial increase compared with the Global Forum's estimate of US$ 105.9 billion for 2001. The 2003 figure comprises three major components, with US$ 56.1 billion (45%) coming from the public sector, US$ 60.6 billion (48%) from the private for-profit sector and US$ 9.0 billion (7%) from not-for-profit organizations. This distribution between the three components is essentially unchanged from that in 2001.

Spending among high-income countries (HICs) accounted for most of the increase globally and followed a similar distribution, with the public sector accounting for 43% of total spending on R&D for health, the private-for-profit sector for 47% and the private-not-for-profit sector for 7%.

The private for-profit sector is estimated to be the largest investor in health research globally. Pharmaceutical companies accounted for 50% of overall funds for research for health in high-income countries and 32% in low- and middle-income countries. The private not-for-profit sector includes private universities, foundations and charities. It contributes approximately the same amount of funding in high-income countries (8%) and low- and middle-income countries (9%). Official Development Assistance (ODA) accounts for 7% of total health research funds in low- and middle-income countries (LMICs).

Public sector contributions to global spending on health R&D are significant not only because of their size, but also because of the influence they have on the directions of basic and applied research. States bear the primary responsibility for the health and rights of their citizens and many are also signatories to international commitments on health. Governments are estimated to be the largest funders after the private sector, accounting in 2003 for 42% of overall health research funds in high-income countries and 59% in LMICs. Governments support research for health through their allocations to ODA, higher education and direct investments in R&D.

Governments in HICs contributed US$ 538.1 billion to health R&D in 2003, up from US$ 44.1 billion reported in 2001 and US$ 36.2 billion in 1998, excluding foreign ODA. The United States government was the biggest spender at US$ 33.8 billion and accounted for more than half of the total in these countries. Japan followed with US$ 5.6 billion, Germany US$ 3.2 billion, France US$ 3.1 billion, the United Kingdom US$ 2.2 billion, Italy US$ 2.0 billion and Canada US$ 1.7 billion. Together, the G7 countries invested more than 92% of publicly funded R&D for health in HICs, with all other HICs combined adding another US$ 4.4 billion.

Few LMICs collect and report data on expenditures on research for health. Governments in those LMICs for which data are available spent at least US$ 2.4 billion on R&D for health in 2003. While this figure is down slightly from US$ 2.5 billion in 2001, the apparent decrease is due to incomplete reporting for LMICs in 2003, and does not reflect a real drop in R&D funding.

Allocations to R&D for health by governments in LMICs are still relatively small. Only a few of such countries have met the target proposed by the 1990 Commission on Health Research for Development for expenditures on R&D for health to total at least two per cent of national health expenditures. Among LMICs, only Argentina and Brazil met this level in 2003, according to the data reported.

The private not-for-profit sector has an increasingly strong commitment to R&D for health – estimated at US$ 9.0 billion in 2003, up from US$ 8.0 billion in 2001 and US$ 6.0 billion in 1998. Almost all of this funding (US$ 8.6 billion) came from private foundations and universities in HICs for R&D carried out in these countries. In contrast, in 2003, domestic private foundations and universities in LMICs funded health research costing just US$ 0.08 billion (roughly the same amount as in 2001 and 1988). Foreign not-for-profit organizations, such as foundations and universities also provided US$ 0.3 billion for R&D for health in LMICs in 2003, a figure that has remained relatively stable since 1998.

Foundations are substantively involved in key global and country level partnerships. This 'third sector' creates institutional diversity, contributes to innovation, and adds an important actor to a field dominated by governments and markets. The financial contribution of private foundations to international development activities in recent years has been estimated at US$ 3 billion annually, although it was probably higher than that in 2000 and 2001 due to large contributions from the Gates Foundation.

Global patterns in mortality and morbidity, 2003–2030

Worldwide, 57.5 million people died in 2003. One third of these deaths were due to communicable, maternal, and perinatal conditions and nutritional deficiencies ('Group I' in the Global Burden of Disease, or GBD, classification). This proportion has remained almost unchanged from 1990. Among Group I causes, HIV/AIDS accounted for 2% of deaths in 1990, but 17% in 2003, rising from 0.3 million deaths to 3.0 million in 2003. HIV/AIDS represented 5% of total global deaths in 2003. Excluding deaths due to HIV/AIDS, deaths due to Group I conditions fell from one-third of total deaths in 1990 to less than one-fifth in 2003. In all, 97% of the 'non-HIV/AIDS Group I' deaths occurred in low- and middle-income countries.

Ischaemic heart disease (IHD) and cerebrovascular disease (stroke) were the leading causes of death in both HICs and LMICS in 2003, together responsible for more than 20% of all deaths worldwide. Four of the top 10 causes of death in the world are related to smoking (IHD, stroke, chronic obstructive pulmonary disease and lung cancer). Of the 7.3 million deaths from IHD worldwide, 1.4 million occurred in HICs. In all, 5.6 million people died of stroke, of which fewer than one million occurred in HICs. Lung cancer was the third leading cause of death in HICs, but was not among the top ten causes of death in LMICs, partly due to the prominence of other causes of death. In LMICs, five of the leading ten causes of death remain infectious diseases, including lower respiratory tract infections, HIV/AIDS, diarrhoeal diseases, TB and malaria.

Nearly 20% of deaths (10 million) in 2003 were among children under five years of age. Enormous strides have been made since 1970 when over 17 million child deaths occurred. Nevertheless, today nearly all child deaths (99%) occur in LMICs, with over 40% in sub-Saharan Africa alone. While some African countries have made considerable strides in reducing child mortality, the majority of African children live in countries where the survival gains of the past have been wiped out or even reversed, largely as a result of the HIV/AIDS epidemic.

Child mortality (ages 0-4 years) declined between 1990 and 2003 in all regions of the world. These declines were around 30% or higher in high-income countries, in Latin America and the Caribbean, in the Middle East and North Africa, and in the LMICs of Europe and Central Asia. Death rates from communicable diseases and injuries have declined substantially in these regions, particularly for diarrhoeal and respiratory diseases. Almost half of all child deaths in 2003 were from five preventable and treatable conditions: acute respiratory infection, measles, diarrhoea, malaria, and HIV/AIDS.

In Latin America and some Asian and Middle-Eastern countries, by 2003 conditions arising in the perinatal period, including birth asphyxia, birth trauma and low birth-weight replaced infectious diseases as the leading cause of death and became responsible for 20–36% of child deaths. Such a shift in the cause-of-death pattern has not occurred in sub-Saharan Africa, where malaria, lower respiratory tract infections and diarrhoeal diseases continue to be the leading causes of death in children, accounting for 50% of all deaths. HIV/AIDS is now responsible for over 300,000 child deaths in sub-Saharan Africa – nearly 7% of all child deaths in the region.

Mortality from diarrhoeal diseases fell from 2.4 million deaths in 1990 to about 1.6 million deaths in 2003 reflecting the substantial efforts in diarrhoea case management (e.g. using oral rehydration therapy). Deaths from measles also declined, most likely because of higher vaccination coverage. Death rates from acute respiratory infections declined less in South Asia and Sub-Saharan Africa than in other regions. Malaria mortality appears to have increased during the 1990s, primarily in sub-Saharan Africa.

Noncommunicable diseases ('Group II' in the GBD classification) are now responsible for more than half of adult (aged 15–59) deaths in all regions except South Asia and sub-Saharan Africa where Group I conditions, including HIV/AIDS, remain responsible for one-third and two-thirds of deaths, respectively. In LMICs, 15–59 year

old adults face a 30% greater risk of death from non-communicable diseases than their counterparts in HICs.

Despite the burden of communicable diseases in adults declining globally, HIV/AIDS has become the leading cause of mortality among adults aged 15–59, responsible for 2.5 million deaths or 15% of global deaths in this age group. HIV/AIDS deaths are responsible for a slightly larger proportion of deaths than ischaemic heart disease and cerebrovascular disease combined, and for more than twice as many deaths as road traffic accidents in that age group. Road traffic accidents are the fourth leading cause of death in adults aged 15–59 years, and three-quarters of these deaths are of men. Suicide and violence (homicide) are also among the top ten causes of death in adults aged 15–59 years. Together with war, intentional injuries account for nearly one in 10 deaths in this age range globally.

In 2003, five communicable diseases were among the leading ten contributors to the burden of disease in LMICs. Apart from road traffic accidents, the leading causes in HICs consisted entirely of noncommunicable diseases, including three diseases (unipolar depressive disorders, adult-onset hearing loss, and alcohol use disorders) with few direct deaths but large disability.

Worldwide, there was a 20% reduction in the per capita disease burden due to communicable, maternal, perinatal and nutritional conditions between 1990 and 2003. Without the HIV/AIDS epidemic and the associated persistence of TB, this reduction would have been closer to 30%.

Lost years of full health per capita (as measured by the disability-adjusted life year, or DALY) for LMICs are double those for HICs. The burden of disease is more than four times higher in Africa than in HICs, and just over twice as high in India as in HICs. People in Africa and India comprised one third of the world's population and together bore 53% of the total global burden of disease in 2003.

Around 45% of the disease burden in LMICs is now from noncommunicable diseases, a rise of 10% in its relative share since 1990. Ischaemic heart disease and stroke are the largest sources of this burden, especially in the low- and middle-income countries of Europe and Central Asia where they account for 21% of the total disease burden. Injuries accounted for 17% of the disease burden in adults aged 15–59 years in 2003. In Latin America and the Caribbean, the Middle East and North Africa, and Europe and Central Asia, more than one quarter of the entire burden of disease among men aged 15 to 44 years was from injuries. Violence is the third leading cause of burden in Latin America and Caribbean countries

The World Health Organization (WHO) undertook recently a major analysis to provide reliable data on the mortality and burden of disease attributable to 26 major risk factors, across all regions of the world, using comparable methods and a common currency (the DALY) for health outcomes. This analysis limited itself to 'proximal risk factors', thereby excluding 'distal risk factors' such as poverty and others. The regional distribution of the burden of disease attributable to 20 risk factors is summarized here.

One-fifth of the global disease burden can be attributed to the effects of under-nutrition. The five leading global risks causing burden of disease are being underweight due to malnutrition, unsafe sex, raised blood

pressure, tobacco smoking and alcohol. Risks are extraordinarily concentrated in low income countries, and relatively few risks are responsible for a considerable proportion of the burden of disease. For example, almost 15% of the total burden of disease in India and Africa is attributed to under-nutrition and being underweight. The burden from these risks alone exceeds that of the high income countries' entire disease and injury burden. Unsafe sex is the second leading risk in LMICs, and in Africa accounts for almost one-fifth of the disease burden.

In HICs, tobacco is the leading risk factor, accounting for 12% of the disease burden. Alcohol and blood pressure are responsible for 7-8% of healthy life years lost, with cholesterol and being overweight accounting for 5-6%. LMICs now face a double burden of disease from risk factors and diseases of poverty and lack of development, as well as the chronic diseases associated with smoking, overweight, diet and physical inactivity.

Almost one half (47%) of all deaths in the year 2002 can be attributed to the 20 leading risk factors, when joint effects are taken into account. More than two-fifths (42%) of global deaths can be attributed to the leading 10 risk factors, and almost one third to the leading five. These top five risk factors are responsible for one quarter of the total loss of healthy years of life globally.

The role of established risk factors is much greater than commonly thought, and the causes are known for more than two-thirds of major diseases, such as ischaemic heart disease, stroke, diabetes, HIV/AIDS. The potential is huge for improving health and reducing mortality through research to develop cost-effective interventions that reduce a relatively small number of risks.

WHO has prepared updated projections of future trends for mortality and burden of disease from 2002 to 2030, based largely on projections of economic and social development, and using the historically observed relationships of these with cause-specific mortality rates. Separate projections for HIV/AIDS mortality were prepared by UNAIDS and WHO, under a scenario in which coverage with anti-retroviral drugs reaches 80% by 2012, thereafter remaining constant, and assuming that there are no changes to current transmission rates due to increased prevention efforts.

Large declines in mortality between 2002 and 2030 are projected for all of the main Group I causes with the exception of HIV/AIDS. Total deaths due to other Group I causes are predicted to decline from 15.5 million in 2002 to nine million in 2030. Unfortunately, this would be substantially offset by the projected doubling in HIV/AIDS mortality from the current annual toll of three million deaths. Avoiding this scenario must remain a major global health priority.

Although age-specific death rates for most Group II conditions are projected to decline, as populations age over the next thirty years there will be a significant increase in total deaths due to most of these conditions. Global cancer deaths are projected to increase from 7.3 million in 2003 to 11.5 million in 2030, and global cardiovascular deaths from 17 million in 2003 to 23.3 million in 2030. Overall, Group II conditions will account for almost 70% of all deaths in 2030 under the baseline scenario. Major failures with tobacco and obesity control efforts could dramatically alter this prediction, as was seen in several industrialized countries in the 1950s and 60s.

The projected 40% increase in global deaths due to injury between 2003 and 2030 is largely due to rising numbers of road traffic accidents, together with increases in population numbers more than offsetting small declines in age-specific death rates for other causes of injury. Road traffic accident deaths are projected to increase from 1.2 million in 2003 to 2.1 million in 2030, primarily associated with economic growth in LMICs.

The three leading causes of burden of disease in 2030 are projected to include HIV/AIDS, unipolar depressive disorders and ischaemic heart disease. HIV/AIDS becomes the leading cause of burden of disease in middle-income countries, as well as low-income countries, by 2015. For some causes, projected changes in disease burden over the next 30 years are likely to result in dramatic changes in global importance. Lower respiratory tract infections and diarrhoeal diseases are expected to fall to 9th and 13th place in the global DALYs 'league' table, from 2nd and 5th place respectively in 2003. Malaria is also expected to decline in relative importance, as are congenital anomalies. Conversely, by 2030, HIV/AIDS is expected to be the leading global cause of DALYs, followed by depression, ischaemic heart disease, chronic obstructive pulmonary disease and perinatal conditions. This rather diverse set of conditions will require very flexible and innovative responses from health systems worldwide in order to avoid what are largely avoidable or treatable conditions. Further research will help to focus these disease control efforts.

These projections predict a dramatic shift in the distribution of deaths from younger to older ages and from communicable, maternal, perinatal and nutritional causes to non-communicable disease causes. The risk of death for children aged under five is projected to fall by nearly 50% between 2003 and 2030. Total tobacco-attributable deaths are projected to rise from 5.4 million in 2005 to 6.4 million in 2015 and 8.3 million in 2030. Tobacco is projected to kill 50% more people in 2015 than HIV/AIDS, and to be responsible for 10% of all deaths globally.

The information presented can be summarized as follows:

- Mortality estimates are higher in LMICs than HICs, and people in LMICs die younger than in HICs.
- There is large mortality variation between LMICs: China has a higher mortality of populations above 60 years while in Africa younger populations die prematurely, a large proportion being of young children and caused by infectious diseases.
- Deaths due to noncommunicable diseases are highly prevalent in LMICs.
- Contrary to common belief, noncommunicable diseases play a key role in the disease burden in many LMICs, with rates comparable to those in HICs (two-thirds of the burden in China). Conversely, in Africa infectious diseases are predominant.
- Trends over time reflect increases in infectious diseases in Africa and increases in noncommunicable diseases in other LMICs.
- A large proportion of the disease and injury burden attributable to risk factors is preventable.

Burden of disease estimates reflect, in contrast with mortality estimates, the importance of noncommunicable diseases in LMICs other than African nations. Disease burden captures not only premature death but also years living with disability. As such,

the weight of conditions before death can be quantified. While some of this disease burden can be averted through known interventions, applying and scaling up such interventions in LMICs is not straight forward. Research can help in identifying tools and programmatic pathways to put knowledge into action.

The public sector and research for health

Overall, resourcing the research that will lead to significant health benefits in developing countries will require greater effort by the public sector across the world. Some key points emerge regarding crucial public sector actions on resources and policy needed to achieve the necessary levels of resources and ensure that they are deployed effectively:

Public sector in high-income countries should:

- give greater priority in national research programmes, such as those funded through the United Kingdom's Medical Research Council and the National Institutes of Health in the United States of America, to basic research on diseases endemic in poor countries;
- ensure the inclusion of more health research in development programmes funded through bilateral and multilateral channels – at least achieving the target of 5% of health aid being earmarked for research and for strengthening research capacity;
- give greater support to product development partnerships creating drugs, vaccines and microbicides; and
- support research into the social, economic and political determinants of health and into finding ways to give all people the opportunity to be healthy.

Public sector in low- and middle-income countries should:

- commit greater resources to health research – at least achieving the target that an amount equal to 2% of government spending on health is allocated to research and to strengthening research capacity;
- engage with stakeholders including researchers and communities in setting priorities for research based on health needs, using a broad definition of health;
- develop funding streams and policy environments that foster capacity building across all aspects of research for health;
- develop and strengthen national health research systems that ensure that research capacities are effectively utilized on priority research and that results are translated into policy and action; and
- support the development of innovation systems that will enable new industries to produce the products needed to address endemic diseases and conditions.

Chapter 1

The changing scene

The changing scene

1.1 Introduction

The first decade of the 21st century may well be seen, with hindsight, as a turning point in the history of health research – a decade in which a wide range of policy-makers, funders and researchers began to appreciate the contributions that health research can and must make to improving the health of populations in all countries; and a decade in which the resources to ensure that this potential benefit is achieved began to become more readily available both globally and nationally.

Having now passed the mid-point of this decade, it is a good time to review the milestones that have been reached, take stock of the current landscape and consider the directions in which recent developments are pointing.

In this context, the decade opened with the International Conference on Health Research for Development in Bangkok in September 2000. The Council on Health Research for Development (COHRED) initiated the conference in collaboration with the Global Forum for Health Research, WHO and the World Bank to review the status of health research 10 years after the Commission on Health Research for Development published its findings and recommendations in 1990. The commission's report, *Health Research: Essential link to equity in development*[1], made the observation that health research was significantly skewed towards diseases that affected the developed world. The commission estimated that only 5% of global spending on health research in 1986 was devoted to health problems in developing countries, where 93% of the world's burden of 'preventable mortality' occurred. Later in the 1990s, while the size of the imbalance had become increasingly more complex and difficult to measure quantitatively, the term '10/90 gap' began to be used as a shorthand reference to the issue. It has come to symbolise the gross mismatch between needs and investments in health research for development.[2]

The Commission made four main recommendations to reduce this imbalance: 1) all countries, no matter how poor, should invest at least some resources in conducting essential national health research and, in the long-term, in building and sustaining capacity for health research; 2) productive research partnerships should link national health research efforts in developing and developed countries; 3) greater and more sustained funding for health research should be made available internationally; and 4) an international mechanism should be set up to monitor progress and promote financial and technical support for research on health problems of developing countries. The Commission's report resulted, in 1993, in the establishment of COHRED, which initially focused on working at country-level to promote the production and use of essential national health research.

Further efforts to draw attention to the continuing health research gap were made by

the Ad Hoc Committee on Health Research Relating to Future Intervention Options, created under the auspices of WHO in 1994. Its 1996 report[3] asserted a continuing conviction that research and development (R&D) had a vital role to play in the prevention and treatment of health problems, and that more resources were required for the whole spectrum from biomedical to health policy research. It highlighted that a new set of threats to health had joined the familiar problems of infection and malnutrition in developing countries, and predicted that noncommunicable diseases would become the leading causes of disability and premature death within 25 years.

At the same time, HIV/AIDS and drug-resistant strains of major pathogens were becoming global challenges. The committee recommended that a 'forum for investors in international health R&D' should be formed to provide a mechanism to review the needs and opportunities for global health R&D – making use of analytical data on disease burden, on R&D opportunities and on the level of ongoing efforts to help focus resources more sharply on the highest priorities. In 1997, parties interested in health research – including donors, development agencies and health research leaders – met and launched the Global Forum for Health Research, which began formal operations in January 1998. The Global Forum's overall objective is to help focus research efforts on the health problems of the poor through improvement in the allocation of research funds, support of better priority setting processes and methodologies, promotion of relevant research, support for concerted efforts in health research and dissemination of research findings.

By the time of the Bangkok conference in 2000,[4] it was clear that the landscape of health research for development was poised for major changes. As noted by the Commission, the previous decade had opened dismally, with very few resources devoted to the field and very few actors engaged in it:

- In the area of communicable diseases, the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) was the only significant global effort. It was complemented by research sponsored by a handful of nationally-based programmes with an international focus on infectious diseases. These included those of the National Institutes of Health (NIH) and Walter Reed Army Institute for Research in the United States of America, the Medical Research Council and Wellcome Trust in the United Kingdom, the French INSERM and Pasteur Institutes, and tropical research institutes in countries such as Belgium, the Netherlands and Switzerland.
- Similarly, while the area of family planning was recognized to be of vital importance for developing countries, the UNDP/UNFPA/WHO/World Bank Special Programme for Research, Development and Research Training in Human Reproduction (HRP) was the leading but greatly under-resourced global effort. It was complemented by the Program for the Introduction and Adaptation of Contraceptive Technology/ Program for Appropriate Technology in Health (PIACT/PATH) and research programmes and institutes working on reproduction and contraception in a handful of developed and developing countries.
- Funding for these limited national and international efforts came mainly from multilateral organizations (such as the World Bank, UNDP, UNFPA, WHO), the

governments of some member states of the Organization for Economic Cooperation and Development and a small number of philanthropic foundations (e.g. Rockefeller, Ford, McArthur, Mellon).

- There was a striking absence of significant interest on the part of the private sector in becoming involved in areas such as tropical (or other neglected) diseases and contraception – an outstanding exception being Merck's donation of ivermectin to treat river blindness[5] – so that support for product development was almost entirely left to the public and philanthropic sectors.
- Few governments of developing countries were investing significantly in health research for their own essential national needs, prompting the Commission on Health Research for Development to recommend[1] that governments devote at least 2% of the health budget to research and to strengthening research capacity, with 5% of donor support to health in these countries being similarly allocated.

But the decade closed with an evolving landscape that was beginning to be more densely populated with a diverse array of actors, including new advocates for health research for development such as COHRED and the Global Forum, new philanthropic actors – in particular the Bill and Melinda Gates Foundation, created in 2000 – and an explosive growth in health product development partnerships[6] such as the International AIDS Vaccine Initiative and Medicines for Malaria Venture. Development assistance partners had begun to focus on improving health as an indispensable aspect of development; and several pharmaceutical giants were becoming involved in large-scale drug donation programmes.

1.2 The evolving landscape

This diversification of the landscape has continued at an increasing pace during the opening years of the 21st century and a number of important milestones have been passed since 2000. At the global level, there has been emphatic recognition of the challenges in tackling major health problems and, most importantly, of the need to create effective instruments to address them.

The Millennium Development Goals (MDGs) were formulated in 2000 following a series of international agenda-setting conferences including two with a major health component – the International Conference on Population and Development (Cairo, 1994)[7] and the Fourth World Conference on Women (Beijing, 1995)[8]. The MDGs have been criticized in some quarters for being too limited in ambition, too narrowly focused on a few issues and lacking in explicit reference to the vital area of sexual and reproductive health. Nevertheless, they have galvanized efforts to tackle some major health problems (including maternal and child mortality and communicable diseases) and there are now substantially greater resources available to ensure people have access to pharmaceuticals they need:

- Following efforts by the G8, the European Commission and the United Nations, the Global Fund to Fight AIDS, Tuberculosis and Malaria was launched in 2002. Its aim is to raise money from governments, businesses and individuals worldwide and channel it into grant programmes. By the end of 2005, the Global Fund had disbursed a total US$ 1.9 billion in grants; 384,000 people had begun antiretroviral therapy through Global Fund-supported programmes (nearly triple the number of recipients funded one year earlier); programmes to combat malaria had distributed 7.7 million insecticide-treated bed nets (a 150% increase in six months); and tuberculosis (TB) programmes had detected and treated more than one million TB cases (a 67% increase from May 2005). By mid-2006, the Global Fund had approved a total of US$ 5.5 billion in allocations to nearly 400 grants in 132 countries.[9]
- In parallel, the United States of America announced the President's Emergency Plan for AIDS Relief (PEPFAR) in 2003. It is providing US$ 15 billion in funding over five years to combat HIV/AIDS in more than 120 countries. By the end of March 2006, PEPFAR had supported antiretroviral therapy for 561 000 men, women, and children through bilateral programmes in 15 of the most afflicted countries in Africa, Asia, and the Caribbean.[10]
- The Global Fund and PEPFAR have been complemented by the '3x5 Initiative' launched by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and WHO in 2003. It aimed to provide three million people living with HIV/AIDS in low- and middle-income countries (LMICs) with antiretroviral therapy by the end of 2005. While this specific target was not achieved (by mid-2005, around 1 million people in LMICs were receiving antiretroviral therapy), the initiative was an important step towards the goal of making HIV/AIDS prevention and treatment universally accessible for all who need them, as a human right.[11]
- Pre-dating the MDGs, but given additional impetus by their targets, is the GAVI Alliance (formerly known as the Global Alliance for Vaccines and Immunization) – a public-private partnership formed in 1999 with the mission of ensuring that every child in the world will be protected against vaccine-preventable diseases. At present, roughly one child in four receives no vaccinations and the gap between the vaccines readily available to children in the poorest countries and to those in the industrialized world is growing, with the result that almost 3 million people, the majority children, still die annually from diseases that could be prevented with available vaccines. The GAVI Alliance works to close this gap through a global network of partners, including national governments, UNICEF, WHO, the World Bank, the Bill and Melinda Gates Foundation, the vaccine industry, public health and research institutions, and nongovernmental organizations. The GAVI Fund now has over U$ 3 billion in commitments over the next ten years.[12]

As major new resources have begun to be made available to address some of the high priority health problems faced by poor countries and as programmes to apply these resources have begun to be implemented, there has been a growing recognition of the essential roles that health research is required to play in the processes of creating, refining, adapting, monitoring and evaluating health initiatives.

The Commission on Macroeconomics and Health (CMH) was launched by WHO

Director-General Gro Harlem Brundtland in January 2000, to analyse the impact of health on development and examine the appropriate modalities through which health related investments could have a positive impact on economic growth and equity in developing countries. Its report[13] recommended measures designed to maximize the beneficial effects of health sector investment on poverty reduction and economic development. These included increases in funding for health and development by both donors and developing countries. The CMH also recognized the vital role that research plays and called for a significant scaling up of financing for global R&D on the heavy disease burdens of the poor (see Box 1.1), to be financed through a new funding channel (see Box 1.2).

Box 1.1

The vital role of health research

A sound global strategy for health will also invest in new knowledge. One critical area of knowledge investment is operational research regarding treatment protocols in low-income countries. There is still much to be learned about what actually works, and why or why not, in many low income settings, especially where interventions have not been used or documented to date. Even when the basic technologies of disease control are clear and universally applicable, each local setting poses special problems of logistics, adherence, dosage, delivery, and drug formulation that must be uncovered through operational research at the local level. We recommend that as a normal matter, country-specific projects should allocate at least 5 percent of all resources to project-related operational research in order to examine efficacy, the optimization of treatment protocols, the economics of alternative interventions, and delivery modes and population/patient preferences.

There is also an urgent need for investments in new and improved technologies to fight the killer diseases. Recent advances in genomics, for example, bring us much closer to the long-sought vaccines for malaria and HIV/AIDS, and lifetime protection against TB. The science remains complex, however, and the outcomes unsure. The evidence suggests high social returns to investments in research that are far beyond current levels. Whether or not effective vaccines are produced, new drugs will certainly be needed, given the relentless increase of drug-resistant strains of disease agents. The Commission therefore calls for a significant scaling up of financing for global R&D on the heavy disease burdens of the poor. We draw particular attention to the diseases overwhelmingly concentrated in poor countries. For these diseases, the rich-country markets offer little incentive for R&D to cover the relatively few cases that occur in these rich countries. We also stress the need for research into reproductive health - for example, new microbicides that could block the transmission of HIV/AIDS and improved management of life-threatening obstetric conditions.

We need increased investments in other areas of knowledge as well. Basic and applied scientific research in the biomedical and health sciences in the low-income

countries needs to be augmented, in conjunction with increased R&D aimed at specific diseases. The state of epidemiological knowledge—who suffers and dies and of which diseases—must be greatly enhanced, through improved surveillance and reporting systems. In public health, such knowledge is among the most important tools available to successful disease control. Surveillance is also critically needed in the case of many NCDs, including mental health, the impact of violence and accidents, and the rapid rise of tobacco and diet/nutrition-related diseases. Finally, we need a greatly enhanced system of advising and training throughout the low-income countries, so that the lessons of experience in one country can be mobilized elsewhere. The international diffusion of new knowledge and "best practices" is one of the key forces of scaling up, a central responsibility of organizations such as the World Health Organization and the World Bank, and a goal now more readily achieved through low-cost methods available through the internet.

Extract from the report of the Commission on Macroeconomics and Health.[13]

Box 1.2
Proposed new financing for health research

To help channel the increased R&D outlays, we endorse the establishment of a new Global Health Research Fund (GHRF), with disbursements of around $1.5 billion per year. This fund would support basic and applied biomedical and health sciences research on the health problems affecting the world's poor and on the health systems and policies needed to address them. Another $1.5 billion per year of R&D support should be funded through existing channels. These include the Special Programme for Research and Training in Tropical Diseases (TDR), the Initiative for Vaccine Research (IVR), the Special Programme of Research, Development and Research Training in Human Reproduction (HRP) (all housed at WHO) and the public-private partnerships for AIDS, TB, malaria, and other disease control programs that have recently been established. In both cases, the predictability of increased funding would be vital, as the necessary R&D undertakings are long-term ventures. The existing Global Forum for Health Research could play an important role in the effective allocation of this overall assistance. To support this increased research and development, we strongly advocate the free internet-based dissemination of leading scientific journals, thereby increasing the access of scientists in the low-income countries to a vital scientific research tool.

Extract from the report of the Commission on Macroeconomics and Health.[13]

The WHO Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) was set up in February 2004 to collect data and to analyse how incentives and funding mechanisms may be created for research into, and the development of, new diagnostics, vaccines and medicines for diseases that disproportionately affect developing countries. Its report[14] noted that recent developments had created real momentum for change but cautioned against complacent thinking that current efforts are yet sufficient, or commensurate with the scale of suffering.

CIPIH saw continuing innovation to be crucial but recognized that it would be pointless without favourable conditions for poor people in developing countries to access existing, as well as new, products. Intellectual property rights (IPR) are important, but as a means not an end, with their relevance in the promotion of the needed innovation depending on context and circumstances. CIPIH considered that IPR can do little to stimulate innovation in the absence of a profitable market for the products of innovation, a situation which can clearly apply in the case of products principally for use in developing–country markets. In successive phases of the innovation cycle – from fundamental research to the discovery, development and delivery of new products – the multiplicity of financial and other incentive mechanisms, and the scientific and institutional complexities of biomedical innovation have to be considered. In each phase, IPR may play some role in facilitating the innovation cycle, but other incentive and financing mechanisms to stimulate R&D of new products are equally necessary, along with complementary measures to promote access. CIPIH concluded that, in spite of the progress made in the past decade, the basis for continued progress in the development of new products needed by developing countries remains fragile. To assure sustainability, and guarantee that medicines, vaccines and diagnostics produced reach the people who need them, additional efforts are needed. Much more must be done to increase the funds available on a sustainable basis and to promote synergy among different partners. Governments have the major responsibility to mobilize funds and promote new financing and incentive mechanisms to meet the goals.

An important development that coincided with the publication of the CIPIH report was that Brazil and Kenya sponsored a resolution[15] on R&D at the January 2006 Executive Board of the WHO. The resolution was later debated at the May 2006 World Health Assembly, resulting in the establishment of a working party to consider how to stimulate and reward innovation in health research for product development that will benefit poor countries. At the same time, WHO has been making efforts to consolidate and clarify its own role and responsibilities in health research.[16]

The WHO Commission on Social Determinants of Health was created in March 2005 to draw the attention of governments, civil society, international organizations, and donors to pragmatic ways of creating better social conditions for health. It brings together leading scientists and practitioners to provide evidence on policies that improve health by addressing the social conditions which people live and work. The commission's main goals are:

- to support policy change in countries by promoting models and practices that address effectively the social determinants of health;
- to support countries in making health a shared goal to which many government departments and sectors of society contribute;

- to help build a sustainable global movement for action on health equity and social determinants, linking governments, international organizations, research institutions, civil society and communities.

While these global initiatives have addressed diverse aspects of the overall framework affecting access to basic health services and essential products, there has also been a new impetus given to financing health research for the needs of developing countries. Thus, although no significant moves have been made to create a single global research fund on the scale recommended by the Commission on Macroeconomics and Health, several separate funding channels are substantially increasing the flow of investments into the field. Three elements of this are noteworthy: an overall growth in funding for health research, especially research related to product development for tropical and other neglected diseases; attention by national institutions, such as research councils and institutes of health, to priority health problems of LMICs; and a growing interest in tracking funding allocations and estimating funding needs.

At the end of 2003, *Business Week Magazine* documented the unprecedented growth in philanthropic giving that was taking place in the United States of America.[17] It listed the 50 most generous philanthropists, headed by the Bill and Melinda Gates Foundation, who were collectively responsible for donations of more than US$ 50 billion during the previous five years – a significant proportion of this going to health and related areas. The magazine noted the rise of a new conception of 'responsible philanthropy', characterized by a demand for measurable results, efficiency, and transparency, that was bringing a businesslike rigor to philanthropy. In addition, many of the leading givers are handing over the bulk of their fortunes to be used during their own lifetimes to tackle the worst problems plaguing society, instead of making promises to be fulfilled by bequest on their deaths.

With an endowment of US$ 29.2 billion, the Bill and Melinda Gates Foundation (Gates Foundation) has already committed US$ 10.5 billion to development projects since its inception in 2000. In the health field, the foundation focuses on accelerating access to existing vaccines, drugs, and other tools to fight diseases that disproportionately affect developing countries, and supports research to discover new health solutions that are effective, affordable, and practical for use in such countries. Key criteria for the foundation's grant-making are diseases and conditions that (a) cause the greatest illness and death in developing countries (b) represent the greatest inequities in health between developed and developing countries and (c) receive inadequate attention and resources (see Figure 1.1). Grants allocated by the Gates Foundation's global health programmes up to June 2006 totalled US$ 6.5 billion (Table 1.1).

Figure 1.1

Priority diseases and conditions addressed by the Bill and Melinda Gates Foundation[18]

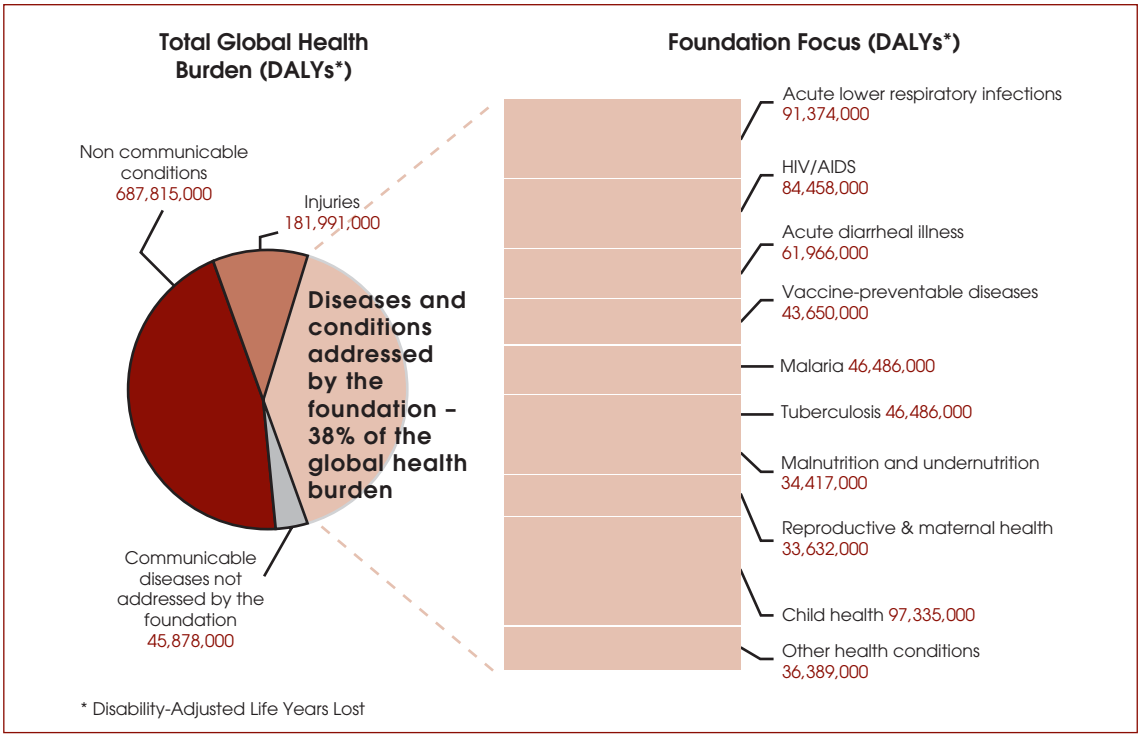


Table 1.1

Bill and Melinda Gates Foundation: support for global health, to June 2006[19]

Global health programmes	Amount, US$
HIV, TB and Reproductive Health	1 900 821 297
Infectious Diseases	1 592 621 889
Global Health Strategies	2 424 965 606
Global Health Technologies	443 286 269
Global Health Research, Advocacy and Policy	147 623 830
Total	6 509 318 891

As part of its overall effort, the Gates Foundation has partnered with the Canadian Institutes of Health Research, the Foundation for the National Institutes of Health, and the Wellcome Trust to develop fourteen 'grand challenges' in global health research, which focus on the needs of developing countries (Box 1.3). By mid-2006, the initiative had offered 43 grants totalling US$ 436.6 million to teams of scientists working in 33 countries on a broad range of innovative research projects.[20]

Box 1.3
Fourteen Grand Challenges in Global Health

An initiative of the Bill and Melinda Gates Foundation, the Canadian Institutes of Health Research, the Foundation for the National Institutes of Health and the Wellcome Trust, with seven long-term goals to improve health in the developing world:

Improve childhood vaccines
1: Create effective single-dose vaccines
2: Prepare vaccines that do not require refrigeration
3: Develop needle-free vaccine delivery systems

Create new vaccines
4: Devise testing systems for new vaccines
5: Design antigens for protective immunity
6: Learn about immunological responses

Control insects that transmit agents of disease
7: Develop genetic strategy to control insects
8: Develop chemical strategy to control insects

Improve nutrition to promote health
9: Create a nutrient-rich staple plant species
Improve drug treatment of infectious diseases
10: Find drugs and delivery systems to limit drug resistance

Cure latent and chronic infection
11: Create therapies that can cure latent infection
12: Create immunological methods to cure latent infection

Measure health status accurately and economically in developing countries
13: Develop technologies to assess population health
14: Develop Versatile Diagnostic Tools

Considerably more philanthropic funds will be available to support global health research in the coming years, following Warren Buffett's announcement[21] that from 2006 he would begin contributing the bulk of his US$ 44 billion assets to the Gates Foundation.

Philanthropic foundations took the lead in the creation of a large number of public-private partnerships (PPPs) in the health field, some of which have focused on the creation of new drugs, vaccines, diagnostics and microbicides to address 'neglected' diseases mainly endemic in developing countries.[6] In particular, the Rockefeller Foundation made major and innovative contributions to this field, fostering the creation of the International AIDS Vaccine Initiative (IAVI), which became an independent legal entity in 1996. IAVI was followed by other ventures launched after 'incubation' by the Rockefeller Foundation. These include the Global Alliance for Tuberculosis Drug Development (TB Alliance) in 2000, the International Partnership for Microbicides (IPM) in 2001 and the Pediatric Dengue Vaccine Initiative (PDVI) in 2001. These and other initiatives also benefited from funding from the Bill and Melinda Gates Foundation, which included support for the Medicines for Malaria Venture (MMV) Sequella Global TB Vaccine Foundation, the Tuberculosis Diagnostics Initiative (the antecedent of the Foundation for Innovative New Diagnostics, FIND), the Institute for OneWorld Health, the Human Hookworm Vaccine Initiative (HHVI) and the Malaria Vaccine Initiative (MVI).

The Rockefeller Foundation also created two additional initiatives to help facilitate and catalyse efforts to ensure more attention to products for neglected diseases. The Initiative on Public-Private Partnerships for Health[22] (IPPPH) and the Centre for the Management of Intellectual Property in Health Research and Development[23] (MIHR).

IPPPH operated from 2000 to 2004 under the auspices of the Global Forum for Health Research. Its role was to monitor, analyse, and support the emerging field of public-private collaborations. It focused on partnerships targeting diseases predominantly affecting poor populations in developing countries, and those where the pharmaceutical or other health product companies were significant participants.

MIHR was set up in 2002 on the premise that improved management of innovation and intellectual property by the public sector can make an important contribution to the goal of improving the availability of health products needed by the poorest in developing countries.

As IPPPH noted,[24] public-private partnerships were already a known concept in the mid 1990s, but many of the new entities emerging since then (see Box 1.4) were distinguished by an important and novel aspect: instead of focusing on identifying and developing a single candidate, they adopted a 'portfolio' approach that was more characteristic of industry, creating and managing a pipeline of several candidates for each targeted disease to manage the risks of failure and improve the chances of a successful outcome.

Box 1.4
Examples of product development initiatives taking a portfolio approach

HIV/AIDS
International AIDS Vaccine Initiative (IAVI)
South African AIDS Vaccine Initiative (SAAVI)
Global Microbicide Project (GMP)
International Partnership for Microbicides (IPM)
Microbicide Development Project (MDP)

Malaria
Medicines for Malaria Venture (MMV)
Malaria Vaccine Initiative (MVI)
European Malaria Vaccine Initiative (EMVI)

Tuberculosis
Global Alliance for Tuberculosis Drug Development (TB Alliance)
Aeras Global Tuberculosis Vaccine Foundation (Aeras)
Foundation for Innovative New Diagnostics (FIND)

Other 'neglected infectious diseases'
Drugs for Neglected Diseases initiative (DNDi)
Institute for OneWorld Health (IOWH)
Pediatric Dengue Vaccine Initiative (PDVI)
Human Hookworm Vaccine Initiative (HHVI)
Rotavirus Vaccine Accelerated Development and Introduction Plan (RotaADIP)
Pneumococcal Vaccine Accelerated Development and Introduction Plan (PneumoADIP)

The IPPPH identified a number of significant underlying characteristics common to these product development partnerships. In particular, they use some private sector approaches to attack R&D challenges; target one or more 'neglected diseases'; use or intend to use variants of the multi-candidate/ portfolio approach; have public health rather than a commercial goal as their primary objective; and focus on developing products suited for use in developing countries.[24]

These similarities stem from a range of common needs that arise from the nature of the product development process:

- engagement of industry, public/ governmental agencies and civil society organizations as necessary;
- sufficient resources to implement their chosen strategies;
- strategies for management of intellectual property and leveraging R&D investments to assure product access for the poorest populations.
- access to clinical trial capacity;
- access to regulatory experience including that relevant to LMICs;
- access to expertise in assessing need, demand and markets for their products particularly in LMICs.

- access to expertise in assessing production options and their costs.
- knowledge of the best strategies for delivering products to the poorest, including ways to work effectively with/within the existing health services infrastructure.
- ways of measuring progress, in product development or delivery, or health status.
- strategies for ensuring that non-contractual allies in the collective efforts to develop and improve access to health products actually fulfil their responsibilities and obligations.

Ten years after the launch of the first of this new breed of product development partnerships, they appear to hold considerable promise for fulfilling the expectations that have been generated. A review[25] of the new landscape of neglected disease drug development, published in 2005, concluded that the drug development partnerships were performing well by industry standards. Whereas only 13 new drugs had been developed for neglected tropical diseases in the last quarter of the 20th century, by the end of 2004 there were over 60 neglected disease drug development projects in progress, including two new drugs in registration stage and 18 new products in clinical trials, half of which were already at Phase III. PPPs were conducting three-quarters of all the identified projects and, assuming sufficient funding and standard attrition rates, these PPP activities alone would be expected to deliver six to seven new drugs within five years.

However, in terms of financing for these activities, the picture was worrying. The breakdown of cumulative philanthropic and public funding allocated and committed to the drug development partnerships up to April 2005 (amounting to US$ 255 million), showed that the major contributors had overwhelmingly been the philanthropic foundations (responsible for 78.5% of the total), with governments (United States of America, United Kingdom, the Netherlands, Switzerland, European Commission) contributing only 16.2%. Noting the substantial increases in funding that would be necessary as a number of promising candidates began to progress to Phase III clinical trials, the report concluded that large increases in public sector funding would be necessary within the next few years if the product development partnership approach is to succeed in delivering products into clinical use.

Since the publication of the report, there have been some encouraging signs in this regard, with major new commitments to support product development partnerships announced by several governments, including Ireland,[26] the Netherlands,[27] the United Kingdom[28] and United States of America[29]. Another welcome step was the formation of a coordinating group of the main donors that support PPPs for product development, which first met in Mexico at the time of Forum 8 in 2004.

The expanding pipelines of candidate products for fighting a number of diseases has created an awareness of the need to ensure that these candidates can be efficiently tested and brought into clinical use. With a few notable exceptions, such as IAVI, the majority of product development partnerships have concentrated their meagre resources on the immediate challenge of identifying potential products and bringing these towards clinical trials. A crucial gap has become apparent in the capacities of many disease-endemic countries to conduct appropriate clinical trials. The European and Developing Countries Clinical Trials Partnership was established as a partnership

between 14 European Union countries, Switzerland and Norway on one hand, and African countries on the other. Its mission is to accelerate the development of new or improved drugs and vaccines against HIV/AIDS, malaria and tuberculosis, with a focus on Phase II and III clinical trials and on sub-Saharan Africa.[30]

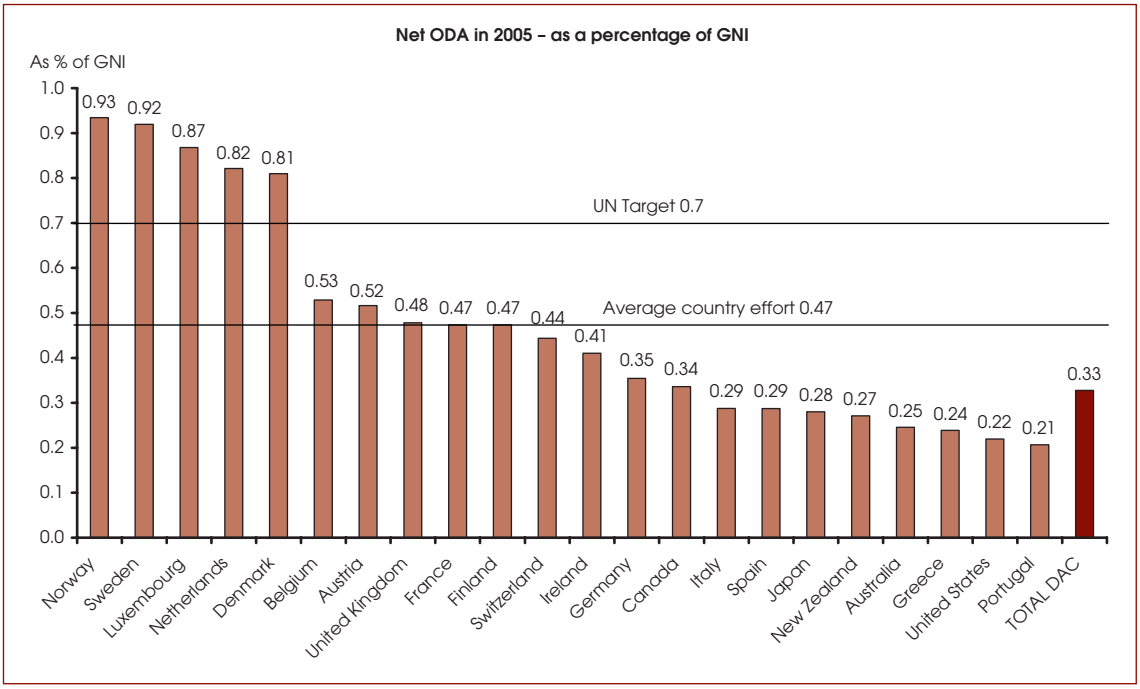
Despite the welcome signs of growing attention to the 'big three' diseases, a number of other tropical diseases continue to be severely neglected. According to one study, hookworm, schistosomiasis, leprosy, and 10 other neglected tropical diseases affect at least as many poor people as the big three, while for US$ 0.4 per person a year, four existing drugs could be used to quickly reduce the harm caused by seven of these scourges.[31]

There have been increasing signs of commitments by governments to tackling global development and health priorities, including finding the necessary funds.

At the 2002 International Conference on Financing for Development in Monterrey, Mexico,[32] world leaders pledged "to make concrete efforts towards the target of 0.7%" of their gross national income (GNI) being used in Official Development Assistance (ODA) – a target first pledged in a 1970 United Nations General Assembly resolution. In 2003, total aid from the 22 richest countries to the world's developing countries amounted to US$ 69 billion – a shortfall of US$ 130 billion from the 0.7% promised for international aid each year and equivalent to an average of 0.25% of GNI in ODA. Five countries have already met or surpassed the 0.7% target: Denmark, Luxembourg, the Netherlands, Norway and Sweden (Figure 1.2).[33]

Collectively, the European Union (EU) is the world's largest donor, contributing over half of the world's development assistance. In May 2005 development ministers from the original 'EU-15' member states met in Brussels and announced that they would all set timetables to meet the 0.7% target by 2015. In addition, the 'new' EU countries (which joined the EU after 2002) will achieve 0.33% by 2015.[34] Several countries including Belgium, Finland, France, Ireland, Spain and the United Kingdom (Box 1.5), have committed to a timeline to reach the target before 2015, but other countries still have much to achieve in this regard (Figure 1.3).[35] Furthermore, as noted by the president of the World Bank (Box 1.6), the United States of America is paradoxically the world's largest donors of ODA in cash terms, but along with Japan is one of the smallest contributors (as a percentage of GNI) of OECD members.[36]

Figure 1.2
Official Development Assistance in 2005 as a percentage of GNI



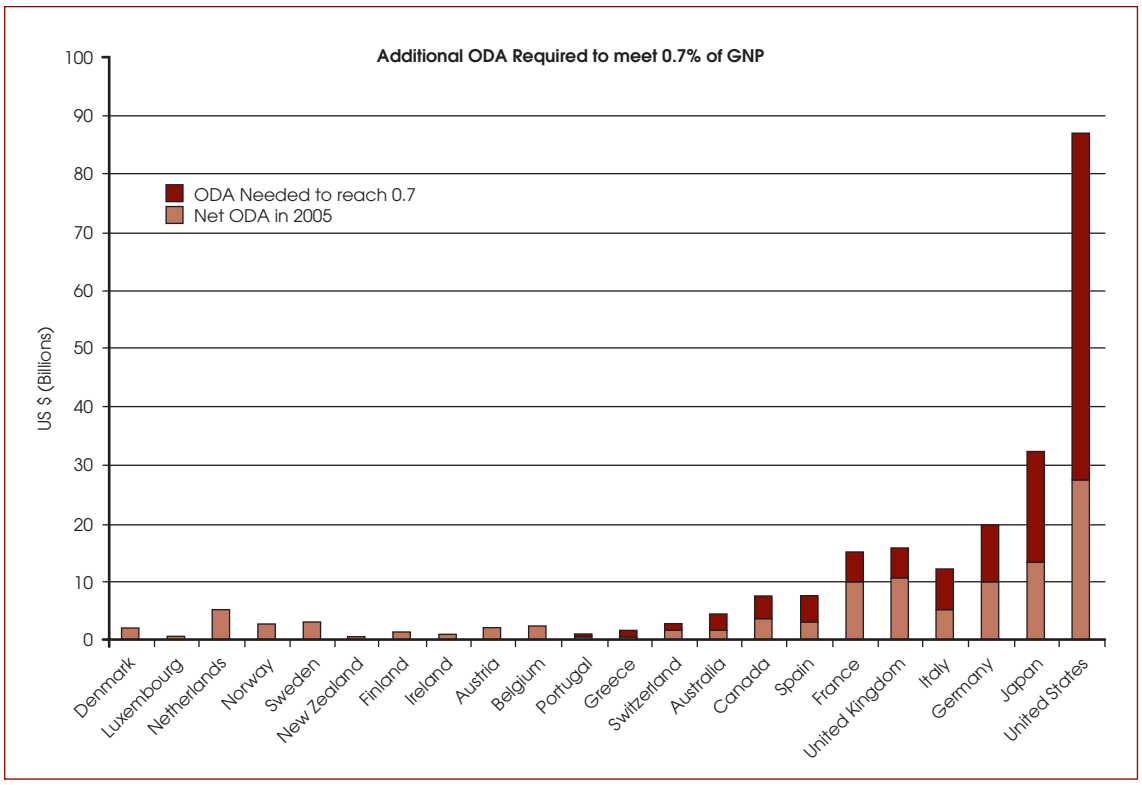
Source: OECD[33]

Box 1.5
Commitments to Reach 0.7% GNI

Belgium	0.7% by 2010
Finland	0.44% by 2007 and 0.7% by 2010
France	0.5% by 2007 and 0.7% by 2012
Ireland	0.7% by 2007
United Kingdom	0.47% by 2007-2008 and 0.7% by 2013
All members of the EU 15	0.56% by 2010 and 0.7% by 2015

Data from Sachs[35]

Figure 1.3
Additional ODA required to meet 0.7% of GNP



Box 1.6
Foreign Aid: Challenges and opportunities

The Gleneagles summit of G-8 countries in 2005 made a commitment to double aid to Africa from US$ 25 billion to US$ 50 billion by 2010, and to provide complete debt relief to some of the poorest countries in the world, most of them in Africa, with a debt cancellation package that will amount to US$ 37 billion when it is completed.

The United States is one of the largest sources of development assistance in the world today. According to the OECD, US ODA in 2005 was US$ 27.5 billion, up from nearly US$ 20 billion the year before. But still… it's only barely 0.2 percent of the gross national income. It's also true that Americans are doing a lot with security assistance, and it's also true that Americans are doing a lot as individuals. Americans give private charitable contributions to poor countries totaling approximately $10 billion per year. And it may well be argued that some of that is more effective than official assistance. That generosity is laudable in its flowering, but I don't think it removes either the moral obligation or the necessity for the U.S. government to do more.

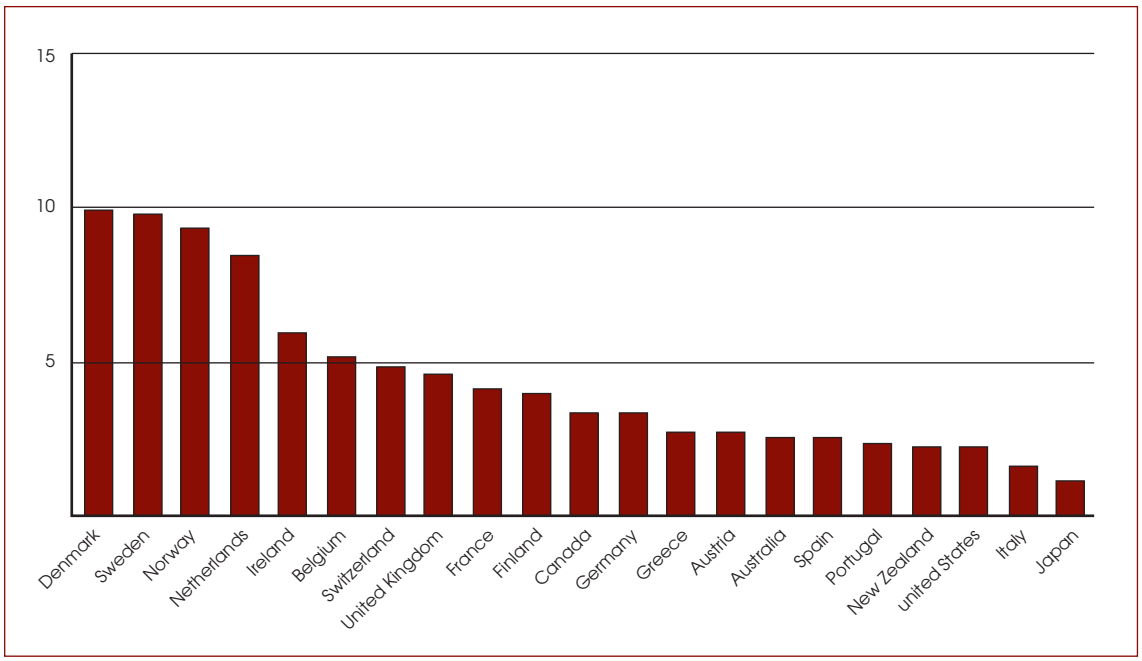
In 2005, the U.S. committed to doubling its aid to sub-Saharan Africa by the year 2010. That's a welcome step toward increasing overall aid and concentrating more of it in countries that need it the most. The United States continues to be an important source of funding for the World Bank, including for more than 13 percent of IDA funding. However, U.S. commitment to IDA has declined from a historical level of 20 percent to the current 13. And when the U.S. wavers in its support, that becomes deeply worrying, because other donor countries look to the U.S. for leadership and adjust their own contributions in response. The discussions for replenishing IDA, the so-called IDA 15 replenishment, will start early next year, and I hope there will be a strong and positive U.S. engagement.

Extract from speech by World Bank president Paul Wolfowitz at the Heritage Foundation, Washington, DC, 31 July 2006

The quality of development assistance is as important as its quantity, if the aid is to be effective. Much aid that currently is given is unpredictable, driven by donor objectives, and tied to contractors from donor countries. In low-income countries, only about 24% of bilateral aid actually finances investments on the ground.[35] A report from ActionAid[37] says that too much development aid is swallowed up by high consultancy fees, excessive administration costs, and poorly targeted actions that favour the interests of donors rather than recipients, so that only 50% of development aid is reaching the poor. According to ActionAid, 47% of the US$ 62 billion worth of global development aid is redundant because it is poorly allocated, tied to donor's own goods and services, highly conditional, badly coordinated and exaggerated through double counting of debt relief measures. The EU-15 doesn't score too badly compared to other donors, with eight countries (Belgium, Denmark, Finland, Ireland Luxembourg, the Netherlands, Sweden and the United Kingdom) among the top ten 'real aid' donors. Nevertheless, because only around 57% of aid from EU countries is targeted effectively, ActionAid argues that real EU development aid amounted to only 0.2% of GNI in 2004 – far from the 0.7% target. Furthermore, four EU members (Austria, Greece, Italy and Spain) are at the bottom of the donor league along with the USA and Japan.[38]

The Center for Global Development publishes an annual Commitment to Aid Index which assesses both quantity and quality of development assistance. On the series of criteria used, some of the countries committing the lowest proportion of their wealth to international development assistance are also making this aid least effective (Figure 1.4).[39]

Figure 1.4
2006 Commitment to Development Index (aid effectiveness in 2005)



Source: Center for Global Development[39]

In addition to the efforts by individual governments to increase their spending on development assistance, collective mechanisms have also gained attention:

- While the 2002 International Conference on Financing for Development had pledged to provide an additional US $16 billion a year from 2006, this still falls short of the estimated additional US$ 50 billion a year required to finance achievement of the MDGs. In January 2003 the United Kingdom launched a proposal for an International Finance Facility (IFF) to bridge this gap. The IFF mechanism would frontload aid, providing up to an additional US$ 50 billion a year in development assistance until 2015. This would be achieved through leveraging money from the international capital markets by issuing bonds, based on legally-binding long-term donor commitments; donors would be responsible for repaying bondholders using future donor payment streams; and the resources would be disbursed through existing multilateral and bilateral mechanisms.[40]
- Pending an agreement among all major donors to adopt the IFF, in September 2003 the United Kingdom, together with France, Italy, Spain and Sweden, initiated an International Finance Facility for Immunization (IFFIm) which will provide an extra US$ 4 billion over the next 10 years. IFFIm will support the work of the Vaccine Fund and GAVI to improve access to underused vaccines and to speed up the development and introduction of new vaccines in poorer countries. It is hoped that, by giving up-

front long-term financial commitments from donors to provide additional resources in a more stable and a more predictable way, the facility will not only enable immediate vaccination of a much larger number of people than would otherwise have been possible, but will also provide more certainty for manufacturers to invest in new and under-used vaccines and accelerate the reduction of vaccine prices.[41]

- In March 2005, France called for a tax on airline fuel and tickets to provide funds to fight epidemics in Africa[42] – a variation of the 'Tobin Tax', named after American Nobel laureate James Tobin who in 1971 suggested taxing capital flows as a way of reducing speculation on global markets.[43] On 1 July 2006, France and Gabon became the first countries to introduce a tax on aeroplane tickets to finance development aid for poor countries.[44] In France, the tax will range from €1 to €40, depending on the distance travelled and the type of ticket, and is expected to raise around €200 million a year. Gabon will impose a levy of €1 to €4. France has announced that 90% of the funds collected will be used to pay for AIDS drugs for the poor and the remaining 10% will be allocated to the International Finance Facility launched by the United Kingdom. The airline levy was approved, on a voluntary basis, by EU finance ministers in May 2005, despite strong opposition from the airline industry. By August 2006, Brazil, Chile, Congo, Côte d'Ivoire, Cyprus, Jordan, Luxembourg, Madagascar, Mauritius, Nicaragua, Norway and the United Kingdom had committed to join the initiative.

One important channel for the overall increases in development assistance in recent years has been in the form of debt relief to heavily indebted poor countries (HIPCs). Through the HIPC Initiative, nominal debt service relief of more than US$ 59 billion of multilateral debt to the World Bank and International Monetary Fund had been approved for 29 countries by mid-2006, reducing their net present value of external debt by approximately two-thirds. Of these countries, 19 reached the completion point and have been granted unconditional debt service relief of over US$ 37 billion.[45] Poverty reducing expenditures are expected to rise from less than twice that of debt-service payments to more than four times, financed in part from resources freed by HIPC debt relief. Some of this extra financing will support development of the health sector.

Within high-income countries, some of the major agencies involved in funding and conducting health research have given increased attention to diseases endemic in developing countries. Estimates of funding for various diseases, conditions, research areas by the NIH are displayed in Table 1.3 and show significant increases in allocations for a number of areas of relevance to LMICs.[46]

Table 1.2
Estimates of funding for various diseases, conditions, research areas by the US National Institutes of Health

Research/Disease Areas (US$ in millions and rounded)[a,b]	2003 Actual	2004 Actual	2005 Actual	2006 Estimate	2007 Estimate
Antimicrobial resistance	181	203	217	218	216
Emerging infectious diseases	1,362	1,807	1,872	1,882	1,814
HIV/AIDS[c]	2,718	2,850	2,921	2,904	2,888
HPV and/or cervical cancer vaccines	15	14	16	16	16
Infectious diseases	2,441	3,055	3,188	3,165	3,137
Malaria	72	89	104	104	107
Malaria vaccine	23	30	44	44	48
Topical microbicides	58	66	66	75	74
Tuberculosis	122	137	158	158	158
Tuberculosis vaccine	13	18	26	26	26

[a] Note: the table is not additive. Funding included in one area may also be included in other areas.
[b] Table updated 10 March 2006. The data are based on actual grants, contracts, research conducted at NIH, and other mechanisms of support in 2003 through 2005. The 2006 and 2007 figures are estimates, and are based on the 2005 levels, the 2006 enacted level, and the 2007 Budget.
[c] Includes research on HIV/AIDS, its associated opportunistic infections, malignancies and clinical manifestations as well as basic science that also benefits a wide spectrum of non-AIDS disease research.

The United Kingdom's Medical Research Council (MRC) collaborates with the Department for International Development (DFID) to tackle the priority health problems of people in developing countries. MRC funding for research in this area is focused on combating infectious diseases, including malaria, HIV/AIDS, TB and childhood infections. The MRC has an agreement with DFID to coordinate policies for research into the health of developing societies, and to help share resources. In 2002/3 the total MRC/DFID portfolio amounted to £22.5 million per annum, to which DFID contributed approximately £4 million. The MRC is currently funding extensive programmes of work on poverty-related disease in Africa, in the Gambia, Tanzania, Kenya and Uganda. The MRC also supports research programmes in China, India and Jamaica, addressing a narrower range of conditions including reproductive health, nutrition, and sickle-cell disease. MRC-funded research in developing countries is intended to help identify the mechanisms underlying infection, to design and test new therapeutic interventions which could be used globally, and to help strengthen research capacity within the host countries.[47]

Commitments by developing countries to increase their own financing of health and health research have also increased. The Abuja Declaration[48] was issued in 2001 at a special summit of heads of state and government of the Organization of African Unity (now the African Union, or AU) devoted to addressing the exceptional challenges of HIV/AIDS, tuberculosis and other related infectious diseases. It

acknowledged the need to secure adequate financial and human resources at national and international levels. The participants committed themselves to take all necessary measures to ensure that the needed resources are made available from all sources. They pledged to set a target of allocating at least 15% of their annual budgets to the improvement of the health sector. They also recognized the need to intensify their efforts in all areas of research such as traditional medicines and vaccine development.

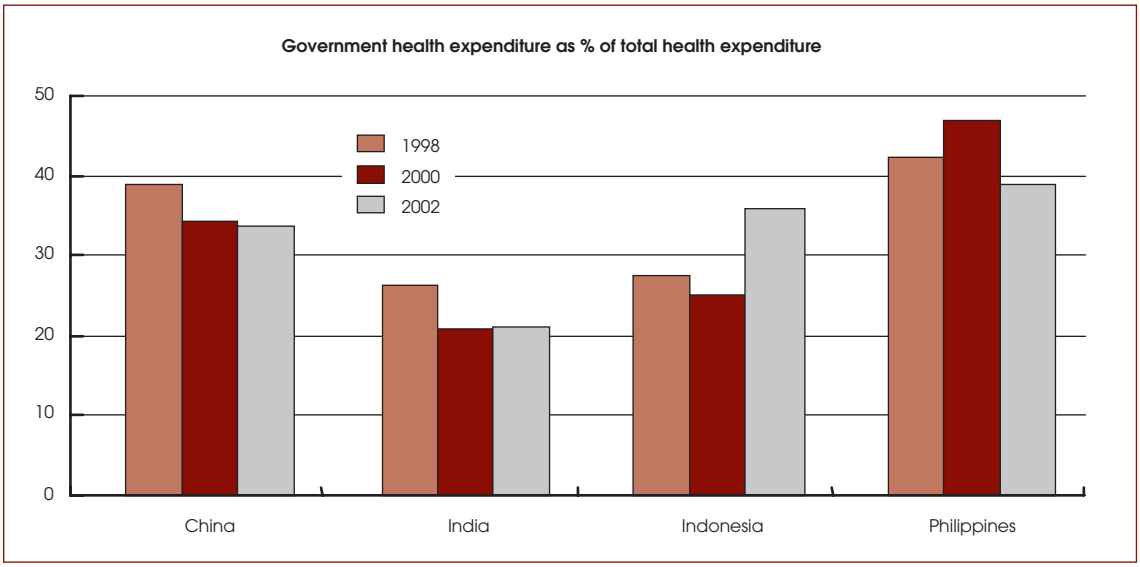
Four years after the International Conference on Health Research for Development in Bangkok, WHO convened a Ministerial Summit on health research, which was held alongside and interfaced with Forum 8 in Mexico City in November 2004. Both meetings had the overall theme of the health research needed to achieve the MDGs and the Ministerial Summit issued a declaration that included commitments to strengthen support for health research and for the translation of its results into effective policy and practice.[49]

Fourteen health ministers and heads of delegations from Africa, Asia, the Middle East and South America met in Accra, Ghana on 17 June 2006 and called for collaborative efforts among countries and regional, bilateral and multilateral organizations to improve upon health research and its application to health needs.[50] They committed themselves to striving to ensure the allocation of at least 2% of the national health budget for health research and to further mobilize other resources from national and international sources.[51]

Government-provided health services in India accounted for only about 18 percent of the overall health spending and 0.9 percent of the gross domestic product (GDP) in 1998. The Indian government has announced its intention to increase the national health budget from less than 1% of GDP to 2% of GDP and to double the proportion of the health budget devoted to health research to 2% by 2010.[52]

In China, as in India, the major share of public expenditure for health is borne at the sub-national levels and the national government spends a low proportion of its GDP on health (see Figure 1.5),[53] with substantial imbalances in provision between urban and rural areas. In 1999, public expenditures on health amounted to 11% of total health expenditures – a fall from 28% of total health costs in 1978, while health costs spiralled up from 3% of GDP in 1981 to 5% in 2001.[54] Total investment in health by the government in 2003 represented 4.54% of total government expenditure and accounted for 17% of the total expenditure on health. Government health spending was 0.95% of GDP, while according to the World Bank, it should ideally be about 2.4% of GDP, given China's existing per capita income level.[55] However, China's government has reaffirmed its determination to take on health system reforms as one of the top public policy issues.[56,57]

Figure 1.5
Government health expenditure as a percentage of total health expenditure



In recent years, a number of developing countries have begun to demonstrate strengthening performance in innovation, characterized by a growing capacity to conduct research, generate intellectual property in the form of patents and translate inventions into manufactured products that are accessible to the public. These 'innovative developing countries' (Figure 1.6),[58] which include Brazil, China, India Malaysia, South Africa and Thailand, have the potential to contribute significantly to the production of health-related products for low income countries.[59,60] To do so, they will require policy and legal frameworks that need to be set nationally and globally – in effect, pointing to the need for a 'global health innovation system,[61] as well as significant levels of public sector investment to ensure that the system delivers products that are accessible and affordable to the poor. One of roles that the innovative developing countries can play is in South-South cooperation, exemplified by the recent announcement by Brazil that it plans to launch a project to boost public-health research in Portuguese-speaking countries in Africa.[62]

Figure 1.6
Economic strength and innovation capability – Innovative Developing Countries

	Low — Innovation Capability — *High*	
High Economic strength *Low*	Natural resource-rich countries and small OECD countries	G8
	Least developed countries and other non-IDC developing countries	Innovative developing countries (IDCs)

The private sector, which accounts for almost half of global health R&D, has been giving more attention to health products for developing countries – in particular, through a range of partnerships that have encompassed research to develop new drugs and programmes to enhance their availability, accessibility and affordability in developing countries.[63,64] According to a survey conducted by the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)[65] and validated by a group at the London School of Economics,[66] in the five years since the setting of the MDGs, 126 health partnerships created by the pharmaceutical R&D industry (see Box 1.7) provided health interventions to help up to 539 million people. In the process, the industry made available medicines, vaccines, equipment, health education and manpower worth US$ 4.38 billion, with the cost of donated medicines valued conservatively at their wholesale price.

Box 1.7

Pharmaceutical industry partnerships to improve health in developing countries

HIV/AIDS

Abbott Access to HIV Care
Accelerating Access Initiative (AAI)
African Comprehensive HIV/AIDS Partnership (ACHAP)
Call to Action
Cambodia Treatment Access Program
China-MSD HIV/AIDS Partnership
Diflucan® Partnership Program
Enhancing Care Initiative (ECI)
Gilead Access
GlaxoSmithKline's Positive Action on HIV/AIDS
GSK's HIV-collaborative research program for resource-poor settings
HIV/AIDS Awareness and Education
HIV South Africa
Infectious Diseases Institute
Integrated Approach to addressing HIV/AIDS in the Caribbean
International AIDS Vaccine Initiative (IAVI)
International Partnership for Microbicides (IPM)
Mission for Essential Drugs & Supplies (MEDS)
PMTCT Donations Program
Secure the Future®
Step Forward - Abbott Program Helping Children & Families Affected by AIDS
Tanzania Care - Abbott Program for Strengthening Health Systems
Viramune® Donation Program
Women's Global Health Imperative

Tropical Diseases

Bayer HealthCare Dengue Fever Health Campaign
Global Alliance to Eliminate Lymphatic Filariasis (GAELF)
Guinea Worm Eradication Program (GWEP
International Trachoma Initiative (ITI)
Leprosy Elimination
Merck Mectizan® Donation Program
Singapore Dengue Consortium
Sleeping Sickness Program

Vaccine-Preventable Diseases

Cervical Cancer
EPIVAC
GAVI Alliance
Global Polio Eradication Initiative
Infectious Disease Research Institute (IDRI)
IFPMA Influenza Vaccine Supply International Task Force
Merck Vaccine Network - Africa (MVN-A)
Pediatric Dengue Vaccine Initiative (PDVI)
Rotavirus Vaccine Program

Additional Health Initiatives

Abbott
AstraZeneca
Bayer HealthCare
Bristol-Myers Squibb (BMS)
GlaxoSmithKline (GSK)
Johnson & Johnson

Malaria

ACCESS - Understanding and Improving Access to Effective Malaria Treatment
Artekin® International Development Program
Chlorproguanil-dapsone (Lapdap™) - Artesunate (CDA) Drug Development Program
GSK African Malaria Partnership
Impact Malaria
JPMW Alliance (Japanese Pharmaceutical Companies, Japanese Ministry of Health, Labor and Welfare, WHO)
Malaria Vaccine Initiative (MVI)
Medicines for Malaria Venture (MMV)
Multilateral Initiative on Malaria (MIM)
Novartis Coartem®
sanofi-aventis - DNDi Malaria Drug Development

Tuberculosis

Aeras Global TB Vaccine Foundation
AstraZeneca-AMREF Partnership - Strengthening TB control in South Africa
AstraZeneca Bangalore Research Institute
AstraZeneca in Partnership with the Red Cross - Fight against TB in Central Asia
Global Alliance for TB Drug Development (TB Alliance)
GSK - TB Alliance Drug Discovery Program
Lilly MDR-TB Partnership
Moxifloxacin Clinical Trials to Shorten TB Treatment (Bayer HealthCare)
Novartis Institute for Tropical Diseases (NITD)
Novartis TB DOTS Donation
Stop TB Partnership
TB Free
Eli Lilly & Co.
Merck & Co.
Novartis
Pfizer
Roche
sanofi-aventis
Schering AG
VFA German Pharma Association
Wyeth

Emergency Relief Efforts

Abbott
AstraZeneca
Bayer HealthCare
Boehringer Ingelheim
Bristol-Myers Squibb (BMS)
Johnson & Johnson
Eli Lilly & Co.
Merck & Co.
LEEM
Novartis
Pfizer
Roche
sanofi-aventis
Wyeth

Source: IFPMA (2006)[64]

With the multiplication of funding sources and initiatives during recent years, a number of issues have emerged as being of vital importance in health research for development:

- the need to track resources, so that gaps and needs can be clearly identified within the complex pattern of myriad activities under way;[67]
- the requirement for rational mechanisms for setting priorities, so that the available resources can be mobilized in the most effective ways to address the gaps and needs;
- the importance of partnerships to optimize resource mobilization and use;
- the shortage of sufficient numbers of adequately trained health researchers in

developing countries, as well as the lack of systematic organizational mechanisms to harness available capacities.

The Global Forum for Health Research now undertakes the systematic tracking of resources for health research. This tracking is conducted at the level of global aggregates every 2-3 years,[68,69] based on the cycle of production of key data – in particular, by the OECD. In the intervening years the Global Forum produces further reports[70] that analyse segments of the overall picture, such as flows to specific diseases (e.g. HIV/AIDS and malaria) or the contributions of countries and of product development partnerships. The Global Forum has undertaken work with Brazil, India and South Africa, funded by a grant from the Rockefeller Foundation and in collaboration with COHRED, on tracking resource flows for health research. COHRED has also undertaken work in other countries to track research resources.[71] The Global Forum, COHRED and WHO have collaborated in this area to encourage country capacity building and recently, in collaboration with the Pan American Health Organizationm, have assisted in the publication of a study by Brazil's Ministry of Health on the funding of health research in that country.[72] Other work by WHO has examined the inclusion of health research data in National Health Accounts.[73]

In addition to providing information that is essential for policy-makers, the collecting and publishing of information on expenditures in health research is vitally important to build public understanding and support for these investments. For example, studies[74,75] demonstrate that Americans rate research as a high national priority, and they strongly support greater investment by public and private funders, while at the same time they greatly overestimate how much their government spends on health research.

Several approaches to priority setting have evolved since the 1990 report of the Commission on Health Research for Development. COHRED has played a leading role in priority setting in the context of its promotion of essential national health research in developing countries[76] and has continued to develop work on the management of the priority setting process.[77] Synthesizing the approaches of the WHO Ad Hoc Committee on Health Research[78] and others, the Global Forum created a 'combined approach matrix' as a methodology to assist priority setting. This enables a 'mapping' of the available information, as a key step in identifying the gaps in knowledge and tools and in the opportunities to address them.[79]

New partnership arrangements have emerged as a major factor in achieving a critical mass of financial, human and institutional resources for health research applied to the needs of developing countries. As indicated in many of the examples above, these partnerships are extremely varied in their nature, encompassing a wide range of combinations and permutations of the public, philanthropic and private sectors; policy-makers, financers and researchers; and institutions and individuals (separately and in regional and global networks) in high-middle- and low-income countries. COHRED and the Global Forum have built upon a long-standing, informal partnership with a new, formal agreement aimed at strengthening collaboration, reducing fragmentation of effort and increasing efficiency in their efforts to promote more health research for development.[80]

A major focus on human resources for health has been seen during 2006, with the critical

shortages, especially in Africa but also in many other LMICs, being highlighted in the World Health Report and in the World Health Assembly.[81] Alongside this, an initiative led by COHRED and supported by the Global Forum has drawn attention to the critical shortage of human resources for health research. In collaboration with several networks in sub-Saharan Africa, a meeting supported by Canada's International Development Research Centre was held in Nairobi in July 2006 to examine this subject and to initiate work by the African networks to address the critical gaps.[82]

1.3 The way ahead

The great scope of changes observed in the landscape of funding for health research for development in recent years – changes both in the range of actors and in the magnitude of funding available – offers encouragement that this decade may indeed be seen as a turning point in history.

However, for this hope to be fulfilled, several further questions need to be answered:

- Will the increases in resources for health research continue, eventually reaching the scale needed to ensure adequate financing for the full range of activities required, including product R&D and research at country level to improve services, eliminate health inequities, elucidate the social determinants of health and provide evidence-based pathways to better health for all?
- Within this overall set of goals, will funding allocations take account of the changing epidemiological and demographic profiles of developing countries, or remain concentrated on a few high-profile diseases and conditions?
- Will countries take up the challenge of building and resourcing national health research systems, to ensure that they create and systematically utilise research capacities as an integral part of their efforts to improve health?
- Will those countries that are rapidly developing their innovation capacities create legal frameworks and practical environments, including state investments with public resources where necessary, to ensure that innovation works to benefit the health of needy populations, rather than producing only expensive products for rich markets?
- Will the public sectors of all countries show the individual and collective commitments needed to finance the required spectrum of research for health – research not only into disease states but also into the wider, underlying causes of ill health (e.g. social and other determinants of health that lie outside the health sector) and into developing a deeper understanding of the factors necessary for people to achieve and sustain overall good health and well-being?

The following two chapters present the most recently available data, covering the year 2003, on the world's resources for health research, and examine global trends in mortality and morbidity. The final chapter looks at how far this information answers the questions about the road ahead.

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77 *Working Paper 1: Priority Setting for Health Research: Toward a management process for low and middle income countries*. Geneva, Council on Health Research for Development, 2006 (http://www.cohred.org/priority_setting/COHREDWP1%20PrioritySetting.pdf).

78 WHO Ad Hoc Committee on Health Research Relating to Future Intervention Options, 1996. *Investing in health research and development*. WHO, Geneva (http://www.who.int/tdr/publications/publications/investing_report.htm).

79 Ghaffar A, de Francisco A and Matlin SA., eds. *The Combined Approach Matrix: A priority-setting tool for health research*. Geneva, Global Forum for Health Research, 2004 (http://www.globalforumhealth.org/filesupld/90.pdf).

80 COHRED and the Global Forum for Health Research. *Memorandum of Agreement*. 2005 (http://cohred.org/cohred/RenderDocument.action?DocumentId=3326&CategoryId=57).

81 *The World Health Report 2006 – Working together for health*. Geneva, World Health Organization, 2006 (http://www.who.int/whr/2006/en/).

82 Council on Health Research for Development, 2006. *Human Resources for Health Research: an African Perspective. Executive Summary of an Expert Workshop, Nairobi, 2-5 July 2006* (http://www.cohred.org/HR-HR/HRHR-Africa/Home.htm).

Chapter 2

Global financing and flows

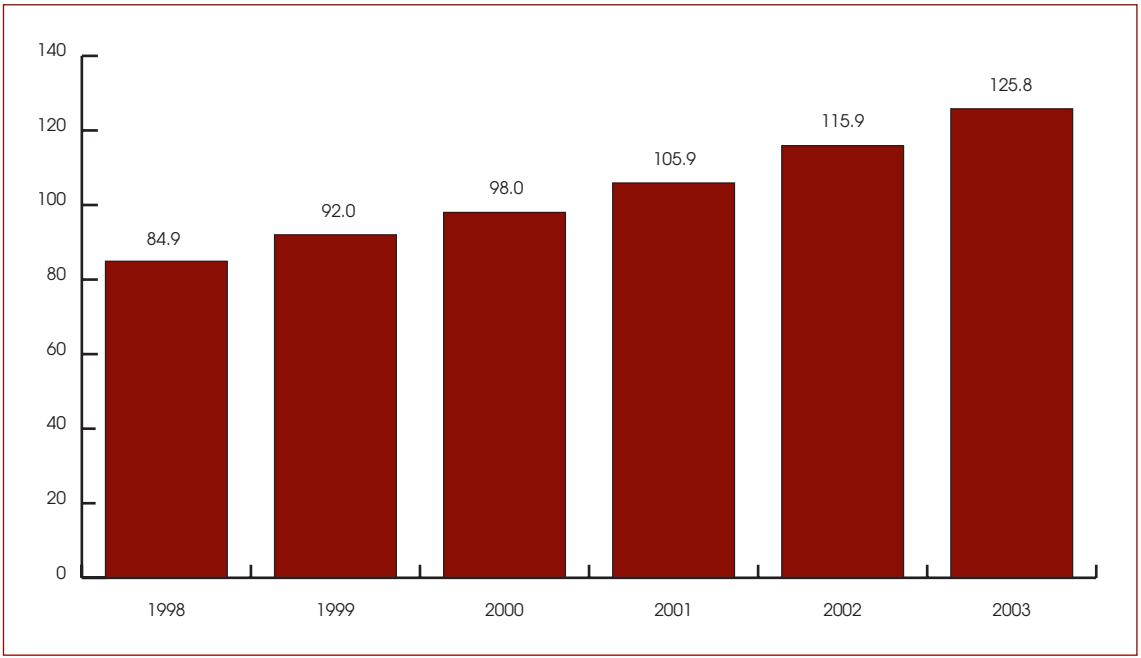
Global financing and flows

2.1 Total global spending on R&D for health

2.1.1 Global spending

Global spending on research and development (R&D) for health continues to increase. In 2003, an estimated US$ 125.8 billion were spent globally on such R&D, up from US$ 105.9 billion in 2001 and US$ 84.9 billion in 1998, see Figure 2.1. R&D spending represented 3.6% of total estimated national health expenditures worldwide in 2003, up from 3.5% in 2001 and 2.8% in 1998.

Figure 2.1
Estimates of total expenditures on research for health (US$ billions)



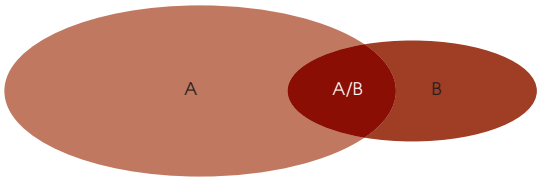
Source: Global Forum for Health Research estimates based on data from official reports to OECD and RICYT, national surveys, pharmaceutical association and other publications

As in the 2001 and 2004 editions of this report, the expenditures described above correspond to the R&D for health funded by and carried out in high income countries (HICs – corresponding to Area A in Figure 2.2, below); that funded by and carried out in low and middle income countries (LMICs – Area B); and, where these efforts converge and overlap – R&D primarily funded by HICs and carried out in and for the primary benefit of LMICs (Area A/B)

Figure 2.2
Graphic representation of global research for health funding

A = R&D by high-income countries (HICs)
B = R&D by low and middle-income countries (LMICs)
A/B = R&D funded by HICs in or for application in LMICs and in LMICs for the benefit of HICs (see text for details)

1 Proportions for surfaces A, B and A/B are indicative only



Since 1990 when the Commission on Health Research for Development made the first attempt to track global spending on R&D for health, considerable efforts have been made to increase understanding of how much is being spent on research for health and by whom, what types of research it encompasses, how research funds flow within and among countries, and in particular, how well these expenditures are addressing the health needs of low- and middle-income countries.

Since the commission's estimate of US$ 30 billions in 1990, WHO, COHRED, the Global Forum for Health Research, and others have continued to call for country-level tracking of investment in R&D for health, and have carried out various pilot projects, multi-country and one-off studies over the years. Despite these efforts, there is still not a single country in the world that routinely collects and reports on data on expenditures on R&D for health.[1]

The data in this report, as in previous reports, are therefore very rough estimates derived from a sophisticated estimation methodology developed over years.[2] These estimates of R&D for health expenditures are calculated as a proportion of overall spending on R&D reported to the Organization for Economic Cooperation and Development (OECD) and to the Network on Science and Technology on Science and Technology Indicators – Ibero-American and Inter-American (RICYT), and in the cases of non-reporting countries, from national data, and from pharmaceutical associations.

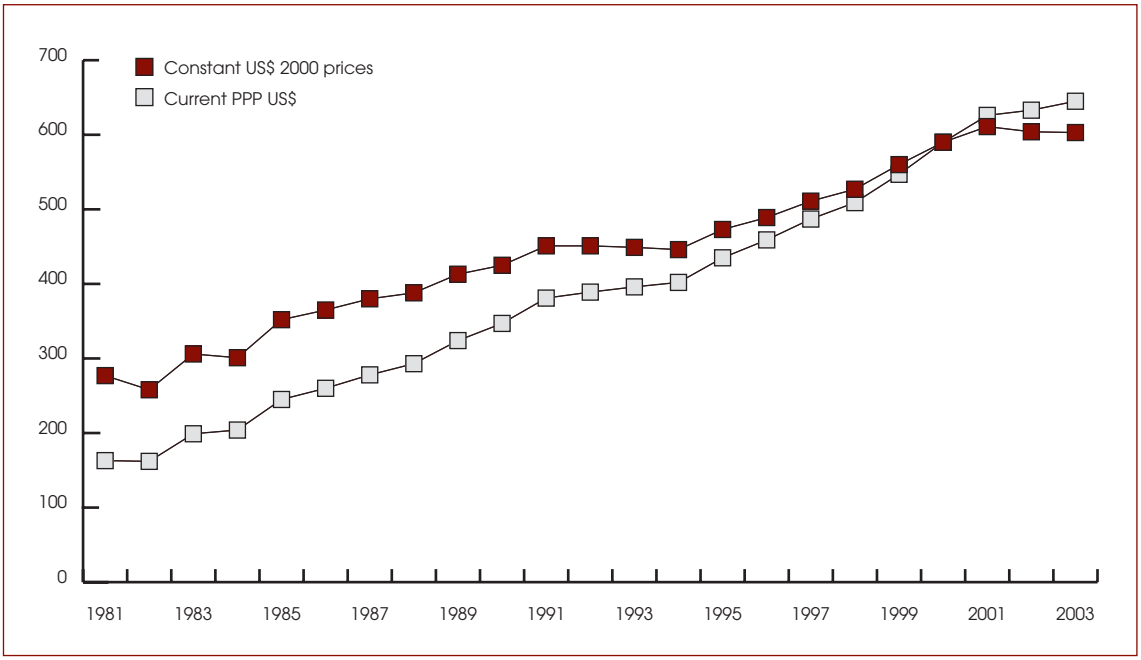
2.1.2 Growth in global investments in R&D for health

While the overall estimated growth in global investments described in this report reflects a growing worldwide commitment to invest in R&D for health, it is clear that some of the increase is a function of the model used to produce the estimates. In the absence of real data, the model assumes a certain degree of stability in the relationship between total R&D expenditures and R&D for health expenditures over time. As such, caution should be exercised in analysing trends over time and among countries.

Nonetheless, it is likely that there has been a real increase in global expenditures on R&D for health, given the steadily growing global commitment to overall R&D reported to the OECD. For example, in 2003, the global overall R&D spending reported to the OECD totalled US$ 603 billion in constant 2000

US$, reflecting a relatively steady increase in expenditures since 1981 when the data were first collected and reported on by the OECD, see Figure 2.3.

Figure 2.3
Global total R&D expenditures, in constant 2000 US$ and current Purchasing Power Parity (PPP) adjusted US$



Source: OECD Science, Technology and R&D Statistics, Volume 2005/2

Figure 2.3 shows a much steeper and more continuous increase in overall R&D expenditures when dollars are adjusted using Purchasing Power Parities (PPPs), increasing to US$ 645 billion in 2003 from US$ 163 billion in 1981. Section 2.2.4 of this chapter examines data adjustment issues in more detail, focusing on R&D for health expenditures among OECD-reporting countries.

2.1.3 Global resource flows on research for health

In 2003, approximately 20% of the total global R&D expenditure is estimated to have been for health research. As Table 2.1 shows, the increase in estimated expenditures on research for health has come from both the public and private sectors. Globally, public expenditures on such research accounted for an estimated US$ 56.1 billion, and private sector expenditures were US$ 69.6 billion, split between for-profit companies (US$ 60.6 billion) and not-for-profit organizations (US$ 9 billion). This distribution remains relatively unchanged from previous years, with the public sector accounting for 45% of overall R&D for health, the private-for-profit for 48%, and the private-not-for-profit for 7%, see Table 2.1.

Of the estimated US$ 20 billion increase in R&D for health expenditures since 2001, 48% or US$ 9.5 billion came from the public sector, 47% or US$ 9.4 billion from the private-for-profit sector, and 5% or US$ 0.9 billions from the private-not-for-profit sector.

Spending among high-income countries (HICs) accounted for most of the increase globally and followed a similar distribution with the public sector accounting for 43% of total global R&D for health expenditures, the private-for-profit sector for 47% and the private-not-for-profit sector for 7%.

The decrease in expenditures in 2003, noted for low- and middle-income countries (LMICs) in Table 2.1, is more reflective of data gaps then a real drop in spending. Of the 19 LMICs for which data were reported in 2001, just 11 reported new data for 2003. As such, the LMICs estimate for 2003 includes data from 2001 for the remaining countries, making it difficult to analyse changes over time. Some of the decrease in expenditures attributable to this data gap has been offset by the inclusion of data from several new LMICs to the data set, notably China (which includes expenditure data for China, province of Taiwan) and the Philippines.

Table 2.1

Estimated global total R&D for health funding, 2003 (in current billion US$) compared with 2001 and 1998

	2003		2001		1998	
	$	%	$	%	$	%
Total	125.8	100	105.9	100	84.9	100
Total public sector	56.1	45	46.6	44	38.5	45
Total private sector	69.6	55	59.3	56	46.4	55
Total private for profit	60.6	48	51.2	48	40.6	48
Total private not for profit	9.0	7	8.1	8	5.9	7
HICs [a]						
Public sector	53.8	43	44.1	42	36.2	43
Private for profit sector	59.3	47	49.9	47	40.0	47
Domestic pharmaceuticals [b]	53.2	42	44.1	42	35.0	41
Foreign pharmaceuticals [b]	6.1	5	5.8	5	5.0	6
Private not-for-profit [c]	8.6	7	7.7	7	5.6	7
Total HIC	*121.7*	*97*	*101.6*	*96*	*81.8*	*96*
LMICs [d]						
Public sector	2.4	1.9	2.5	2.4	2.3	2.7
Public sector domestic	1.9	1.5	2.0	1.9	1.8	2.1
Public funding from foreign ODA [e]	0.4	0.3	0.4	0.4	0.4	0.5
Public funding for international research [e]	0.07	0.1	0.07	0.1	0.07	0.1
Private for profit sector: foreign and domestic pharmaceuticals	1.4	1.1	1.35	1.3	0.98	1.2
Domestic private not-for-profit	0.08	0.1	0.08	0.1	0.08	0.1
Foreign private not-for-profit [e]	0.3	0.2	0.3	0.3	0.2	0.3
Total LMIC	*4.1*	*3.3*	*4.3*	*4.0*	*3.6*	*4.2*

Sources: Global Forum for Health Research estimates based on data from official reports to OECD and RICYT, national surveys, pharmaceutical association and other publications.

(a) HIC: Israel 2001, Singapore 2001.

(b) Foreign pharmaceutical R&D stands for R&D expenditure outside the United States by US-owned Pharmaceutical Research and Manufacturers of America (PhRMA) member companies and R&D conducted abroad by the US divisions of foreign-owned PhRMA member companies. Domestic pharmaceutical R&D corresponds to the global estimates for the pharmaceutical R&D in HICs reduced from foreign pharmaceuticals R&D.

(c) Private not-for-profit includes US$ 3.1 billion estimated for private General University Funds (GUF) in 2001, and $ 2.5 billion in 1998.

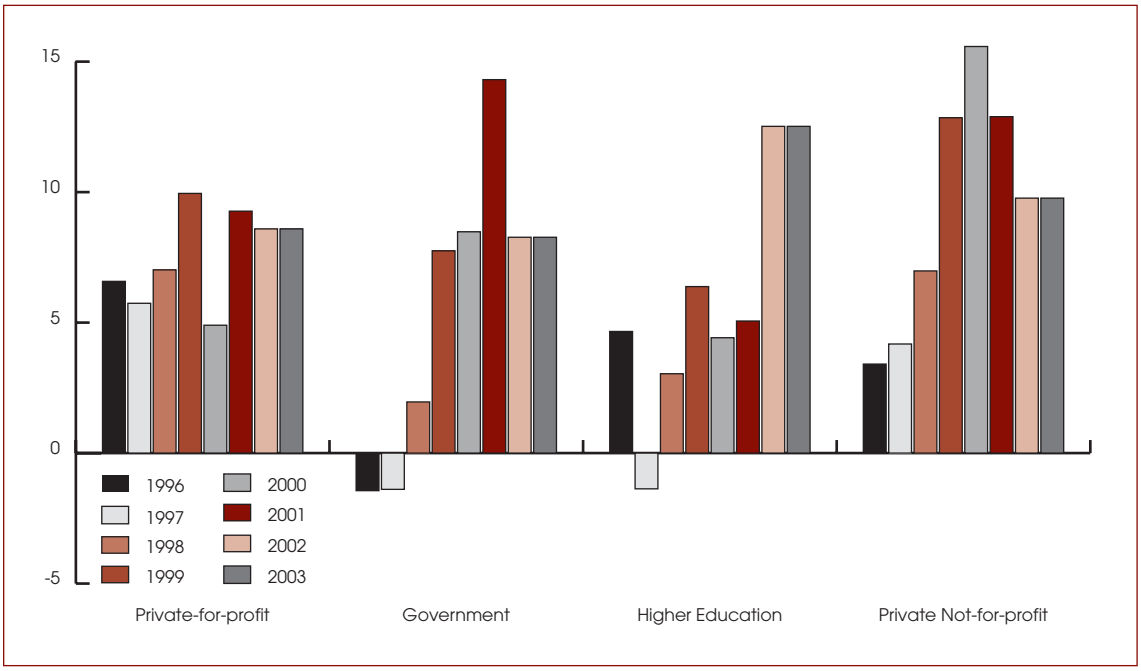
(d) The decline in expenditures noted for LMICs is due to data gaps as many LMICs did not report new data for 2003. Data for China (including China, Province of Taiwan) are from 2001; Brazil for the private sector for 2001 and the public sector 2003; Chile 2001; Cuba 2001; the Philippines 2001; Romania 2001; Russia 2001; Slovenia 2001; South Africa for the private sector for 2001 and the public sector 2003; and Venezuela 2001.

(e) International research, foreign PNP and foreign ODA data are very rough estimates.

2.1.4 Growth in global investments in R&D for health

Among HICs, all sectors experienced growth in expenditures on R&D for health during 2001–2003, although growth varied across sectors. The higher education and private not-for-profit sectors experienced the highest growth, followed by the private-for profit and government sectors. Growth in spending in the higher education sector more than doubled in 2002 and 2003, while growth dropped in all other sectors. The private not-for-profit sector expenditure growth dropped to about 10% from its peak of 16% in 2000, while the for-profit sector dropped only slightly. Growth in government expenditures on R&D for health returned to levels of 1999-2000, following the large spike in growth in 2001 (see Figure 2.4).

Figure 2.4
Annual R&D for health expenditures growth for HIC



Source: Global Forum for Health Research estimates based on OECD data.

2.2 Sectors of performance and sources of funds

2.2.1 Performance sectors

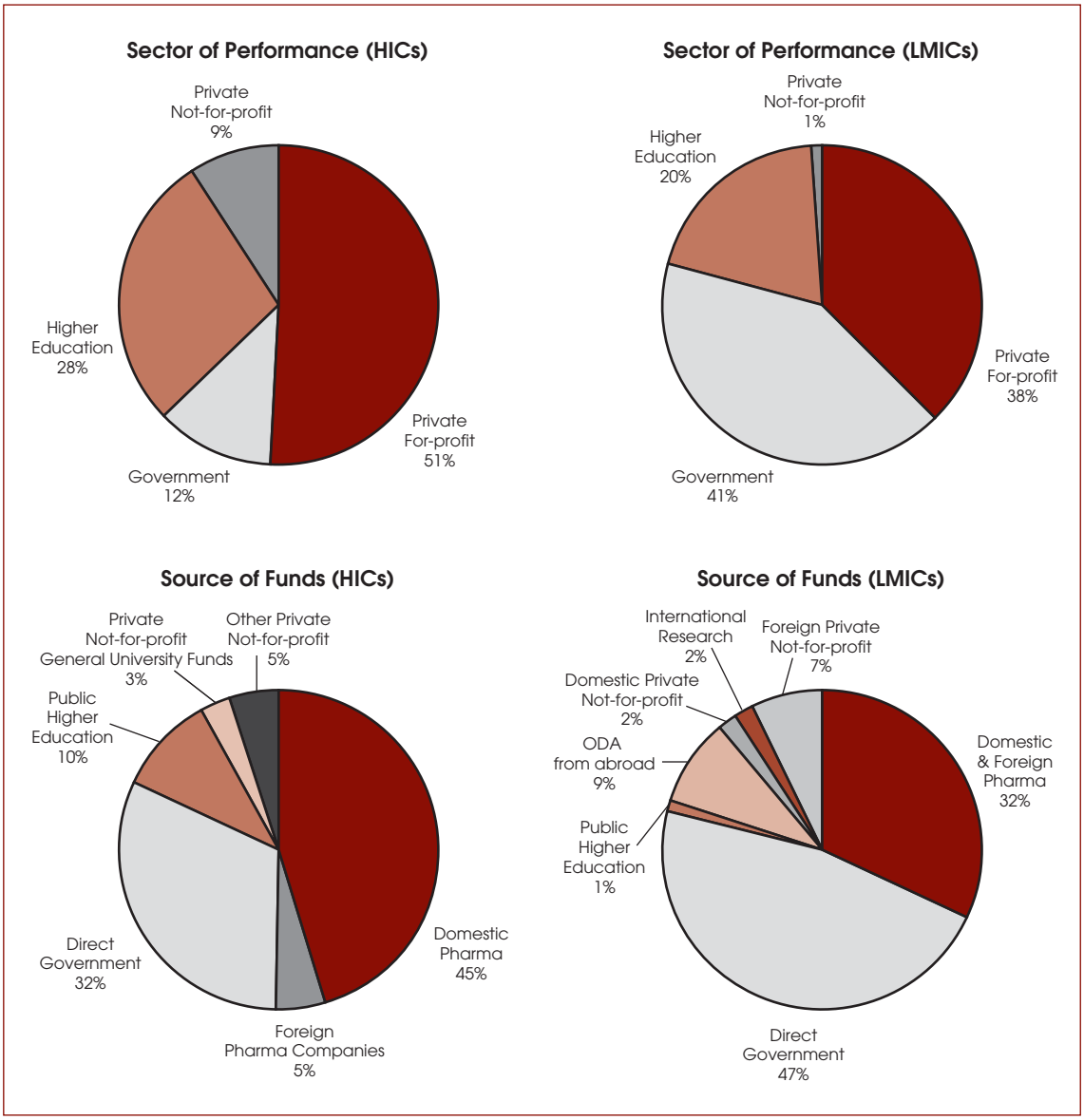
R&D for health tends to be carried out by the same four sectors in both high-income and low- and middle-income countries (see Figure 2.5). Based on officially reported data, the 2003 estimates indicate that the private for-profit sector carried out the majority of research in HICs, accounting for

51% of total R&D for health, compared to 40% for the public sector. Research funded by the private not-for-profit sector accounts for the remaining 9%, and is carried out by independent researchers in universities.

In LMICs, most research was carried out within the public sector (61%), while 38% was carried out in the private-for-profit sector, and the remaining 1% by private-not-for-profits.

Figure 2.5

Sectors of performance and sources of funds for health research, 2003



Source: Global Forum for Health Research estimates based on data from official reports to OECD and RICYT, national surveys, pharmaceutical association, and other publications.

2.2.2 Funding sources

As in earlier years, there were four main sources of funds for health research in 2003:

- private for-profit sector;
- public sector;
- not-for-profit sector;
- various public and private non-domestic sources.

Private for-profit sector

The private for-profit sector is estimated to be the largest investor in research for health globally, according to officially reported data. Pharmaceutical companies accounted for half of all funds for research for health in HICs and 32% in LMICs, see Figure 2.5. Companies based in high-income countries invested in their home countries, in other HICs and to a lesser extent, in LMICs.

Private not-for-profit sector

The private not-for-profit sector includes private universities, foundations and charities. It contributes approximately the same amount of funding in high-income countries (8%) and low- and middle-income countries (9%). ODA accounts for 7% of total funds in LMICs (see Figure 2.5).

Public sector

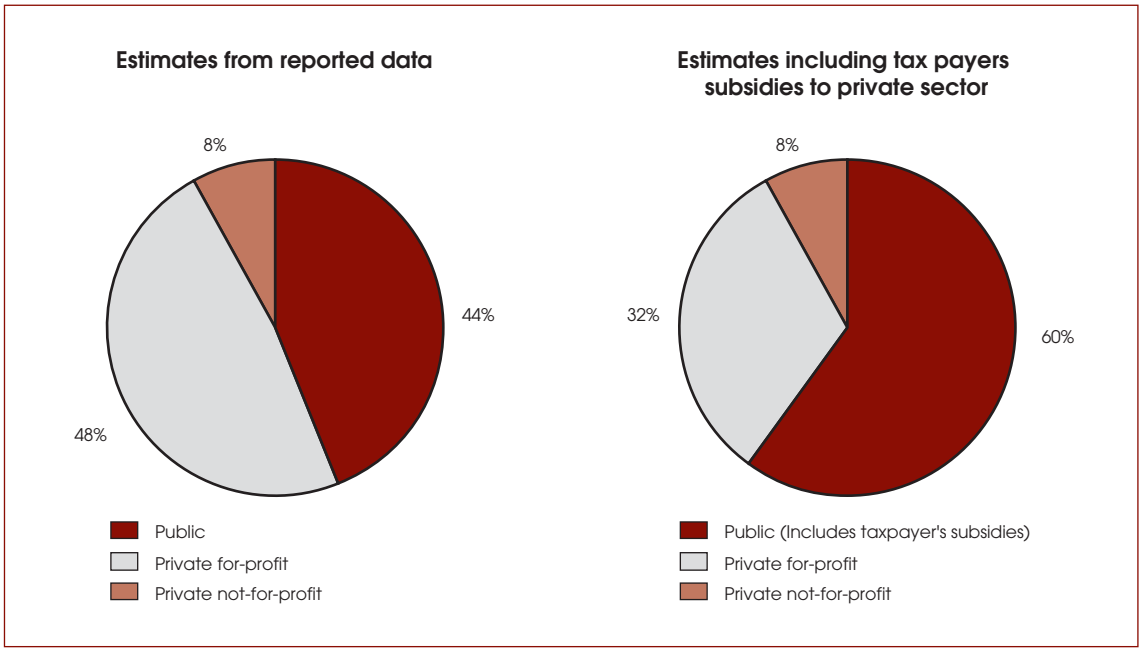
Public contributions to global expenditures on R&D for health are quite significant in size. They are also important as states bear the primary responsibility for the health and rights of their citizens and many are also signatories to international commitments on health. Governments are estimated to be the next-largest funders, in 2003 accounting for 42% of overall funds in high-income countries and 59% in low- and middle-income countries. Governments support research for health through their allocations to ODA, higher education, and direct investments in R&D.

New evidence on public funding to industry

A recent study[3] suggests, however, that estimates based on reported expenditures do not reflect accurately the division between funds provided by the public and private sectors. By factoring in tax deductions, credits and other indirect support private sector companies receive from government, for example as payments for graduate and advanced training of researchers and for the laboratories they use, the study estimates that taxpayers' subsidies to industries would shift an additional 16% of overall global expenditures on R&D for health to the public sector. While acknowledging that "these estimates and calculations are necessarily crude, because the industry does not provide verifiable figures and details about its R&D budget", the study suggests that estimated taxpayers' subsidies to industry may in fact be underestimated.

If these estimates are correct, the public sector would be the largest contributor globally to R&D for health. Taking this estimated taxpayers' subsidy to industry into account, the public sector's share of global expenditures in 2003 would increase from 44 to 60%. Conversely, the private sector share would drop from 48 to 32%, see Figure 2.6.

Figure 2.6
Estimates of R&D for health funding by sector, with and without taxpayers' subsidies to industry, 2003

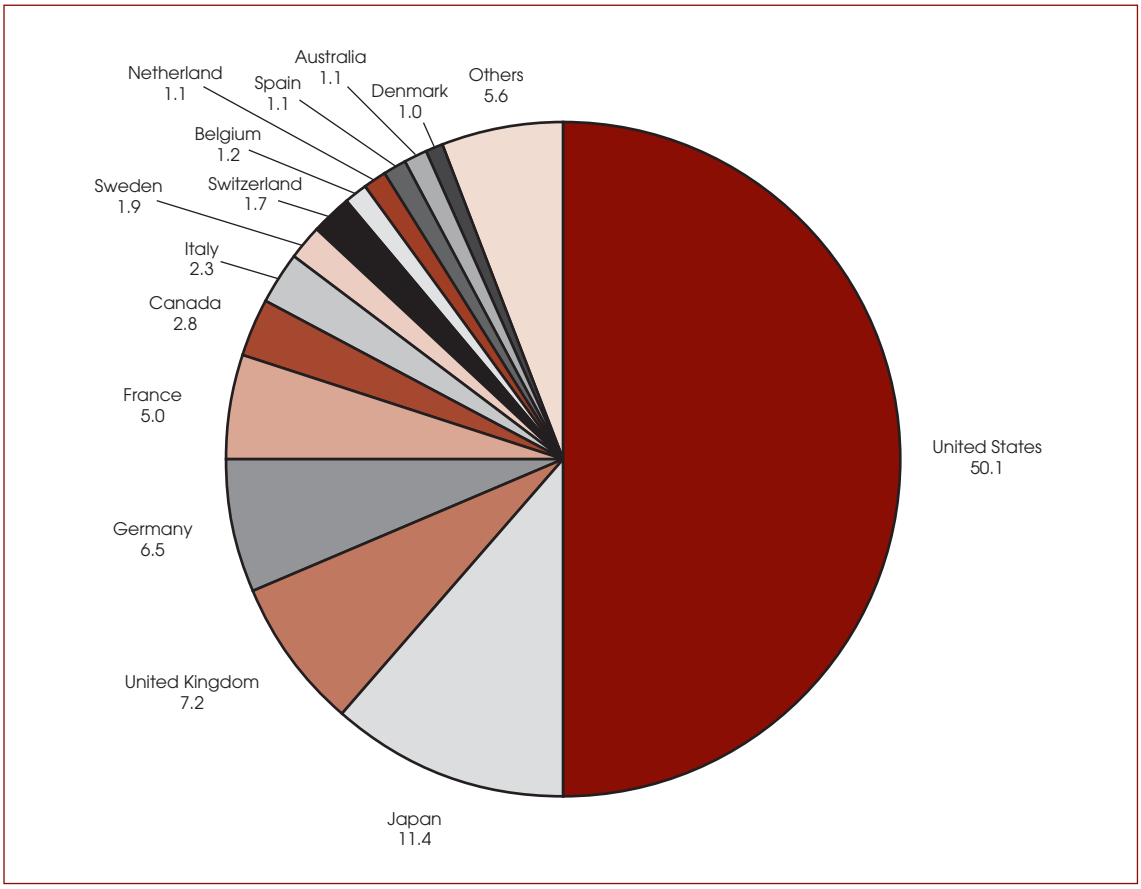


Source: GFHR estimates based on OECD and RICYT databases, national surveys, pharmaceutical associations and calculations from D. Light[3]

2.2.3 Global distribution of expenditures

Global investments in R&D for health remain heavily dominated by just a few countries, led by the United States, which accounts for 50%. Japan (11%), the United Kingdom (7%), Germany (6.5%), France (5%) and Canada (3%) are the next largest investors, see Figure 2.7.

Figure 2.7
Global distribution of R&D for health expenditures, 2003



Source: Global Forum for Health Research estimates based on data from official reports to OECD and RICYT, national surveys, pharmaceutical association and other publications.

National commitments to R&D for health

When a more complex measure than absolute dollars is used, it is evident other countries are also investing significantly in R&D for health. As in *Monitoring Financial Flows for Health Research 2004*, the following section analyses expenditures on research for health along four key dimensions:

1) national R&D expenditure as a percentage of GDP;
2) national R&D for health as a percentage of GDP;
3) national R&D for health as a percentage of national health expenditures; and
4) national R&D for health as a percentage of total R&D.

Countries that score high on the first measure are investing in R&D in general. Countries that score well on the remaining three measures make relatively large investments in R&D for health. Scores for a number of countries are plotted on Figures 2.8 and 2.9.

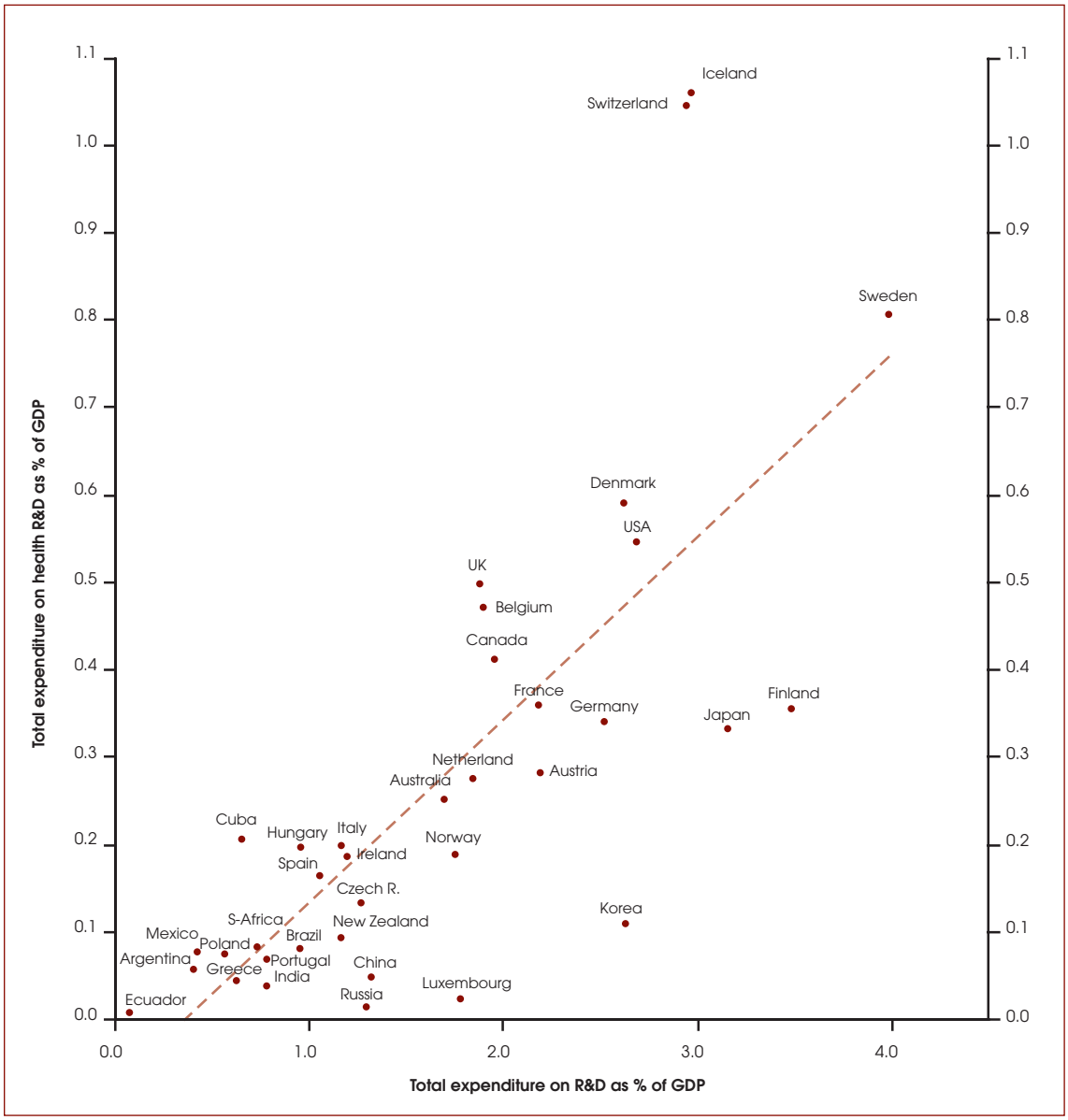
In Figure 2.8, the farther the score is from the vertical axis, the larger the investment in R&D as a proportion of total GDP. The higher up a score is on the vertical axis, the larger the investment in R&D for health as a proportion of GDP. The optimal position on the scatter graph is as far up and to the right as possible.

Sweden scores very high in both overall R&D and R&D for health. Denmark, France and the United States also have strong investments in both areas, as they did in 2001. Finland, Germany, Japan and the Republic of Korea do well in overall R&D but relatively less so in R&D for health than other high-income countries, placing themselves below the diagonal axis, as in 2001. Australia and Austria were below the diagonal in 2003.

Iceland and Switzerland were highest above the horizontal axis in 2003, and with the exception of Sweden, Finland and Japan, had higher expenditures on overall R&D relative to GDP than did other countries. The OECD estimates indicate that Iceland and Switzerland's investments in R&D for health relative to their GDPs are among the highest in the world.[4]

The clustering of low- and middle-income countries at the low end of the diagonal line demonstrates low investments in R&D relative to GDP. Countries that fall above the diagonal line, even if they are near the bottom, such as Argentina, Mexico, Poland and South Africa, have relatively stronger economies and higher investments in R&D for health than countries below the diagonal such as China, India, Russia and Singapore. Typically, developing or transition countries invest first in "bricks and mortar" R&D to get their economies going. When they feel they are on firmer economic footing, they look to build social capital with increasing investment in areas such as R&D for health. Poland and Cuba were above the diagonal in 2003, while Brazil and Russia were below. An appropriate policy goal for all countries is to shift their scores into the upper-right quadrant of the chart.

Figure 2.8
R&D for health and national R&D as a % of GDP



Source: Global Forum for Health Research Estimates based on data from the WHO, the OECD and other publications.

Figure 2.9 looks at countries' investments in R&D for health relative to the size of their health and R&D sectors. In this framework, countries with scores above the diagonal line have above-average investments in R&D for health relative to the size of their health sectors. The farther away the score is from the vertical axis, the higher the investment in R&D for health as a proportion of total R&D.

The data in Figure 2.9 signal a growing commitment to invest in R&D for health in some countries. Once again, Iceland placed first among all countries in its commitment to R&D for health within its overall R&D and in relation to its total health budget, placing it in the far upper right quadrant of the chart.

Sweden has the next highest relative investment in research for health compared to the size of its health and overall R&D sectors, followed by Denmark, Switzerland and the United Kingdom. The relatively low score of the United States and its position below the diagonal once again in 2003, reflects an emphasis on private-sector investments in health in that country.

Finland, Germany and Canada were above the diagonal in 2003, indictating higher spending on R&D for health relative to overall national health expenditures than for countries such as Norway, Ireland, Italy and Mexico, which were all below the diagonal. The Latin American countries and transition countries of the former Soviet bloc whose economies are recovering have relatively higher scores on R&D for health as a proportion of overall R&D than countries above the line such as China, India, the Republic of Korea and Russia. 2003 data for Turkey placed it towards the bottom-left quadrant, close to Poland and Slovakia.

Attention is being paid globally to research developments in a few countries known as Innovative Developing Countries (IDCs). These include: Argentina; Brazil; China; India, Indonesia; Malaysia;, South Africa and Thailand. As our data set includes some of these countries, with the exception of Indonesia, Malaysia and Thailand, we are able to see how they are faring relative to each other and to other countries.

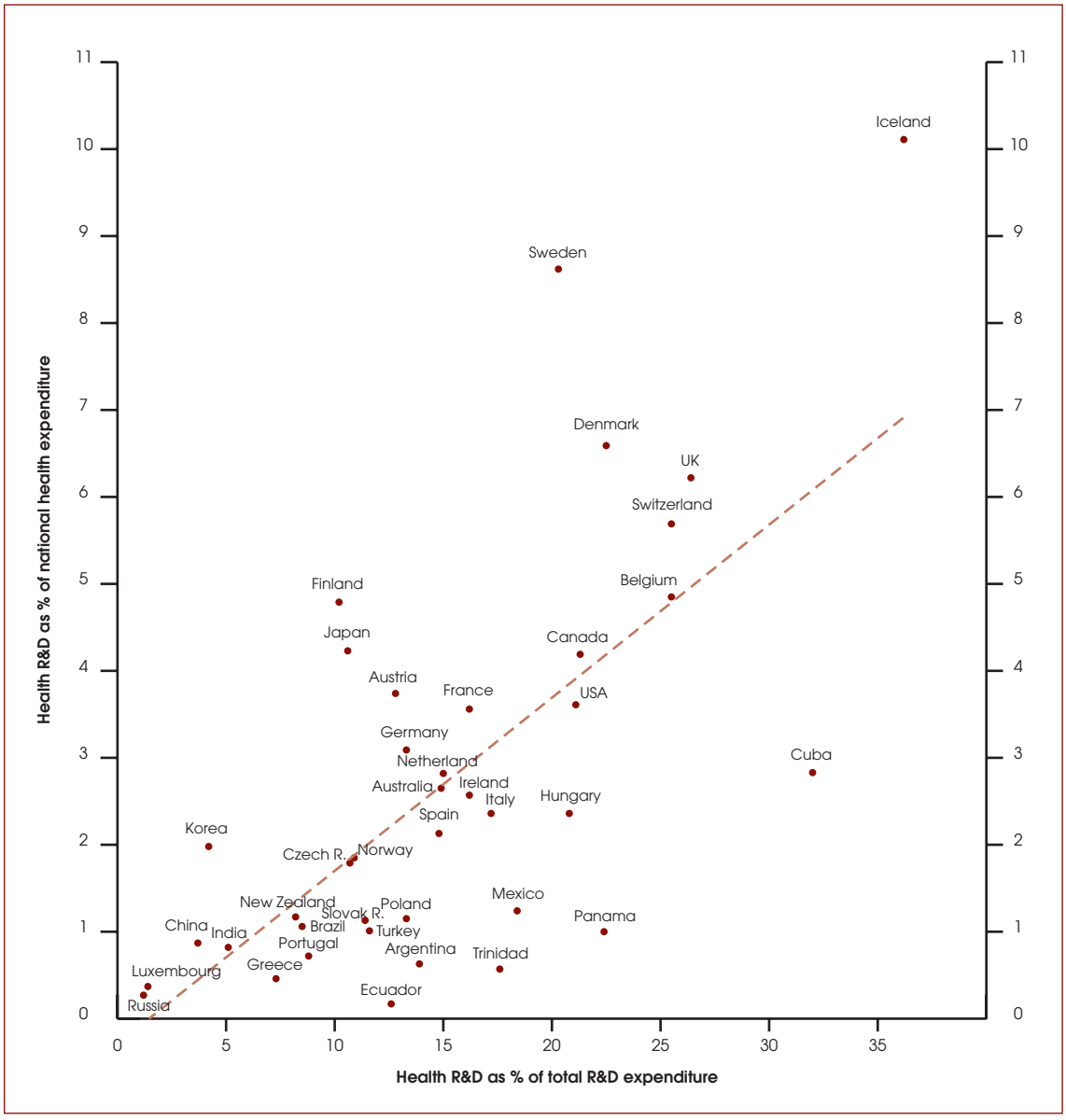
In 2003, these IDCs demonstrated relatively similar commitments to R&D for health as a percentage of total health budgets, hovering around a horizontal line representing investments in R&D for health that accounted for approximately 1% of their national health expenditures. There was considerable difference however in their commitment to research for health as a percentage of their overall R&D sectors, as reflected by their relative distance from the vertical axis. Argentina shows the strongest commitment, followed by South Africa, Brazil, India and China.

Brazil is well positioned along the diagonal relative to the others, although it dropped slightly below the diagonal in 2003, signalling a drop in importance of research for health in its overall health and R&D budgets relative to 2001. Relative to 2001, India and China maintained their positions along the diagonal in 2003. As data for Argentina and South Africa were plotted for the first time in 2003, it is not possible to analyse changes over time.

The 2004 report drew attention to Hungary, as illustrative of a transition country experiencing economic recovery. Data for 2003 show that both Hungary and the Czech Republic are moving towards the upper right quarter of the figure, as expected of countries with expanding economies.

Unfortunately, many low- and middle-income countries could not be plotted due to lack of data. We expect that more countries will be added for the next report.

Figure 2.9
Strength of investments in R&D for health



Source: Global Forum for Health Research Estimates based on data from the WHO, the OECD and other publications.

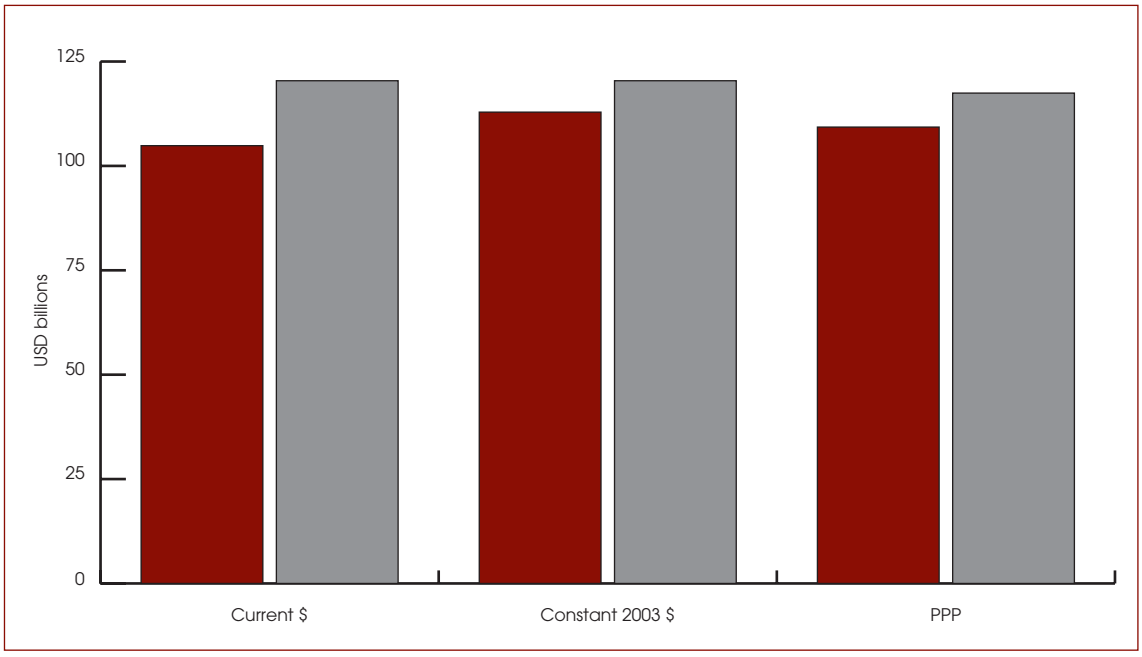
2.2.4 Public expenditures in high-income countries

Governments in high-income countries contributed US$ 53.8 billion to R&D for health in 2003, up from US$ 44.1 billion reported in 2001 and US$ 36.2 billion reported in 1998, excluding foreign ODA (see Table 2.1).

Indications are that this growth in expenditures is real and not just a reflection of inflation or shifts in exchange rates. When data were standardized using either constant 2003 US$ or 2003 Purchasing Power Parities (PPPs), a similar pattern of growth was observed, see Figure 2.10. Work is needed to develop PPPs that reflect the basket of goods specific to R&D for health. This is especially important for LMICs, as using such a basket of goods to assess their expenditures on R&D for health may give a fairer assessment of their investments in R&D. This is because one would assume that the costs of doing R&D in these countries may be considerably lower than in HICs, given differences in labour and other fixed costs.

Figure 2.10

R&D for health expenditures among OECD-reporting countries, in current and constant 2003 USD and Purchasing Power Parities (PPPs), 2001 and 2003



Global distribution of expenditures

The United States government was the biggest spender at US$ 33.8 billion and accounted for more than half of the total in these countries. Japan followed with US$ 5.6 billion, Germany US$ 3.2 billion, France US$ 3.1 billion, the United Kingdom US$ 2.2 billion, Italy US$ 2.0 billion and Canada US$ 1.7 billion. Together, the G7 countries invested more than 92% of publicly funded R&D for health in high-income countries. Together, all other high-income countries added another US$ 4.4 billion.

Table 2.2
Public funding of R&D for health in HICs, 2003, 2001 and 1998

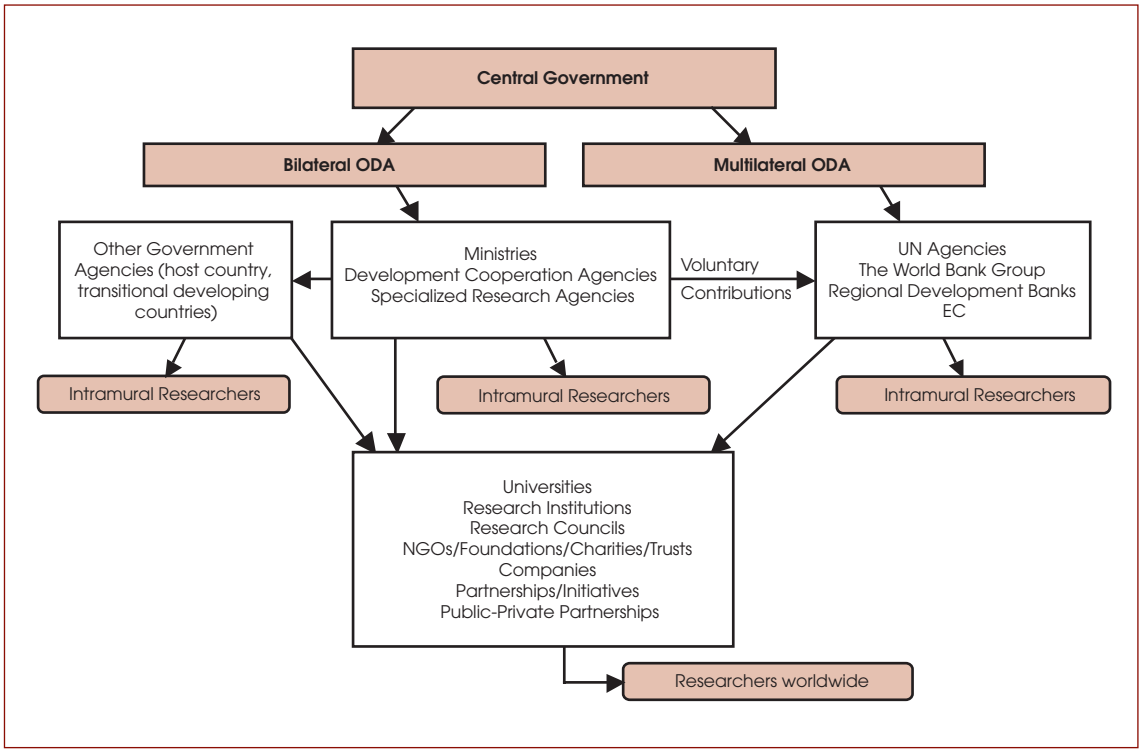
	2003 Current million US$	2001 Current Million US$	1998 Current Million US$	2003 % of GDP	2003 % of public expenditure on health
Funder reported					
Austria	532	408	375	0.21	4.1
Belgium	208	117		0.07	2.3
Denmark	287	204	223	0.14	2.1
Finland	287	200	201	0.18	4.1
France	3,142	2,448	2,242	0.18	1.8
Germany	3,154	2,297	2,393	0.13	2.2
Greece	47	35	45	0.03	0.5
Iceland	24	7		0.48	5.5
Ireland	66	23	16	0.04	2.3
Israel	204	179		0.19	2.2
Italy	2,006	1,218		0.14	2.1
Korea	321	169		0.05	2.1
Netherlands	761	605	542	0.15	1.5
New Zealand		20	38	0.05	0.9
Portugal	78	63		0.05	3.0
Spain	620	367	302	0.07	1.3
Sweden	506	369	458	0.17	1.8
United Kingdom	2,184	1,692	1,789	0.12	3.1
United States	33,823	28,600	19,527	0.31	3.1
Performer reported					
Australia	740	553	506	0.14	2.2
Canada	1,650	980	754	0.19	2.8
Japan	5,591	5,341	4,860	0.13	2.3
Norway	298	205	205	0.13	1.6
Switzerland	320	250	-	0.10	1.5
Total	55,997	43,303	32,137		

Sources: Global Forum for Health Research estimates based on data from official reports to OECD and RICYT, national surveys, pharmaceutical association and other publications; revised estimates for Japan for 1998 & 2001 based on OECD Sector of performance data.

Official development assistance (ODA) investment in research for health

Bilateral and multilateral ODA are important sources of funding for health and research for health in low- and middle-income countries. ODA is administered by countries in a variety of ways through specialized development cooperation or development aid agencies. Sometimes these agencies are independent; sometimes they are within ministries of foreign affairs or development cooperation. Bilateral ODA may be administered through a different agency or ministry than multilateral ODA, see Figure 2.11.

Figure 2.11
Distribution of ODA



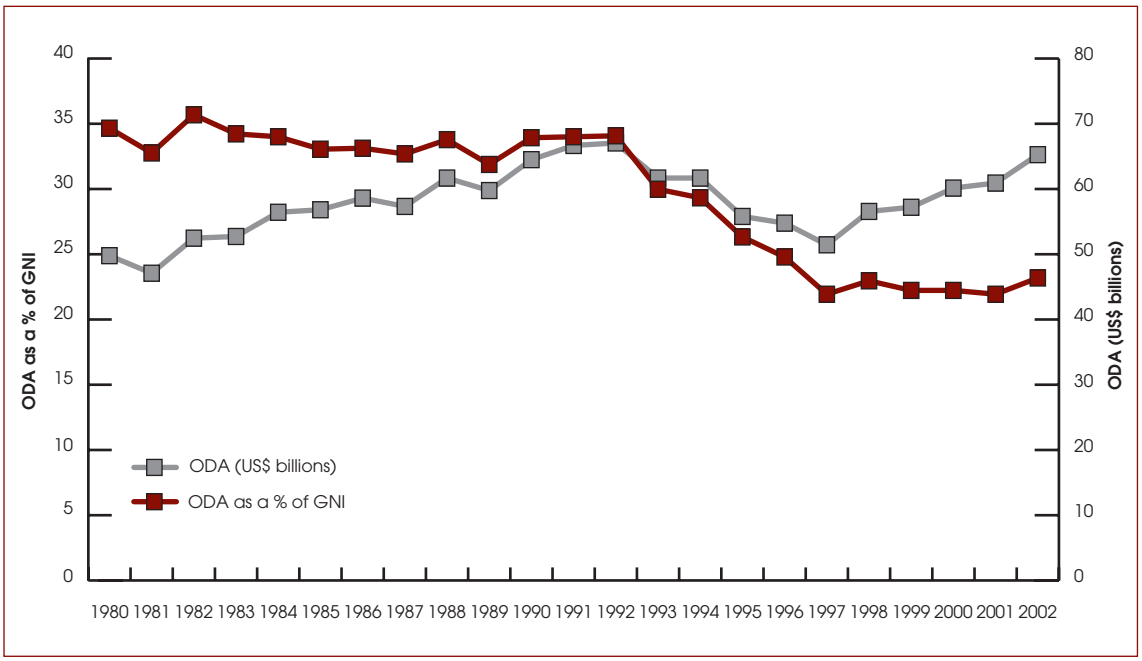
At a supranational level, ODA financial flows are monitored by the Development Assistance Committee (DAC) of OECD. DAC member countries account for at least 95% of worldwide ODA (see Table 2.3). Aggregated health and research for health data are collected annually from DAC members. Selected data are made available to the public in annual reports; health and population data are always reported, but health and population research data are not.

ODA trends in funding[5]

ODA funding has been increasing over the past several years, following a slump in the early 1990s when aid to low- and-middle income countries fell sharply. By 1997, aid reached an all-time low of 0.22% of donor

countries' combined national income. By 2002, there was a 7.2% real increase in ODA (see Figure 2.12) and further increases are projected through 2006 (see Table 2.3).

Figure 2.12
DAC members' total ODA, at 2001 prices as a share of GNI, 1980-2002



Source: OECD

Table 2.3
DAC Members' ODA prospects for 2006

	Net ODA in 2002	ODA/GNI in 2002	Net ODA in 2006	ODA/GNI in 2006	Real change in ODA, 2006 over 2002 (at 2002 prices and exchange rates)[1]	
	US$ millions	%	2002 US$ millions	%	US$ millions	%
Austria	520	0.26	728	0.33	208	0.40
Belgium	1072	0.43	1234	0.46	162	0.15
Denmark	1643	0.96	1531	0.83	-112	-0.07
Finland	462	0.35	598	0.42	136	0.29
France	5486	0.38	7378	0.47	1892	0.34
Germany	5324	0.27	7099	0.33	1775	0.33
Greece	276	0.21	515	0.33	239	0.86
Ireland	398	0.40	671	0.63	273	0.69
Italy	2332	0.20	4195	0.33	1863	0.80
Luxembourg	147	0.77	206	10	60	0.41
Netherlands	3338	0.81	3566	0.80	228	0.07
Portugal	323	0.27	424	0.33	102	0.31
Spain	1712	0.26	2328	0.33	616	0.36
Sweden	1991	0.83	2247	0.87	256	0.13
United Kingdom	4924	0.31	6906	0.40	1982	0.40
EU Members' Total	29949	0.35	39627	0.42	9679	0.32
Australia	989	0.26	1089	0.26	100	0.10
Canada	2006	0.28	2730	0.34	723	0.36
Japan	9283	0.23	10500	0.26	1217	0.13
New Zealand	122	0.22	154	0.26	32	0.27
Norway	1696	0.89	2067	10	370	0.22
Switzerland	939	0.32	1143	0.36	204	0.22
United States	13290	0.13	19539	0.17	6249	0.47
DAC Members' Total	58274	0.23	76849	0.29	18575	0.32

Notes include assumptions/commitments for projections:
1) Assumes average real growth in GNI of 2% per annum (3% for Canada, 4% for Greece, and 0% for Japan) from 2002-06. Austria committed to 0.33 by 2006. 2) Belgium committed to 0.7% by 2010. 3) Denmark committed to more than 0.7%. 4) Finland committed to 0.44% by 2007. 5) France committed to 0.5% by 2007; ODA/GNI ratio for 2006 interpolated between 2002 and the year that the target is scheduled to be attained. 6) Greece committed to 0.33% by 2006. 7) Ireland committed to 0.7% by 2007; ODA/GNI ratio for 2006 interpolated between 2002 and the year that the target is scheduled to be attained. 8) Italy committed to 0.33% by 2006. 9) Luxembourg committed to 1% by 2005. 10) The Netherlands committed to 0.8%. 11) Portugal committed to 0.33% by 2006. 12) Spain committed to 0.33% by 2006. 13) Sweden committed to at least 0.87% in 2006. 14) The United Kingdom committed to 0.4% by 2005-06. 15) Australia committed to 0.26% in 2003-04; estimated ODA/GNI 0.26% in 2003-04; assumes same ratio in future years. 16) Canada committed to 8% annual increase until 2010. 17) Japan committed to 1998-02 average level in 2006. 18) New Zealand commitments under review. 19) Norway committed to 1% in 2005. 20) Switzerland committed to 0.4% by 2010; ODA/GNI ratio for 2006 interpolated between 2002 and the year that the target is scheduled to be attained.

Source: OECD

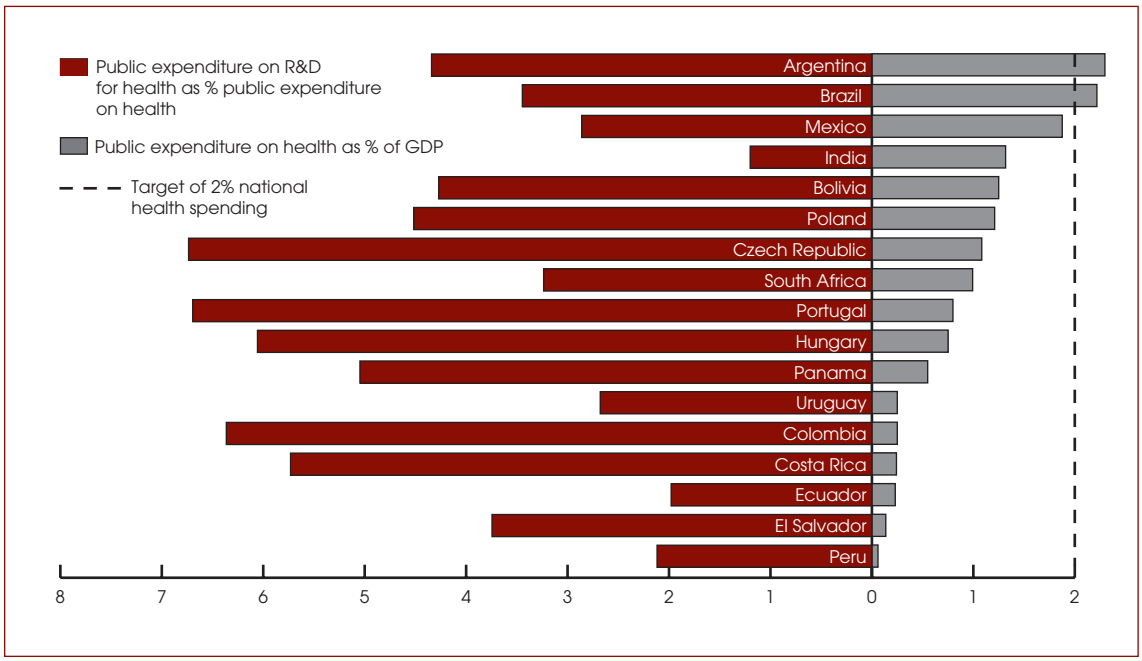
2.2.5 Public Expenditures in low- and middle-income countries

Governments in low- and middle-income countries – for which data are available – spent a minimum of US$ 2.4 billion on R&D for health in 2003, down slightly from US$ 2.5 billion in 2001. This decrease is due to incomplete reporting for LMICs in 2003, and does not reflect a real drop in R&D funding. As more countries report on research for health expenditures and the quality of reporting improves, adjustments to these data will be in order.

Few LMICs collect and report data on expenditures on research for health. Nonetheless, many governments are funding such research, notably in many Central and Eastern European countries, some of which report to the OECD; also in countries in Central and South America, including Argentina, Brazil, Costa Rica, Cuba, Ecuador, El Salvador, Mexico, Trinidad and Tobago that report to RICYT.

R&D for health efforts by governments in LMICs are still relatively small. Only a few LMICs have met the target set by the 1990 Commission on Health Research for Development for expenditures on R&D for health totalling at least 2% of national health spending. Among LMICs, only Argentina and Brazil have met this level, according to data reported for 2003, see Figure 2.13.

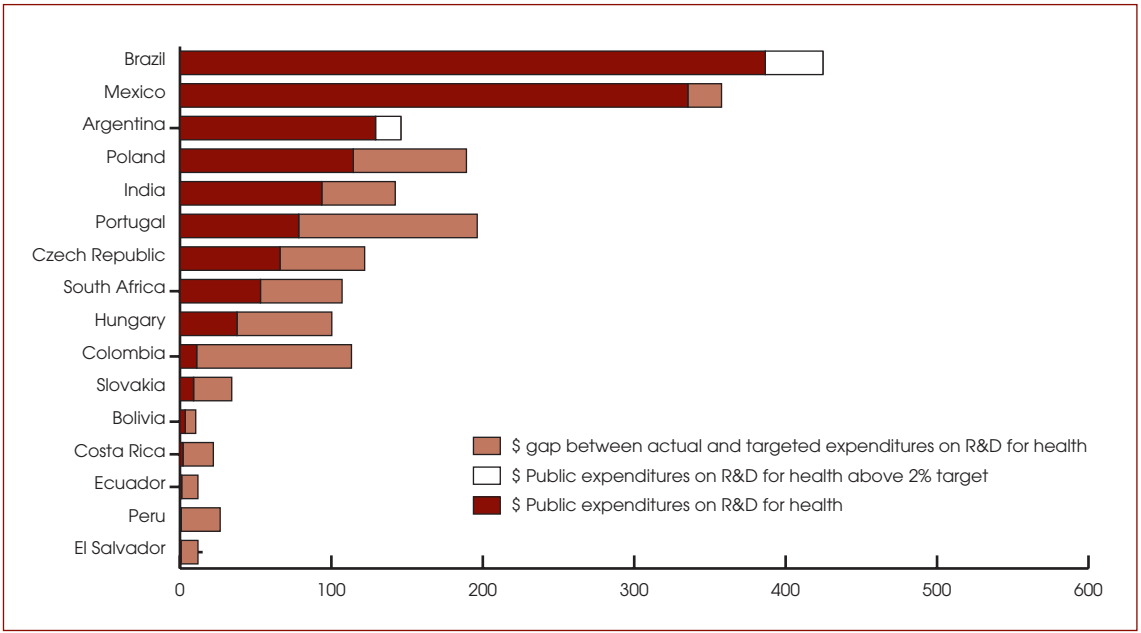
Figure 2.13
Public funding of R&D for health as a % of public expenditure on health and of GDP, 2003



Sources: Global Forum for Health Research estimates of expenditure on R&D for health based on OECD, RICYT, and national surveys for countries reporting public expenditures on R&D for health in 2003; public expenditure on health estimates from the WHO.

While this target may seem insurmountable for some countries, those with the lowest shares of expenditures on R&D for health may make notable gains with little effort. Countries with higher R&D investments relative to total health expenditures may require greater effort in absolute terms to meet the 2% target, see Figure 2.14. While countries with few health resources may need to focus them on delivering services, investing in research on operational issues such as targeting would help to inform governments about how well their spending on service delivery, for example, is meeting the needs of their populations, and where programmes and services could be fine-tuned.

Figure 2.14
Gap between actual and 2% target* for public expenditure on research for health in LMICs, 2003 estimates



Sources: Global Forum for Health Research estimates of expenditure on R&D for health based on OECD, RICYT, and national surveys for countries reporting public expenditures on R&D for health in 2003; Public expenditure on health estimates from the WHO.

BOX 2.1
Update on NBIC Technologies

'NBIC' technologies were flagged in *Monitoring Financial Flows 2004* as an emerging trend to watch. Nanoscience or nanotechnologies enable nanoscience (N); biotechnology and biomedicine (B); information technology (I); and cognitive science, including neuro engineering (C), to converge at the nanoscale. According to Lux Industries, this is a major emerging industry worldwide, with applications that run from antimicrobial refrigerators to nano-reformulated drugs.

> Emerging nanotechnology was incorporated into more than US$ 30 billion in manufactured goods in 2005 – more than double the previous year. In 2014, we project that US$ 2.6 trillion in global manufactured goods will incorporate nanotech, or about 15% of total output. Governments, corporations, and venture capitalists spent US$ 9.6 billion on nanotechnology research and development (R&D) worldwide in 2005, up 10% from 2004.[a]

In his 2006 *State of the Union Address*, President George W. Bush announced that the United States would double the federal commitment to the most critical basic research programs over the next 10 years to support development of nano and other emerging technologies.[b] Updated data from Lux Industries show the size of this industry globally, see Table 2.4.

Table 2.4
Estimated global spending on nanotechnology[c], US$ billions

Year	2004	2005
Total global spending	8.6	9.6
Total global government spending	4.6	4.6
North America (primarily US)	1.6	1.7
Asia (primarily Japan)	1.6	1.7
Europe (primarily Germany)	1.1	1.3
Rest of World	0.133	0.100
Total global corporate spending	3.8	4.5
North America (primarily US)	1.7	1.9
Asia (primarily Japan)	1.4	1.7
Europe (primarily Germany)	0.650	0.850
Rest of World	<0.40	0.70
Venture capitalist spending	0.417	0.497

[a] Holman MW et al. The Nanotech Report 4th Edition, Investment Overview and Market Research for Nanotechnology, Lux Research, 2006 (http://www.luxresearchinc.com/TNR4_TOC.pdf , accessed, 14 July 2006).

[b] see http://www.whitehouse.gov/news/releases/2006/01/20060131-10.html, accessed 27 July 2006.

[c] The Nanotech Report, 2004 (https://www.globalsalespartners.com/lux/# http:www.luxsearchinc.com/).

2.2.6 Private funding

Private for-profit financing

The private for-profit sector accounted for 48% of total global expenditures on R&D for health in 2003, investing US$ 60.6 billion, up from US$ 51.2 billion in 2001 and US$ 40.6 billion in 1998 according to estimates derived from official reports. Multinational pharmaceutical, biotechnology, and medical instrument companies are the main actors in the private for-profit sector. Most of these companies are owned and operate in HICs; however, some operate in LMICs. In 2003, 88% of the US$ 60.6 billion private sector expenditures were domestic expenditures by companies from HICs, and another 10% were foreign expenditures by companies in HICs. Just US$ 1.4 billion, or 2% of investments by private sector companies – both foreign and domestic – were spent in LMICs, see Table 2.1 and Figure 2.15.

Globally, the biggest spenders were US-based companies, followed by companies from Japan, the United Kingdom, Germany, France, Switzerland, Sweden and Canada, see Table 2.5.

Table 2.5

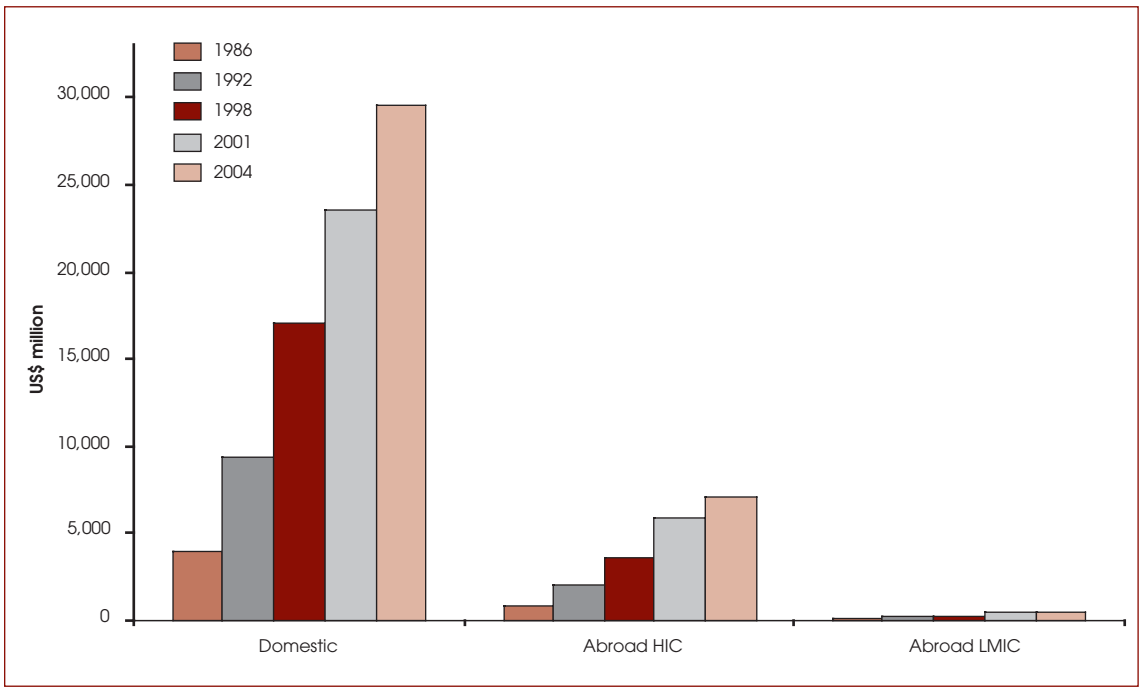
Private-for-profit R&D for health expenditures by funders, 2003 (US$ millions)

Global Total	60,639	100%
United States	27,065	44.6
Japan	8,317	13.7
United Kingdom	5,295	8.7
Germany	4,455	7.3
France	3,128	5.2
Switzerland	1,722	2.8
Sweden	1,624	2.7
Canada	1,105	1.8
Other HICs	6,560	10.8
Total HICs	59,273	97.7
China	303	0.5
India	141	0.2
Other LMICs	921	1.5
Total LMICs	1,366	2.3

Sources: Global Forum estimates based on data from OECD, national sources and pharmaceutical associations.

A few innovative developing countries are also supporting the development of indigenous pharmaceutical and biotechnology industries, which bears watching over the coming years, especially with the explosive growth in investments in genomics research and the newly convergent NBIC technologies among some of these countries. While the NBIC industry may be poised to become a big player in the next few years, the pharmaceutical industry remains the biggest actor in the private-for-profit sector.

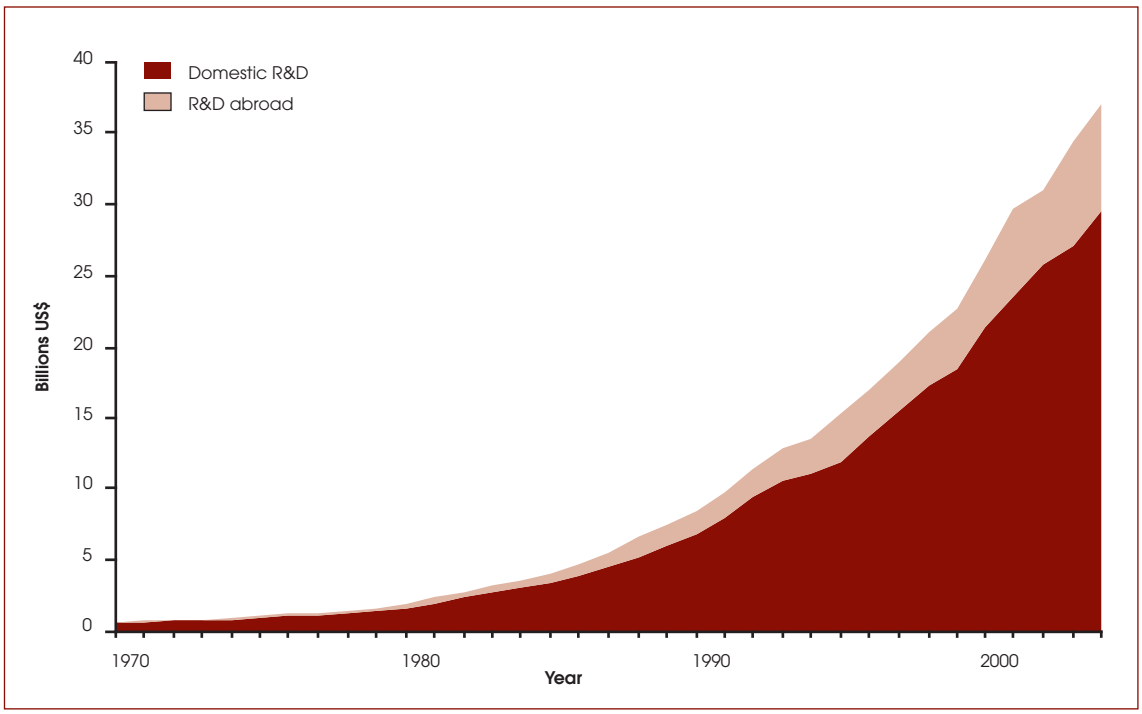
Figure 2.15
Trends in pharmaceuticals R&D by US PhRMA companies, (US$ millions)



Notes: R&D Abroad includes expenditure outside the United Stated by US-owned PhRMA member companies and R&D conducted abroad by the US divisions of foreign owned PhRMA member companies. R&D performed abroad by the foreign divisions of foreign owned PhRMA member companies is excluded. Domestic R&D, however, includes R&D expenditures within the United States by all PhRMA member companies.
Source: Pharmaceutical Industry Profile 2004, PhRMA

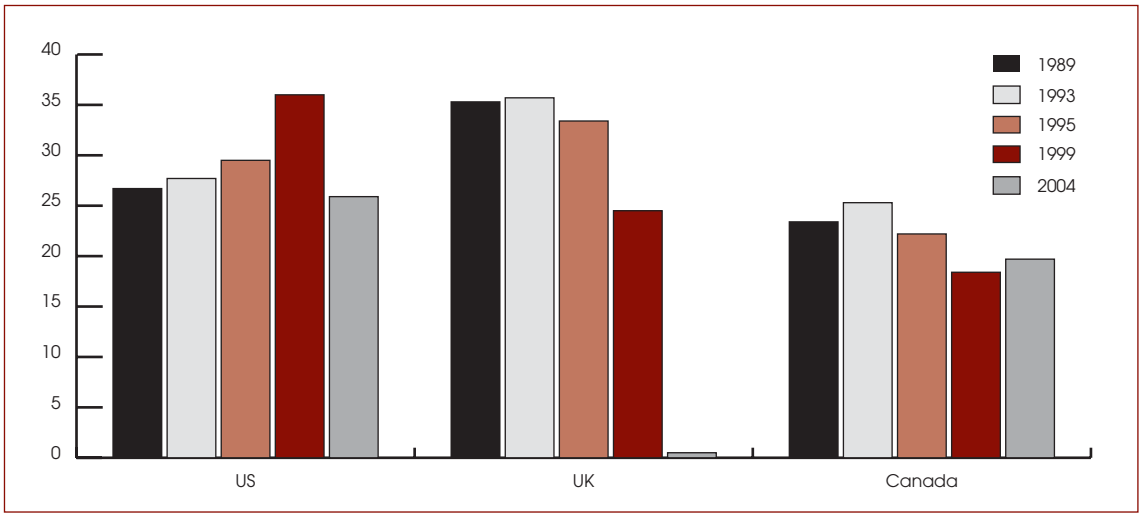
By 2004, R&D expenditures by PhRMA member companies totalled US$ 37 billion. While most of this was spend on domestic R&D, US$ 7 billion or 20% of total PhRMA expenditures were spent abroad, see Figure 2.16.

Figure 2.16
Domestic R&D and R&D abroad, by PhRMA member companies, 1970–2004



Source: Pharmaceutical Research and Manufacturers of America, PhRMA Annual Membership Survey, 2006.

Figure 2.17
Basic research by pharmaceutical companies, as % of total R&D, 2003 (US$ millions)



Note: No available data for 2004 for the United Kingdom.
Sources: A comparison of Pharmaceutical Research and Development Spending in Canada and Selected Countries (2002), PMPRB, PMPRB annual reports, PhRMA report.

According to data from the pharmaceutical industry, the proportion of R&D spent on basic research dropped in the United States to 25.9% in 2004, from 36% in 1999, and increased in Canada to 19.7% in 2004 from 18.6% in 1999. No updated data are available for the United Kingdom.

The portion of overall expenditures by pharmaceutical companies on basic research may be overestimated, according to a recent study.[3] Of the gross reported global expenditure of US$ 9.2 billion by pharmaceutical companies on basic research, US$ 2.9 billion were estimated to be subsidized by tax payers. This leaves a net contribution by private sector companies of US$ 6.3 billion, 32% lower than what industry reports. The study reports that the taxpayers' contribution may in fact be understated, and that in the absence of verifiable data from industry, these estimates and calculations are necessarily crude.

Private not-for-profit financing

The private not-for-profit sector has an increasingly strong commitment to R&D for health – estimated at US$ 9 billion in 2003, up from US$ 8 billion in 2001 and US$ 6 billion in 1998. Almost all of the 2003 funding (US$ 8.6 billion) came from private foundations and universities in high-income countries for R&D for health carried out in these countries. In contrast, in 2003, just US$ 0.08 billion of research was conducted in LMICs and financed by domestic private foundations and universities (roughly the same amount estimated for 2001 and 1988). Foreign not-for-profit organizations, such as foundations and universities also financed R&D for health in LMICs, an estimated US$ 0.3 billion in 2003, a figure that has remained relatively stable since 1998.

Foundations are substantively involved in key global and country level partnerships. That this "third sector" creates institutional diversity, contributes to innovation, and adds an important actor to a field dominated by government and the market has been well documented.[6]

Foundations vary greatly in number and types, but globally support remarkably similar activities – 71% of foundation activities include education, research and health.[6] Public foundations rely mainly on voluntary public subscriptions to fund operations while private foundations typically are supported by endowments.

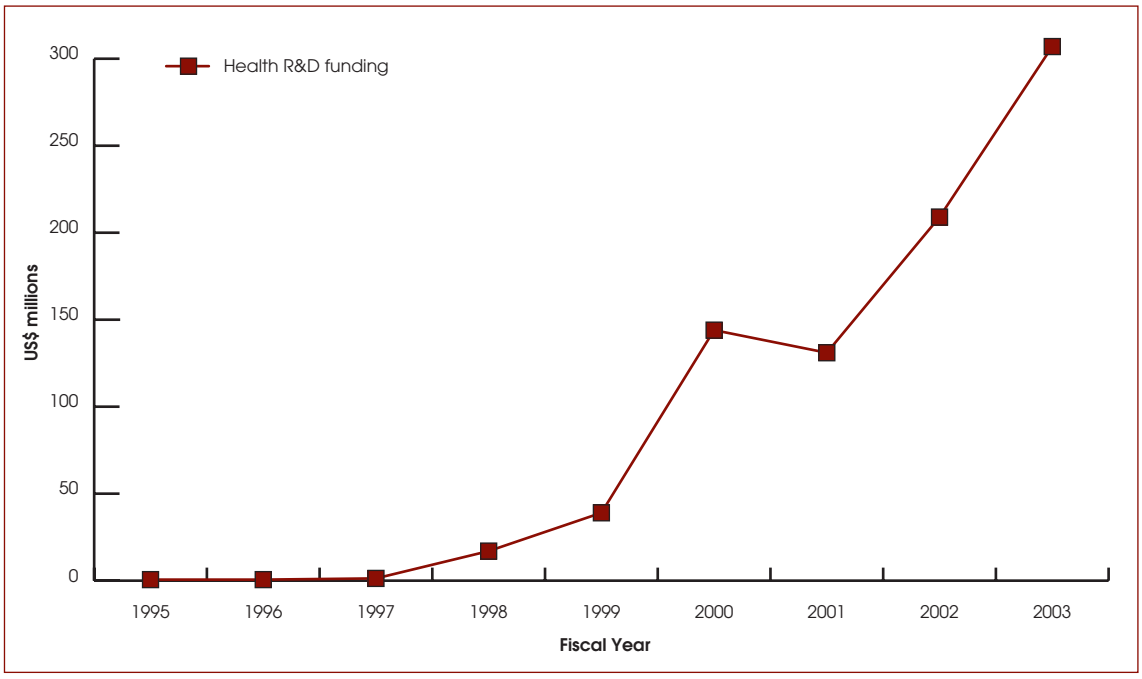
The estimated annual financial contribution of private foundations to international development activities in recent years has been estimated at US$ 3 billion annually, although it was probably higher than that in 2000 and 2001 due to large contributions from the Gates Foundation.[7] More than half of this amount comes from foundations in the United States. The majority of foundations have no overseas activities; most international funding comes from a small number of foundations that directly fund activities abroad (e.g., the Wellcome Trust and Gates Foundation) and/or the activities relevant to international issues are addressed through giving to domestic institutions.

By way of example, Figure 2.18 shows the heavy investment in R&D for health by the Gates Foundation. Its investments picked up beginning in 1997, and have been climbing rapidly since, with the exception of a brief decline over the period 2000-2001.

In principle, foundation expenditures on international / development activities are

reported in OECD/DAC statistics as part of the roughly US$ 7 billion attributed to nongovernmental organizations. However, under-reporting within countries is evident; attempts to improve data collection are underway.

Figure 2.18
Trends in health research funding, Bill and Melinda Gates Foundation*, 1995-2003 (US$ millions)



*1995-1999 William H. Gates Foundation, 2000-2003 Bill & Melinda Gates Foundation
Source: Gates Foundation, personal communication.

Available data for American foundations show the extent of their investment, and the overall importance of this sector. In 2003, they gave an estimated US$ 30.3 billion, up substantially from its contribution of US$ 8.8 billion in 1994. International giving overseas accounted for 5.7% of this total in 2003, see Table 2.6.

Table 2.6
Number of US foundations, total and estimated international giving (US$ billions)

Year	Numbers of foundations	Total giving	International giving	International as a % of total	International giving overseas	International giving overseas as a % of total
2003	66,395	30.3	4.7	*15.4*	1.7	*5.7*
2002	64,843	30.4	4.2	*13.8*	1.6	*5.3*
2001	61,180	30.5	4.5	*14.7*	1.4	*4.6*
2000	56,582	27.6	3.1	*11.2*	1.7	*6.0*
1998	46,832	19.3	1.6	*8.2*	0.8	*4.3*
1994	38,807	11.3	1.0	*8.8*	n/a	*n/a*
1990	32,401	8.8	0.8	*8.7*	n/a	*n/a*

Table provides aggregate financial information on the 56,582 active independent, corporate, community, and grant-making foundations in the United States. Estimates on international giving and international giving overseas are based on the percentage of international giving of a sample of foundations as a proportion of total giving reported by all foundations.
Source: Grantmaker Information, Foundation Center Statistics, http://foundationcenter.org/findfunders/statistics/pdf/03_fund_geo/2004/09_04.pdf, accessed July 2006 and http://fdncenter.org/fc_stats/grantmakerinfo.html, October 2002, and International Grantmaking II, The Foundation Center, 2000, p. 15.

References and notes

1 See page 10 in *Monitoring Financial Flows for Health Research 2005: Behind the numbers*. Geneva, Global Forum for Health Research, 2005.

2 See chapters by Alison Young and Andrew Kennedy in *Monitoring Financial Flows for Health Research: Work in progress for discussion and feedback on the occasion of Forum 7*. Geneva: Global Forum for Health Research, 2003.

3 Light D. Basic research funds to discover new drugs: who contributes how much? Chapter 3 in: *Monitoring Financial Flows for Health Research 2005: Behind the global numbers*. Geneva, Global Forum for Health Research, 2005.

4 OECD Biotechnology Statistics 2006 (http://www.oecd.org/dataoecd/51/59/36760212.pdf).

5 For more details on ODA see: Miller C. *High-income Country Investors: Financial flows for international health research*. Geneva, Global Forum for Health Research, 2005 (www.globalforumhealth.org).

6 This section of the report on private not-for-profit financing draws on material prepared by Caryn Miller in her report: *High-income Country Investors: Financial Flows for International Health Research*. Geneva, Global Forum for Health Research, 2005 (www.globalforumhealth.org).

7 *Philanthropic Foundations and Development Cooperation* (offprint) *DAC Journal*, 2003, 4 (OECD).

Chapter 3

Trends and patterns of morbidity and mortality

Trends and patterns of morbidity and mortality

3.1 Introduction

An important step in understanding the health status of a given population, and the factors that improve or harm health, is to document patterns of morbidity and mortality. These trends, after all, reflect important elements that affect health and can lead to specific interventions which may modify these patterns.

To better understand these patterns, mortality and morbidity trends need to be explored in a disaggregated manner by exploring how they differ within populations by age, gender, social class, geographical distribution, disability status, caste, race and religion among others. This information is, however, scarce at the global level and even national mortality rates are unknown in a large proportion of low and middle income countries (LMICs).

Understanding the relative health impacts of different diseases and injuries, and of risk factors and other determinants, is important for setting priorities in health research.

To better understand these patterns, the Harvard School of Public Health in collaboration with the World Bank and WHO developed the Global Burden of Disease (GBD) methodology to assess the causes of loss of health in all regions of the world using a common currency: the disability adjusted life year (DALY).[1,2] The Ad Hoc Committee on Health Research Relating to Future Intervention Options report used this information to review gaps in information and research, and used the 'five step approach' to identify priorities for health research.[3]

In recent years, WHO has undertaken a progressive reassessment of the GBD for the years up to 2002, and new projections of the GBD forwards from 2002 to the year 2030.[4,5] In the GBD context, this chapter presents estimates for the years 1990 and 2003 for the following two epidemiological indicators:

- mortality figures, which refers to the numbers of people who die and the cause of death;
- burden of disease, using the DALY metric, which quantifies equivalent healthy years of life lost due either to premature mortality or to living in states of less than full health – one lost DALY represents one lost year of full health.

There has been considerable controversy about the burden of disease methodology, particularly in its approach to the dealing with incomplete and missing data, and in the use of age and severity weights in the DALY. The DALY attempts to quantify only losses of individual health, and does not address well-being, quality of life, or other broader social impacts of diseases and injuries. Bearing in mind the wide uncertainty around the estimates in some developing regions, we find it useful to examine global and regional patterns of burden of disease in 2003 and to examine broad trends between 1990 and 2003.

3.2 Mortality – causes and trends

Worldwide, 57.5 million people died in 2003. One-third of these deaths were due to communicable, maternal, and perinatal conditions and nutritional deficiencies (the 'Group I' causes in the GBD classification). This proportion has remained almost unchanged from 1990. Among Group I causes, HIV/AIDS accounted for 2% of deaths in 1990, but 17% in 2003, rising from 0.3 million deaths globally to 3.0 million in 2003. HIV/AIDS represented 5% of total global deaths in 2003. Excluding deaths due to HIV/AIDS, deaths due to Group I conditions fell from one-third of total deaths in 1990 to less than one-fifth in 2003. In all, 97% of the 'non-HIV/AIDS Group I' deaths occurred in low- and middle-income countries.

3.2.1 Comparisons between countries

Table 3.1 summarizes estimated numbers of deaths in 2003 for high-income countries (HICs) and LMICs, for diseases and injuries causing more than 1% of global deaths or global DALYs. Ischaemic heart disease (IHD) and cerebrovascular disease (stroke) were the leading causes of death in both groups of countries in 2003, together responsible for more than 20% of all deaths worldwide. Four of the top 10 causes of death in the world are related to smoking (ischaemic heart disease, stroke, chronic obstructive pulmonary disease and lung cancer). Of the 7.3 millions deaths from IHD worldwide, 1.4 million occurred in HICs. In all, 5.6 million people died of stroke, of which fewer than 1 million deaths occurred in HICs. Lung cancer was the third leading cause of death in HICs, but was not among the leading ten causes of death in LMICs, partly due to the prominence of other causes of death. In LMICs, five of the leading 10 causes of death remain infectious diseases, including lower respiratory tract infections, HIV/AIDS, diarrhoeal diseases, TB and malaria.

Table 3.1
Ten leading causes of death. Comparison between LMICs and HICs, 2003

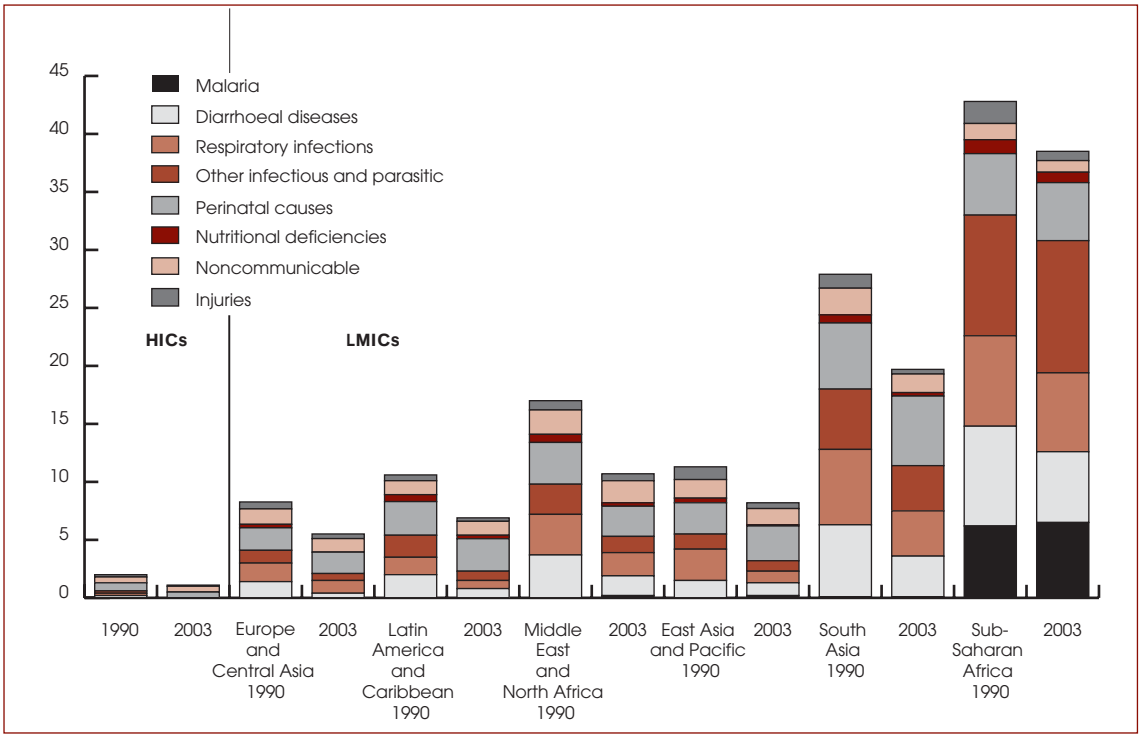
Low- and middle-income countries (LMICs)				High-income countries (HICs)			
	Cause	Deaths (millions)	Percent of total deaths		Cause	Deaths (millions)	Percent of total deaths
1	Ischemic heart disease	5.97	12.1%	1	Ischaemic heart disease	1.35	17.0%
2	Cerebrovascular disease	4.81	9.7%	2	Cerebrovascular disease	0.77	9.6%
3	Lower respiratory infections	3.50	7.1%	3	Trachea, bronchus, lung cancers	0.46	5.8%
4	HIV/AIDS	2.98	6.0%	4	Lower respiratory infections	0.34	4.3%
5	Chronic obstructive pulmonary disease	2.52	5.1%	5	Chronic obstructive pulmonary disease	0.31	3.9%
6	Perinatal conditions	2.38	4.8%	6	Colon and rectum cancers	0.26	3.3%
7	Diarrhoeal diseases	1.79	3.6%	7	Alzheimer and other dementias	0.22	2.8%
8	Tuberculosis	1.52	3.1%	8	Diabetes mellitus	0.22	2.7%
9	Road traffic accidents	1.11	2.3%	9	Breast cancer	0.15	1.9%
10	Malaria	0.90	1.8%	10	Stomach cancer	0.14	1.8%

3.2.2 Death trends in children

Nearly 20% of deaths (10 million) in 2003 were among children under five years of age. Enormous strides have been made since 1970 when over 17 million children of this age-group died. Nevertheless, today nearly all child deaths (99%) occur in LMICs, and over 40% in sub-Saharan Africa. While some African countries have made considerable strides in reducing child mortality, the majority of African children live in countries where the survival gains of the past have been wiped out or even reversed, largely because of the HIV/AIDS epidemic.

While cause-specific death rates for 1990[2] may not be completely comparable to those for 2003 due to changes in data availability and methods, plus some approximations in mapping 1990 estimates to the 2003 regions, some broad conclusions can be drawn about trends in causes of child mortality. Child mortality (ages 0-4 years) declined between 1990 and 2003 in all regions of the world (Figure 3.1). These declines were around 30% or higher in HICs, in Latin America and the Caribbean, in the Middle East and North Africa, and in the LMICs of Europe and Central Asia. Death rates from communicable diseases and injuries have declined substantially in these regions, particularly for diarrhoeal and respiratory diseases. Almost fifty per cent of child deaths in 2003 were from five preventable and treatable conditions: acute respiratory infection, measles, diarrhoea, malaria, and HIV/AIDS.

Figure 3.1
Death rates by disease group and region in 1990 and 2003 for children aged 0-4 years. For all geographical regions, high-income countries have been excluded and are shown as a single group on the left side of the graph.



The situation in 2003 in Latin America and some Asian and Middle-Eastern countries was that conditions arising in the perinatal period, including birth asphyxia, birth trauma and low birth weight replaced infectious diseases as the leading cause of death and became responsible for 20–36% of child deaths. Such a shift in the cause-of-death pattern has not occurred in sub-Saharan Africa, where malaria, lower respiratory tract infections and diarrhoeal diseases continue to be the main causes of death in children, accounting for 50% of all deaths. HIV/AIDS is now responsible for over 300,000 child deaths in sub-Saharan Africa – nearly 7% of all child deaths in the region.

Mortality from diarrhoeal diseases fell from 2.4 million deaths in 1990 to about 1.6 million deaths in 2003 reflecting the substantial efforts in diarrhoea case management (e.g. using oral rehydration therapy). Deaths from measles also declined, most likely because of higher vaccination coverage. Death rates from acute respiratory infections declined less in South Asia and sub-Saharan Africa than in other regions. Malaria mortality appears to have increased during the 1990s, primarily in sub-Saharan Africa (Figure 3.1).

3.2.3 Deaths trends in adults

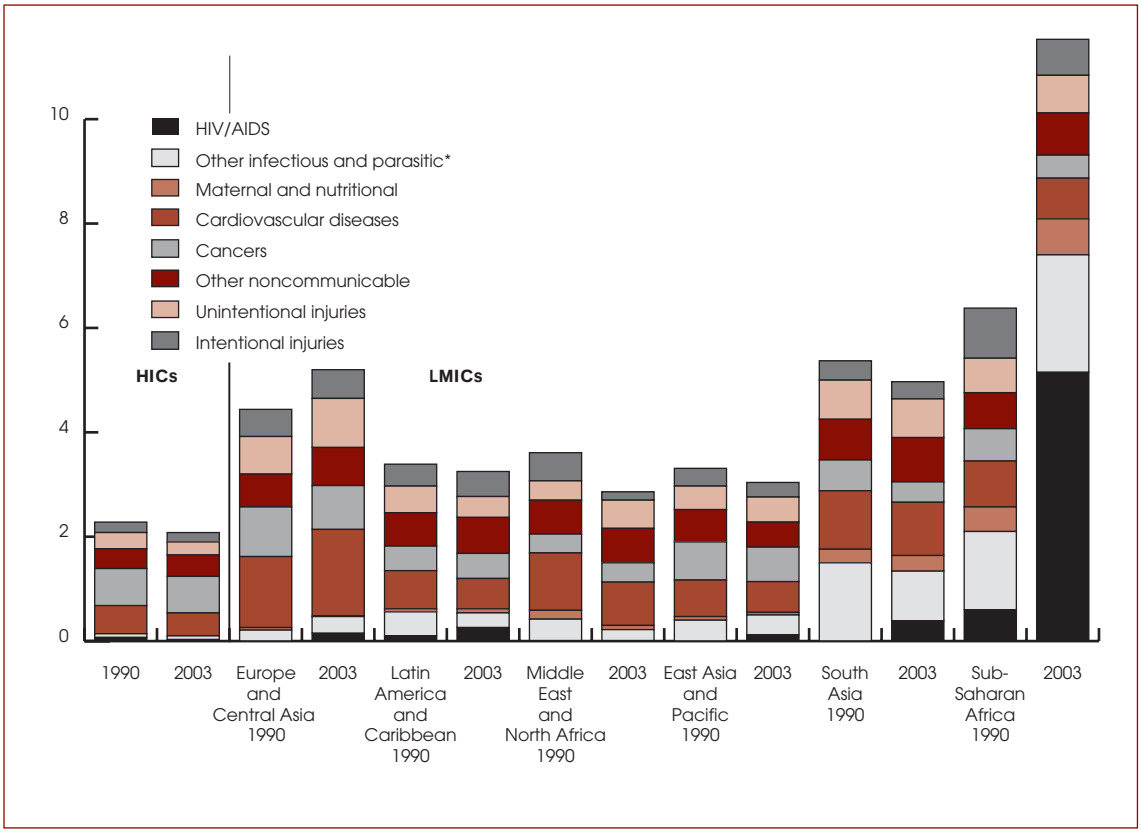
There is a marked difference in the age distribution of mortality between HICs and LMICs. Almost 85% of deaths in the former occur beyond age 60, compared to about 45% in the latter. Adult mortality rates have been declining in recent decades in most regions of the world, with the exception of sub-Saharan Africa and the former Soviet countries of Eastern Europe (Figure 3.2). The probability of premature adult death varies widely between regions. For example, in Africa it is much higher – around three times as high – than that observed in China and some middle income countries of the Western Pacific region. Even within more developed regions there are wide variations. Men in some Eastern European countries are three to four times more likely to die prematurely than men in HICs. Furthermore, male adult mortality in Eastern Europe is much greater than in the LMICs of the Americas, South-East Asia and the Eastern Mediterranean.

Noncommunicable diseases are now responsible for more than half of deaths of adults aged 15–59 in all regions except South Asia and sub-Saharan Africa, where Group I conditions, including HIV/AIDS, remain responsible for one-third and two-thirds of deaths, respectively (Figure 2). Adults aged 15–59 in LMICs face a 30% greater risk of death from non-communicable diseases than their counterparts in HICs.

Despite the burden of communicable diseases burden declining globally in adults, HIV/AIDS has become the leading cause of mortality among adults aged 15–59, responsible for 2.5 million deaths or 15% of global deaths in this age group. HIV/AIDS deaths are responsible for a slightly larger proportion of deaths than ischaemic heart disease and cerebrovascular disease combined, and for more than twice as many deaths as road traffic accidents in that age group. Road traffic accidents are the fourth leading cause of death in adults aged 15–59 years, and three-quarters of these deaths are of men. Suicide and violence (homicide) are also among the top ten causes of death in adults aged 15–59 years. Together with war, intentional injuries account for nearly one in ten deaths in this age range globally.

HIV/AIDS has been a major factor in the rise in mortality in sub-Saharan Africa; the increase in Europe and Central Asia has been due to cardiovascular diseases and injuries. Deaths from cardiovascular disease among adults aged 15–59 years have declined in all regions except the LMICs countries of Europe and Central Asia, although the declines are lower in South Asia and sub-Saharan Africa than elsewhere. Similarly, Europe and Central Asia was the only region where deaths from injuries increased.

Figure 3.2
Death rates by disease group and region in 1990 and 2003 for adults aged 15–59 years. For all geographical regions, high-income countries have been excluded and are shown as a single group on the left side of the graph.



* Includes respiratory infections

3.2.4 Gender differentials

Globally, the male death rate from all causes was 11% higher than that for females in 2003. In all regions, male mortality is higher than female, and the discrepancy between the two sexes in adult mortality risk is much larger in adults than among children.

3.3 Burden of disease and injury

The DALY combines years of life lost from premature death and years of life lived with disabilities in a single indicator that allows the total loss of health from different causes to be assessed. The Global Burden of Disease study introduced the DALY concept and generated a comprehensive and consistent set of estimates of mortality and morbidity by age, sex and region. WHO has undertaken an assessment of the GBD for 2002 and updated projections for years 2003 to 2030 using similar general methods to those of the original GBD study, albeit with substantial improvements in data availability and some methods for dealing with incomplete and biased data[4–6]. This information is used to provide an overview of the main causes of burden of disease in 2003 and of major trends since 1990.

3.3.1 Trends over time

In 2003, the leading ten causes of the burden of disease in LMICs included five communicable diseases (Table 3.2). Apart from road traffic accidents, the leading causes in HICs consisted entirely of noncommunicable diseases, including three (unipolar depressive disorders, adult-onset hearing loss, and alcohol use disorders) with few direct deaths but large disability. Table 2 summarizes estimated DALYs in 2003 for HICs and LMICs, for diseases and injuries causing more than 1% of deaths or DALYs.

Table 3.2
Ten leading causes of DALYs. Comparison between LMICs and HICs, 2003

Low- and middle-income countries (LMICs)				High-income countries (HICs)			
	Cause	DALYs (millions of years)	Percent of total DALYs		Cause	DALYs (millions of years)	Percent of total DALYs
1	Perinatal conditions	95.0	7.0%	1	Unipolar depressive disorders	10.6	9.0%
2	Lower respiratory infections	88.7	6.5%	2	Ischaemic heart disease	7.5	6.3%
3	HIV/AIDS	85.9	6.3%	3	Cerebrovascular disease	5.6	4.7%
4	Diarrhoeal diseases	62.1	4.5%	4	Alcohol use disorders	5.5	4.6%
5	Unipolar depressive disorders	57.5	4.2%	5	Alzheimer and other dementias	4.2	3.5%
6	Ischaemic heart disease	52.3	3.8%	6	Hearing loss, adult onset	4.0	3.4%
7	Cerebrovascular disease	44.0	3.2%	7	Chronic obstructive pulmonary disease	3.9	3.3%
8	Road traffic accidents	36.2	2.7%	8	Trachea, bronchus, lung cancers	3.7	3.1%
9	Malaria	34.3	2.5%	9	Diabetes mellitus	3.3	2.8%
10	Tuberculosis	33.7	2.5%	10	Road traffic accidents	3.1	2.6%

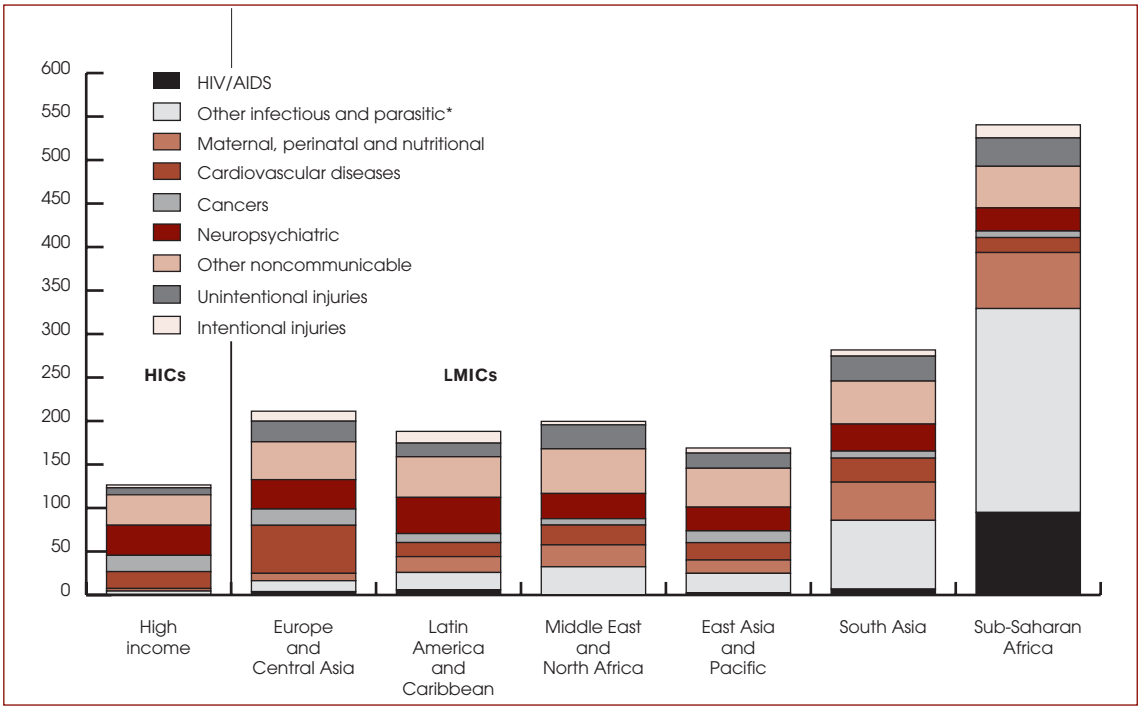
Table 3.2 reveals a marked difference between DALYs in LMICs and in HICs. Of the ten leading causes of DALYs in LMICs, five are infectious diseases. HIV/AIDS was the third leading cause of the burden of disease in LMICs in 2003, the fourth globally, but the leading cause in sub-Saharan Africa, where it was followed by malaria. HICs had mainly noncommunicable disease and injuries among the ten most important causes of DALYs.

Worldwide, the per capita disease burden due to communicable, maternal, perinatal and nutritional conditions fell by 20% between 1990 and 2003. Without the HIV/AIDS epidemic and the associated persistence of the burden of TB, this reduction would have been closer to 30%.

Lost years of full health per capita (as measured by the DALY) for LMICs are double those for HICs (Figure 3.3). The rate of burden of disease is more than four times higher in Africa than in HICs, and just over twice as high in India as in HICs. People in Africa and India comprised one third of the world's population and together bore 53% of the total global burden of disease in 2003.

Around 45% of disease burden in LMICs is now from noncommunicable diseases, a rise of 10% in its relative share since 1990. Ischaemic heart disease and stroke are the largest sources of this burden, especially in the LMICs of Europe and Central Asia where they account for 21% of the total disease burden (Figure 3.3). Injuries accounted for 17% of the disease burden in adults aged 15–59 years in 2003. In Latin America and the Caribbean, the Middle East and North Africa, and Europe and Central Asia, more than one quarter of the entire health burden among men aged 15–44 years was from injuries. Violence is the third leading cause of burden in Latin American and Caribbean countries.

Figure 3.3
DALYs per 1000 people in 2003, by region and cause. For all geographical regions, high-income countries have been excluded and are shown as a single group on the left side of the graph.



* Includes respiratory infections

3.4 Burden attributable to major risk factors

WHO undertook recently a major analysis to provide reliable data on the mortality and burden of disease attributable to 26 major risk factors, across all regions of the world, using comparable methods and a common currency (the DALY) for health outcomes.[7,8] This analysis limited itself to 'proximal risk factors', thereby excluding 'distal risk factors' such as poverty and others. The regional distribution of burden of disease attributable to 20 risk factors is summarized here for HICs and LMICs (Figure 3.4).

One-fifth of the global disease burden can be attributed to the effects of under-nutrition. The five leading global risks causing burden of disease are being underweight due to malnutrition; unsafe sex; raised blood pressure; tobacco smoking and alcohol are the five leading global risks causing burden of disease. Risks are extraordinarily concentrated in low income countries, and relatively few risks are responsible for a considerable proportion of the burden of disease. For example, almost 15% of the total burden of disease in India and Africa is attributed under-nutrition and being underweight. The burden from these risks alone exceeds that of the high income countries' entire disease and injury burden.

Unsafe sex is the second leading risk in LMICs, and in Africa accounts for almost one fifth of the disease burden.

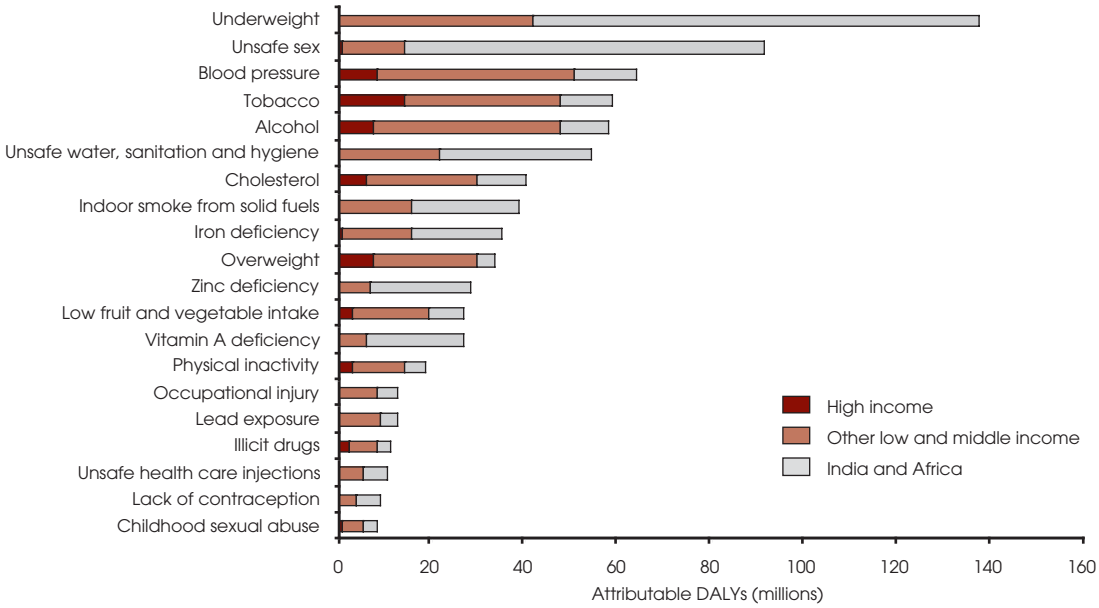
For HICs, tobacco is the leading risk factor, accounting for 12% of the disease burden. Alcohol and blood pressure are responsible for 7-8% of healthy life years lost, with cholesterol and being overweight accounting for 5-6%. LMICs now face a double burden of disease from risk factors and diseases of poverty and lack of development, as well as the chronic diseases associated with smoking, being overweight, poor diet and physical inactivity.

Underweight, under-nutrition, unsafe water and climate change affect children almost exclusively. The burden from addictive substances, unsafe sex, lack of contraception, risk factors for injury, unsafe injections and child sex abuse almost all occurs in middle-aged adults. Diet-related and environmental risks and unsafe sex are about equally distributed between the sexes, but four-fifths of the burden from addictive substances and 60-90% from occupational risks occurs among men. Women suffer most from child sex abuse and exclusively from lack of contraception.

Almost one half (47%) of deaths in the world in the year 2002 can be attributed to the 20 leading risk factors, when joint effects are taken into account. More than two fifths (42%) of global deaths can be attributed to the leading 10 risk factors, and almost one third to the leading five risk factors, which are responsible for one quarter of the total loss of healthy years of life globally.

The role of established risk factors is much greater than commonly thought, and the causes are known for more than two-thirds of many major diseases, such as ischaemic heart disease, stroke, diabetes, HIV/AIDS. The potential is huge for improving health and reducing mortality through research to develop cost-effective interventions to reduce a relatively small number of risks.

Figure 3.4
Burden of disease attributable to leading global risk factors, 2000

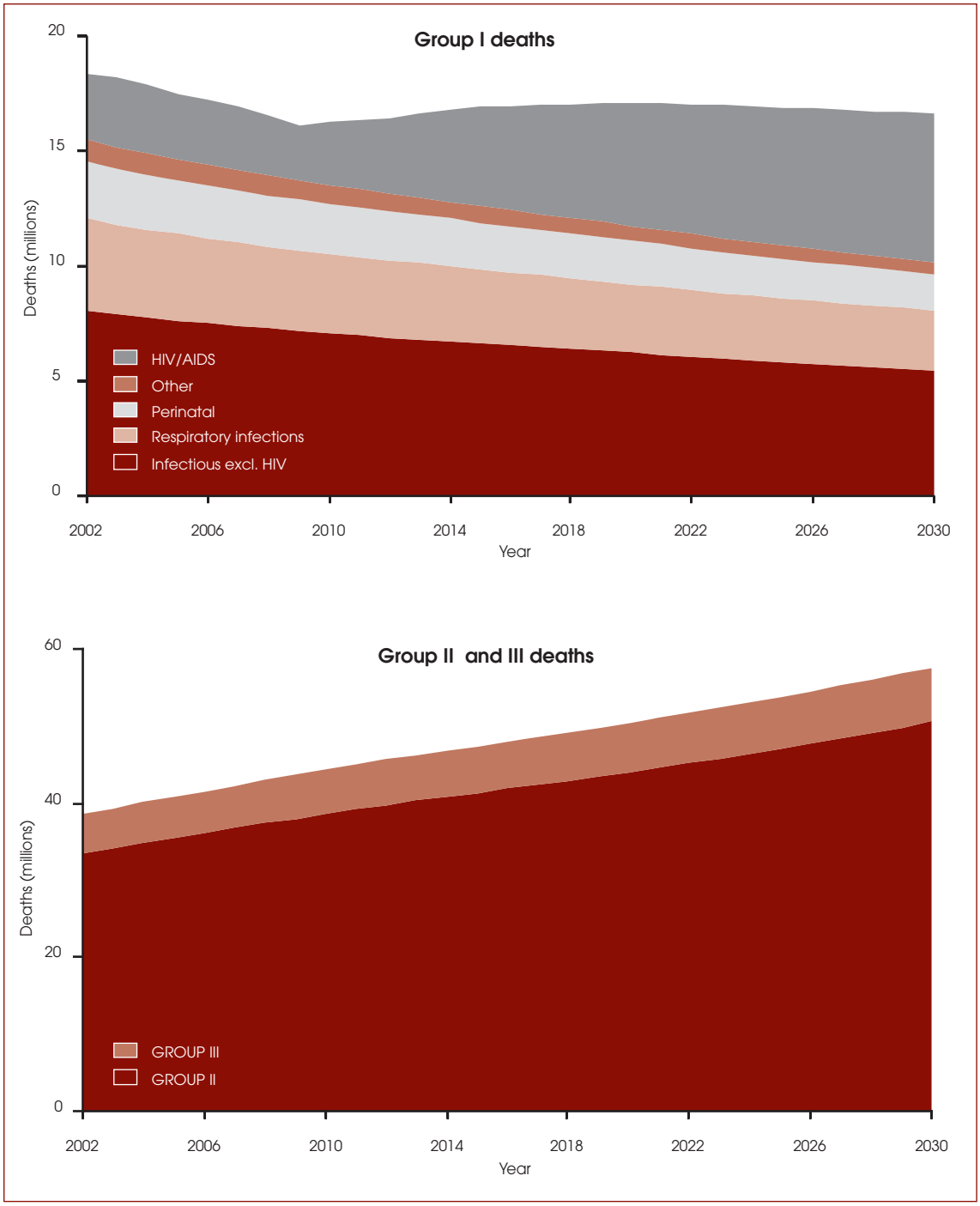


3.5 Projected trends in burden of disease

WHO has prepared updated projections of future trends for mortality and burden of disease from 2002 to 2030 using methods similar to those of the original GBD study.[5] A set of relatively simple models was used to project future health trends based largely on projections of economic and social development, and using the historically observed relationships of these with cause-specific mortality rates. Separate projections for HIV/AIDS mortality were prepared by UNAIDS and WHO, under a scenario in which coverage with anti-retroviral drugs reaches 80% by 2012,thereafter remaining constant, and assuming that there are no changes to current transmission rates due to increased prevention efforts.

Figure 3.5

Baseline projections of deaths from Group I, Group II and Group III causes, world, 2002-2030



Source: Mathers and Loncar[5]

Figure 3.5 summarizes the contributions of major causes to global trends in numbers of deaths for the three major cause groups. Large declines in mortality between 2002 and 2030 are projected for all of the principal Group I causes with the exception of HIV/AIDS. Indeed, by 2030, global HIV/AIDS mortality is expected to double from the current annual toll of 3 million deaths. Avoiding this scenario must remain a major global health priority. Total deaths due to other Group I causes decline from 15.5 million in 2002 to 9 million in 2030. Unfortunately, this is substantially offset by the projected rise in HIV/AIDS deaths.

Although age-specific death rates for most Group II conditions are projected to decline, as populations age over the next thirty years there will be a significant increase in total deaths due to most of these conditions (Figure 3.5). Global cancer deaths are projected to increase from 7.3 million in 2003 to 11.5 million in 2030, and global cardiovascular deaths from 17 million in 2003 to 23.3 million in 2030. Overall, Group II conditions will account for almost 70% of all deaths in 2030 under the baseline scenario. Major failures with tobacco and obesity control efforts could dramatically alter this prediction, as was seen in several industrialized countries in the 1950s and 60s.

The projected 40% increase in global deaths due to injury between 2003 and 2030 is largely due to rising numbers of road traffic accident deaths, together with increases in population numbers more than offsetting small declines in age-specific death rates for other causes of injury. Road traffic accident deaths are projected to increase from 1.2 million in 2003 to 2.1 million in 2030, primarily due economic growth in LMICs.

The three leading causes of burden of disease in 2030 are projected to include HIV/AIDS, unipolar depressive disorders and ischaemic heart disease (Table 3.3). HIV/AIDS is predicted to be the leading cause of this burden in LMICs by 2015. For some causes, projected changes in disease burden over the next 30 years are likely to result in dramatic changes in global importance (Table 3.3). Lower respiratory tract infections and diarrhoeal diseases are expected to fall to 9th and 13th place in the global DALYs 'league' table, from 2nd and 5th place respectively in 2003. Malaria is also expected to decline in relative importance, as are congenital anomalies. Conversely, by 2030, HIV/AIDS is expected to be the leading global cause of DALYs, followed by depression, ischaemic heart disease, chronic obstructive pulmonary disease and perinatal conditions. This rather diverse set of conditions will require very flexible and innovative responses from health systems worldwide in order to avoid what are largely avoidable, or treatable conditions. Further research will help to focus these disease control efforts.

These projections predict a dramatic shift in the distribution of deaths from younger to older ages and from communicable, maternal, perinatal and nutritional causes to noncommunicable disease causes. The risk of death for children under five is projected to nearly halve between 2003 and 2030. Total tobacco-attributable deaths are projected to rise from 5.4 million in 2005 to 6.4 million in 2015 and 8.3 million in 2030. Tobacco is projected to kill 50% more people in 2015 than HIV/AIDS, and to be responsible for 10% of all deaths globally.

Table 3.3
Projected changes in rankings for 15 leading causes of death, in 2003 and 2030

Disease or injury	2003 rank	2030 rank	Change in rank
Within top 15			
Ischaemic heart disease	1	1	0
Cerebrovascular disease	2	2	0
Lower respiratory infections	3	5	-2
HIV/AIDS	4	3	+1
Chronic obstructive pulmonary disease	5	4	+1
Perinatal conditions	6	9	-3
Diarrhoeal diseases	7	16	-9
Tuberculosis	8	23	-15
Trachea, bronchus, lung cancers	9	6	+3
Road traffic accidents	10	8	+2
Diabetes mellitus	11	7	+4
Hypertensive heart disease	12	11	11
Malaria	13	22	-9
Self-inflicted injuries	14	12	+2
Stomach cancer	15	10	+5
Outside top 15			
Nephritis and nephrosis	17	13	+4
Liver cancers	18	14	+4
Colon and rectum cancers	19	15	+3

These projections represent a vision of the future for population health, based on certain explicit assumptions. By their very nature, projections of the future are highly uncertain and should be interpreted with caution. The results depend strongly on the assumption that future mortality trends in LMICs will have a similar relationship to economic and social development as has occurred in the HICs. If this assumption is not correct, then the projections for LMICs will be overoptimistic in the rate of decline of communicable diseases. The projections have also not taken explicit account of trends in major risk factors apart from tobacco smoking, and to a limited extent overweight and obesity. If broad trends in risk factors are for worsening of risk exposures with development, rather than the improvements observed in recent decades in many HICs, then the projections for LMICs would again be too optimistic.

3.6 Discussion and conclusion

This chapter provides an overview of the causes of mortality and burden of disease for high and low-to-middle income countries across the regions of the world in 2003 and of causes predicted for 2030. It also summarizes the contribution of 20 known risk factors for the latest year that figures are available (2000).

Burden of disease analysis offers a comprehensive, comparative overview of the state of population health, and the factors affecting the health of populations, which provide an important input to the assessment of areas of health that require attention. The latest GBD estimates, summarized here, are a much expanded effort compared to the original 1990 GBD study, with the incorporation of much new data and a greater understanding of the limitations of routinely available data sets. Yet, there remains substantial uncertainty about the comparative burden of diseases and injuries in many parts of the world, uncertainty that has substantially greater consequences for policy than the inclusion or otherwise of social choices such as age weighting into the basic burden of disease metric.[4]

The information presented can be summarised as follows:

- Mortality estimates are higher in LMICs than HICs, and people in LMICs die younger than in HICs.
- There is large mortality variation between LMICs: China has a higher mortality of people above 60 years while in Africa younger populations die prematurely, with a large proportion of these deaths being of young children and caused by infectious diseases.
- Deaths due to noncommunicable diseases are highly prevalent in LMICs.
- Contrary to common belief, disease burden due to noncommunicable diseases plays a key role in some LMICs, with rates comparable to those in HICs (two thirds of the burden in China). Conversely, Africa has a pattern of disease burden in which infectious diseases predominate.
- Trends over time in Africa reflect increases in infectious diseases, while those in other LMICs show increases in noncommunicable diseases.
- A large proportion of the disease and injury burden attributable to risk factors is preventable.

Burden of disease estimates reflect, in contrast with mortality estimates, the importance of noncommunicable diseases in LMICs other than African nations. Disease burden captures not only premature death but also years living with disability. As such, the weight of conditions before death can be quantified. While some of this disease burden can be averted through known interventions, applying and scaling up such interventions in LMICs is not straightforward. Research can help in identifying tools and programmatic pathways to put knowledge into action.

Despite a continuing improvement in average health status in many developing countries, there are widening health inequities within countries, and some regions where health reversals have occurred. Across the world, children are at higher risk of dying if they are poor and malnourished, and the gaps in mortality between the haves and the have-nots are widening. In some parts of the world, particularly in sub-Saharan Africa, mortality declines have reversed.

For example, overall, 35% of Africa's children are at higher risk of death than they were 10 years ago. Those that do make it past childhood are confronted with adult mortality rates that exceed those of 30 years ago. Indeed, the state of adult health is characterised by three major trends: slowing down of gains and widening health gaps, increasing complexity of the burden of disease, and the globalisation of adult health risks.

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Chapter 4

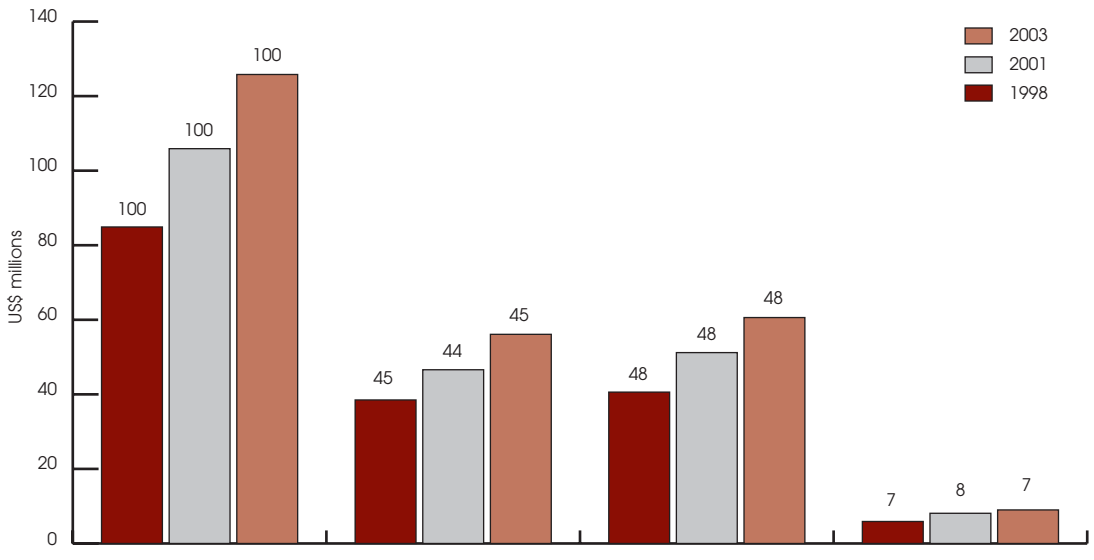
Resourcing research for health: challenges and priorities for the public sector

Resourcing research for health: challenges and priorities for the public sector

4.1 Introduction

The assessment of resource flows presented in Chapter 2 shows that, in 2003, 48% of the global total of US$ 125.8 billion spent on health research was contributed by the private sector, 45% by the public sector and 7% by philanthropic foundations. Thus, while the totals have risen, the spread of contributions has not changed significantly from that observed in the Global Forum for Health Research's previous studies[1] (Figure 4.1).

Figure 4.1
Health research spending by sectors 1998-2003, US$ millions (Y axis) and % of annual total (bar labels)



As noted in Chapter 1, in the 1990s the landscape of research for health was relatively simple, with a few international organizations conducting research directed to the health needs of developing countries, where virtually no private-sector funded research was being conducted. Now, much more international development money is available. And there are also many more players in the field, including philanthropic foundations and public-private partnerships addressing specific areas such as products for neglected diseases. In some developing countries, the public sector has begun to make significant investments in diverse areas of health research, ranging from basic research and pharmaceutical R&D to health policy and systems research, social sciences and operational research. Pharmaceutical companies have become important contributors of resources such as expertise and products and are now substantial investors in health research in many developing countries through their funding of clinical trials.

Within this complex array of actors and initiatives, the multiple roles of the public sector merit close examination. The public sector not only provides funding but also sets priorities and policy and legal frameworks, nationally and globally, within which the initiatives aiming to close health research gaps and to build country capacities operate.

4.2 Addressing the global burden of disease

Globally, most of the public-sector funding for health research (more than US$ 56 billion in 2003) originates in HICs, where it is mainly used to support basic research in universities, medical schools and research institutes. Basic research in the chemical, biological and pharmaceutical sciences gives rise to leads for the creation of new drugs and vaccines. At least in commercially attractive areas, such leads are generally picked up by industry and a process of applied R&D then generates a pipeline of potential candidates for evaluation in clinical trials. In a recent study, Light[2] argued that public sources may be funding as much as 84% of all basic research in the health field either directly or indirectly, such as through subsidies and tax breaks to research conducted by the private sector. Consequently, if products are to be generated that are appropriate to the health needs of developing countries, there is clearly a crucial role for the public sector to ensure that relevant basic research is conducted.

To what extent do the research priorities of major funding bodies reflect this need in practice? Precise data are not easily obtained, since information on research spending is rarely reported in disease-specific or geographically defined categories that can easily be related to health conditions of particular significance to low- and middle-income countries. This information gap is itself significant and requires attention. Moreover, the evidence that can be found points to major gaps in investment in relevant research in all three groups of conditions that contribute significantly to the burden of ill health in LMICs.

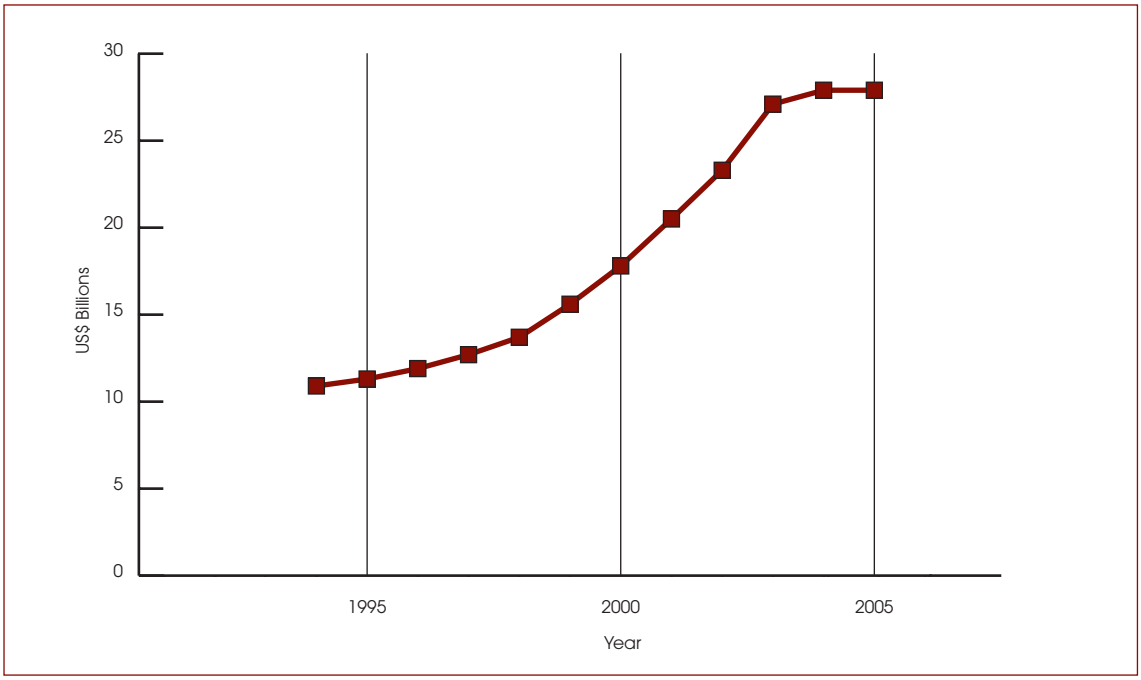
Group I (communicable, maternal and perinatal conditions and nutritional deficiencies) accounted for one third of the 57.5 million deaths worldwide in 2003, the vast majority of which occurred in LMICs (see Chapter 3). Infectious diseases are responsible for about 10 million deaths and 350 million lost DALYs every year, and account for a third of all deaths in low-income countries. Almost half of all child deaths in 2003 were due to preventable and treatable communicable diseases (acute respiratory infection, measles, diarrhoea, malaria, HIV/AIDS) and while deaths from some of these causes have fallen in the 0-4 age group, those due to malaria and HIV/AIDS have risen since 1990.

Research is not the only answer. Much of the observed mortality could be avoided by applying known treatment and prevention measures more effectively. The failure to implement available, proven interventions can be attributed to a complex series of inter-related causes, including poverty, political indifference, socio-cultural factors and, sometimes, corruption that lead to failures to commit adequate human, financial and institutional resources within countries and in the development agencies that assist them. But research certainly has many roles to play. It can demonstrate how well or poorly efforts are progressing and can help uncover which of the possible factors are proving to be the key barriers to implementation that need to be removed; it can provide experimental evidence about how best to adapt what is known to local contexts; and it can provide new knowledge, tools and products where existing ones are inadequate or are beginning to fail due to emerging problems such as drug resistance. Rapid and accurate diagnosis of infectious diseases is an essential prerequisite for timely and effective treatment. Recent research has demonstrated that a number of diagnostic kits for diseases such as TB[3] are unfit for purpose and has pointed to the need both for more such evaluations and for R&D to develop better diagnostic tools.

The spectrum of necessary research requires action on several fronts. The creation of new products – such as drugs, vaccines, diagnostics and microbicides – to combat infectious diseases requires research that is often long-term, expensive and technologically challenging. Such research must take place across a range of biomedical disciplines, beginning with basic research to uncover the biological mechanisms of infection and resistance, progressing through R&D for product development and culminating with clinical trials and implementation studies as the new products are brought into use in disease-endemic countries. The 'market failure' observed in the last quarter of the 20th century, when the pharmaceutical industry developed only a dozen or so new drugs for infectious diseases, clearly demonstrated that the public sector has vital roles to play in filling this gap.

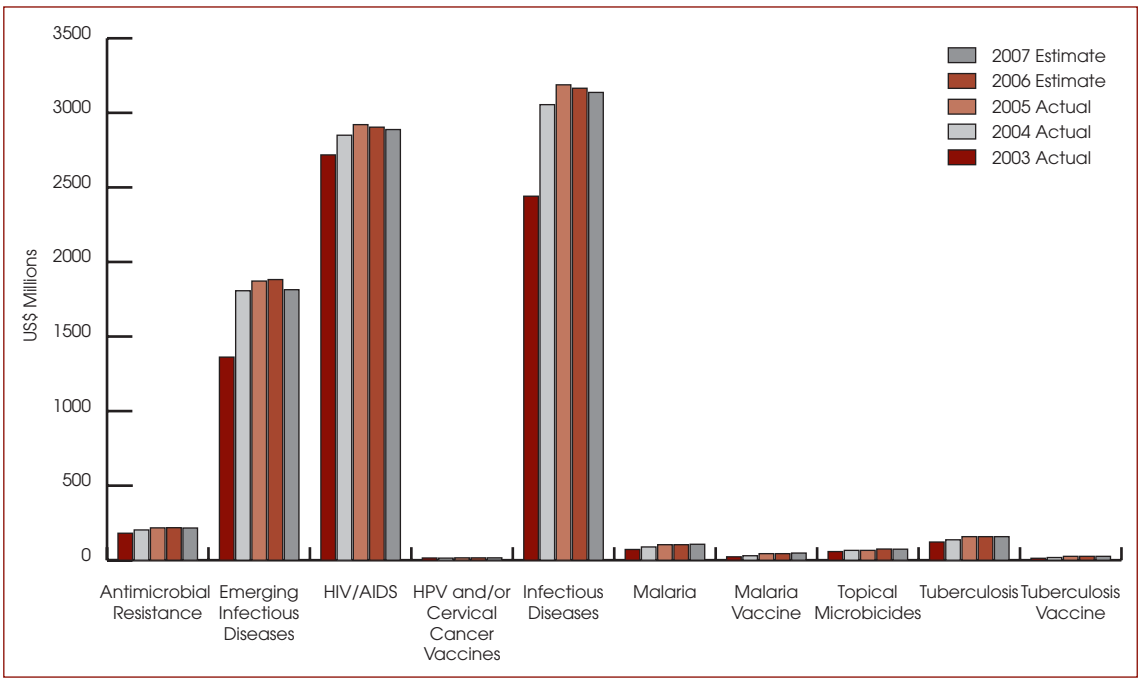
The largest single source of public sector financing for health research is the National Institutes of Health in the United States (NIH), whose appropriations from the United States government rose steeply from the mid-1990s (Figure 4.2).

Figure 4.2
US-NIH appropriations 1994-2005



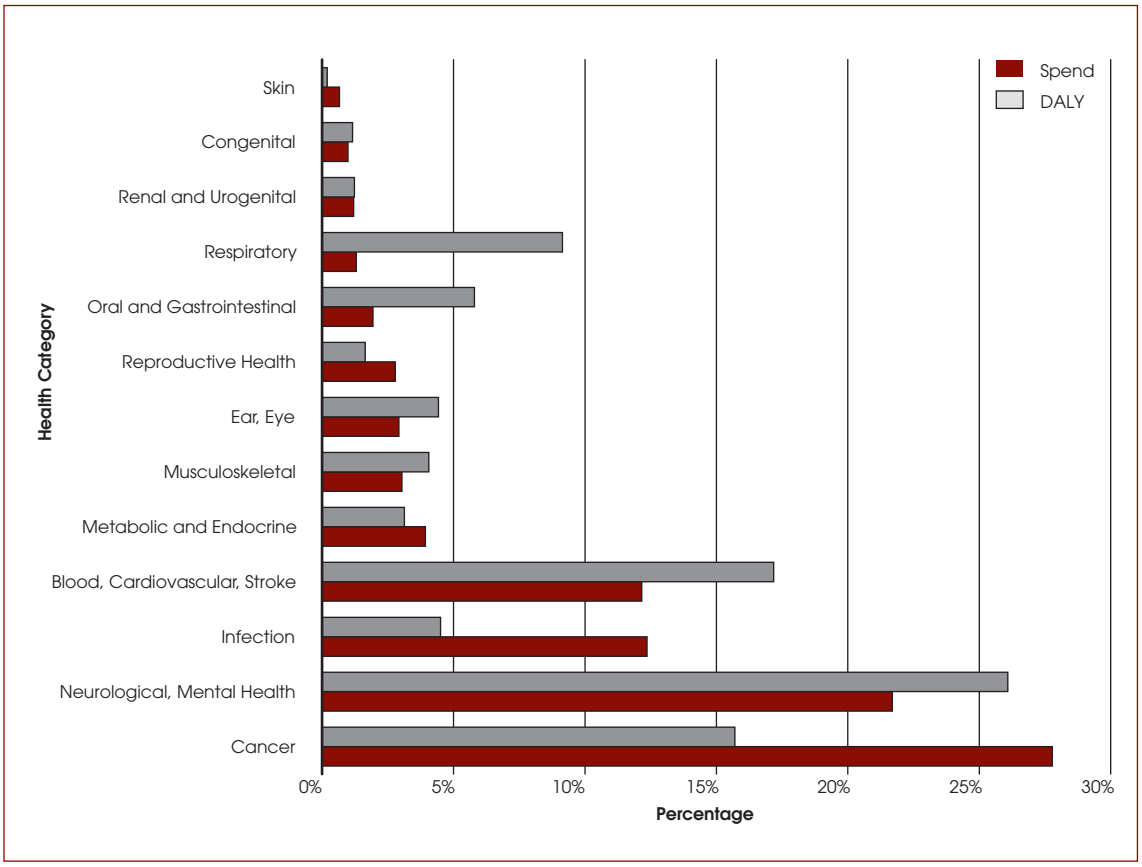
Research conducted or funded by the NIH addresses a range of national and global health challenges. Within the NIH's broad portfolio, annual allocations for infectious diseases currently total around US$ 3 billion, with HIV/AIDS, TB and malaria being the main beneficiaries. Figure 4.3 shows actual and projected NIH funding for the period 2003 to 2007 for a range of infectious diseases (figures are NOT additive between research categories).[4]

Figure 4.3
US-NIH funding for some infectious diseases 2003-2007



Two recent publications from the United Kingdom reflect the growing interest in research funding and its relationship with health problems. The first ever national study detailing the distribution of spending on all types of health research across all areas of health and disease, and comparing public investments in health research with national burden of disease was published in 2006 by the UK Clinical Research Collaboration.[5] Such analyses can be extremely valuable in helping to understand national patterns of spending and to help set priorities. However, the juxtaposition of spending alongside burden of disease must be used with caution, as it is not be expected that there should always be a simple 1:1 relationship between them. For some diseases there may be a lack of optimal drugs and very costly, long-term R&D could be necessary to create these, while for other diseases very effective tools may be available and any research needed may be in relatively inexpensive areas to understand factors such as social determinants or failures of access, compliance, etc. Priority setting should use the burden of disease information as one element of a complete mapping of what is known about disease, for which tools such as the Combined Approach Matrix can provide assistance.[6]

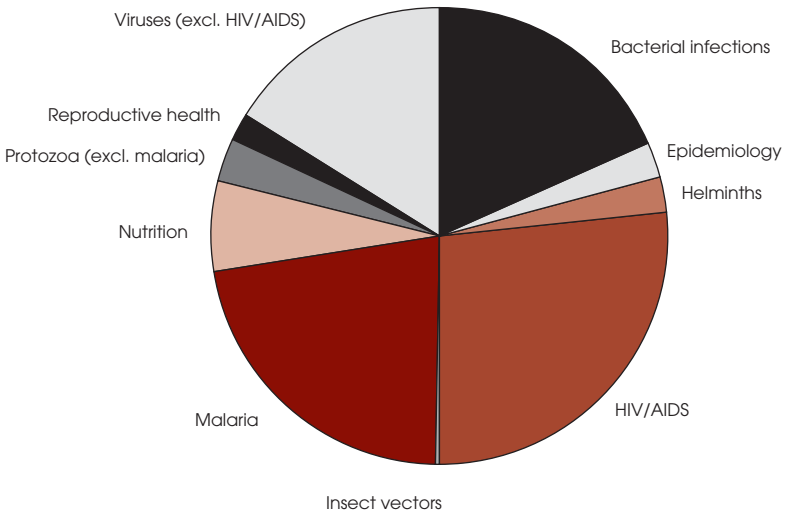
Figure 4.4
Proportion of combined spending on health specific categories compared with DALY rates



Estimated DALYs for United Kingdom 2002 (WHO Global Burden of Disease Project)
Data excludes R&D support for NHS providers funded by the UK Health Departments, core support costs (e.g. for the Wellcome Trust Sanger Institute) and research taking place outside the UK.

The United Kingdom's Medical Research Council (MRC) has reported its spending on 'global health research' for 2005. This research focused on Group I conditions (Figure 4.5) and cost £30 million (c. US$ 55 million).[7]

Figure 4.5
UK-MRC investment in global health research 2005



The size of the investment necessary to address a particular disease or condition cannot simply be related to the burden of disease:

- If there are no effective drugs or vaccines for a particular infectious disease, large investments will be required to create them. Estimates of the cost of creating a new drug vary substantially: industry-based figures place the 'full' cost of development of certain drugs, which includes the opportunity cost of the capital invested, as high as around US$ 1 billion,[8] while other sources[2] suggest that more typical costs may be one-tenth of this.

  In principle, if the technological challenges are similar, it should cost about the same to develop a safe and effective drug for an infection that kills a thousand people a year as for one that kills a million. Burden of disease data can be used to help determine relative priorities for the allocation of scarce resources – but if the health of individuals is taken as a human right, the lives of each of the one thousand dying from one infection should be valued equally with each of the million dying from another infection.

  For diseases that cause significant mortality (e.g. more than 1% of global deaths or DALYs annually) and where new drugs or vaccines are required, a combination of investment and burden of disease data can, however, provide a rough guide to whether the resources being committed are commensurate with the scale of the problem.

- Using such data for 2001-2002, the Global Forum for Health Research estimated that the average expenditure on all health research amounted to

about US$ 72 per DALY. But for the 'big three' MDG-targeted diseases, HIV/AIDS, TB and malaria, which together accounted for over 11% of the global burden of disease in 2001, and which each require the development of new drugs and/or vaccines; the combined investments in research averaged around US$ 8 per DALY in 2001.

- The finance data for this assessment were drawn from the Global Forum's estimates of research spending based on reports of OECD, industry and other sources. In a related investigation, bibliometric techniques reviewing the costs of published research were used to assess spending. Compared to the previously described approach, the methodological differences result in some quantitative differences in absolute spending levels for research on different diseases and conditions. However, when combined with burden of disease data, a very similar pattern emerges: average spending levels to develop new drugs for conditions that have received considerable attention in high-income countries, such as cardiovascular disease and diabetes, are in the range of around US$ 60–100 per DALY, while investments for diseases like HIV/AIDS, TB and malaria are up to an order of magnitude lower (Table 4.1).

Table 4.1
Relationship between research funding and burden of disease (BoD)

Condition	Global BoD (Million DALYs)	% of Total Global BoD	R&D Funding US$ Millions	R&D Funding US$ per DALY
All BoD[1]	1,470	100	105,900	72
HIV/AIDS + TB + Malaria[1]	167	11.4	1,400	8.4
CVD[2]	148.19	9.9	9,402	63.45
Diabetes[2]	16.19	1.1	1,653	102.07
HIV/AIDS[2]	84.46	5.7	2,049	24.26
Malaria[2]	46.49	3.1	288	6.2
TB[2]	34.74	2.3	378	10.88

[1] Financial data for 2001 from *Monitoring Financial Flows for Health Research, Volume 2*, Global Forum for Health Research, 2004; BoD data from WHO Global Burden of Disease, World Health Organization, 2002.
[2] Based on bibliometric assessment of R&D spending presented by G Lewinson et al. (Forum 8, Mexico City, November 2004) and work by the Malaria R&D Alliance.[9]

- The following are among the necessary new pharmaceutical products that require large investments to bring them into clinical use:
  - Novel antibacterial agents, since older ones are becoming increasingly less useful as bacteria grow resistant to them (e.g. methicillin-resistant *Staphylococcus aureus*, MRSA, is now a major problem throughout both the developed and developing word). There has been very little R&D in this sector for many years as the high investment needed and low expected profits have provided industry with few incentives.
  - New antimicrobial agents to combat re-emerging diseases: in the case of TB, such agents need to be both more effective against resistant strains and to provide a complete cure in a much shorter period of time than current drugs. TB also requires an effective vaccine that can protect adults and children.
  - New treatments for drug-resistant malaria are urgently needed – especially in paediatric formulations, as malaria kills up to a million African children aged under five every year. A malaria vaccine is also urgently required.
  - While there are now a large number of anti-retroviral drugs for treating HIV/AIDS, development of vaccines and microbicides to prevent transmission is an urgent priority.
- Smaller, but still substantial, investments (US$ 1 million – US$ 10 million) are necessary to develop diagnostic kits for a wide range of diseases endemic in poor and tropical countries. The kits must be robust, reliable, sensitive, accurate and be useable by health workers under field conditions.
- Research into health policy and systems is generally less expensive than studies that require laboratories or sophisticated scientific equipment. The scale of costs will vary considerably, however, depending on factors such as duration, numbers of subjects under study and location.
- Similarly, costs of research on implementation of health interventions can vary greatly, depending on whether it involves clinical investigations or field studies related to factors such as access, compliance, etc.

Group II or noncommunicable diseases (NCDs), such as cancers, diabetes, ischaemic heart disease, cerebrovascular disease (stroke) and mental and neurological conditions, have hitherto been largely regarded as 'diseases of affluence' that reflect lifestyle changes (in diet, physical activity, work and the use of tobacco and other substances) as countries develop However, it has been predicted for some time (e.g. by the WHO Ad Hoc Committee on Health Relating to Future Intervention Options in 1996) that, within 1-2 generations, NCDs will increasingly affect poor populations and become the main sources of mortality and morbidity in many developing countries.

Sadly, this prediction is proving to be accurate. NCDs have become the major sources of mortality and morbidity in all regions except Africa. Moreover, according to new projections (see chapter 3), there will be significant increases in total deaths due to most Group II conditions, with global cancer deaths rising from 7.3 million in 2003 to 11.5 million in 2030 and global cardiovascular deaths from 17.0 million in 2003 to 23.3 million in 2030. Rates of NCDs are rising steeply in LMICs, where 15-59 year old adults now face a 30% greater risk

of death from NCDs than their counterparts in high-income countries. Around 45% of the disease burden in LMICs is now from non-communicable diseases, a rise of 10% in its relative share since 1990 (Chapter 3).

In 1999, in recognition of the growing seriousness of this problem, the Global Forum for Health Research created an Initiative on Cardiovascular Health in Developing Countries. This is now an independent foundation with a secretariat based in New Delhi. It conducts an active programme in research and advocacy, raising awareness of the problem and developing appropriate solutions.[10]

This new 'epidemic' of NCDs in developing countries raises important questions. A number of NCD prevention and treatment tools have been developed and effectively applied in high-income countries in recent years. These include long-term oral or injectable drugs for such conditions as diabetes and hypertension; combinations of drugs for reducing risks of cardiovascular events; chemotherapies for cancer; psychotropic and other neurologically active agents for a range of mental and neurological conditions; as well as dietary materials to influence risk factors such as lipid uptake and metabolism. To what extent are these approaches relevant to poor populations and in settings where health services and associated diagnostic facilities are inadequate, inaccessible or unaffordable? What adaptations are needed to prevent and treat chronic conditions, taking account of variations in cultural, economic, environmental, genetic and social contexts? Can developing countries adapt the lessons that have been learnt elsewhere concerning NCDs and avoid many of the mistakes that have proved so costly in lives and resources? How do globalization trends in diet, work, leisure, legislation and other factors impact on health? Should prevention focus on the regulation of food, alcohol and tobacco, or on information, education and communication to promote healthy behaviour? Will an approach based on 'responsibilities' or 'rights' be more effective in different settings, and how should these be defined? How can gender biases in diagnosis and treatment be avoided? What are the public health, ethical and practical issues in the mass treatment of poor populations, often with low average levels of education or scientific knowledge, with dietary and medical products aimed at reducing risk factors such as high serum LDL and blood pressure? Beyond the health issues, what are the economic and social impacts of the chronic disease epidemic for individuals, families and countries?

Overall, it is evident that a substantial research agenda needs to be defined in developing responses to the new challenge of epidemic NCDs in low- and middle-income countries. With the mapping of this priority agenda will come a need to finance the necessary research. Much of the work will need to be done in local settings in developing countries, involving the populations at risk and engaging them not only as subjects but as collaborators in the design, conduct and analysis of the studies. Financing for this work will certainly need to come from public sector sources and be channelled through a range of sectors, disciplines and organizations.

Rates of death and disability due to injuries (Group III) are growing in many developing countries and it is projected that there will be a 40% increase in global deaths due to injury between 2003 and 2030. Road traffic accidents are now the fourth leading cause of mortality in adults aged 15-59 years and such deaths are projected to increase

from 1.2 million in 2003 to 2.1 million in 2030, primarily due increased motor vehicle fatalities associated with economic growth in low and middle income countries (Chapter 3). Like NCDs, road traffic injuries are preventable,[11,12] but this requires a combination of adaptation of existing, effective interventions and research to develop new knowledge and tools. To date, there has been limited funding, particularly in LMICs, for traffic related research.[13] The Global Forum for Health Research, in collaboration with WHO, has established a Road Traffic Injuries Research Initiative to promote appropriate research in developing countries.[14] Investment by the public sector in research and implementation for prevention of road traffic accidents can yield very high rates of return, since these injuries drain developing economies of 1-2% of gross domestic product (about US$ 100 billion) each year, or twice the total development aid received worldwide by developing countries.[15]

In addition to addressing the main categories of disease and disability, research on risk factors is also needed. As discussed in Chapter 3, a large proportion of the world's disease and injury burden, including a growing proportion of that burden in developing countries, is attributable to a handful of known risk factors and is preventable.

4.2.1 Widening the spectrum: research for health

Moving beyond these factors, research into the social, economic and other determinants of health is beginning to emerge as part of the new research agenda. Research for health must have horizons that stretch far beyond the immediate, pressing needs of disease response. As overall resources are now increasing, this is an ideal opportunity to reconsider the patterns of investment. There could be great benefit to public health if the resources needed to develop disease treatments were complemented by funding of research into methods for eliminating malaria-carrying mosquitoes, cleaning up contaminated water, creating sustainable materials for affordable and good quality housing, developing efficient and environmentally friendly processes for handling sewage, and tackling many similar problems that impact on the day-to-day lives of the poor. This would ensure that people treated to cure their diseases do not return to the conditions that made them sick in the first place.

The breadth of issues now encompassed by global health, and the correspondingly wide spectrum of research needed to address them, is illustrated by Finland's decision[16] to make promotion of the principle of '*Health in All Policies*' a core part of its EU presidency in 2006.

The need to map out of a new research agenda and to delineate funding mechanisms and resources needed for such cross-sectoral and multi-disciplinary studies presents new challenges for the future.

4.2.2 The public sector and research for health

Overall, resourcing the agenda of research that will lead to significant health benefits in developing countries will require greater effort by the public sector across the world. Some key points that emerge as crucial to achieving the necessary levels of resources and ensuring that they are effectively deployed are set out in Box 4.1.

Box 4.1:
Financing health research for development: some key public sector actions on resources and policy

High-income countries should:

- give greater priority in national research programmes, such as those funded through the United Kingdom's Medical Research Council and the National Institutes of Health in the United States, to basic research on diseases endemic in poor countries;
- ensure the inclusion of more health research in development programmes funded through bilateral and multilateral channels – at least achieving the target of 5% of health aid being earmarked for research and for strengthening research capacity;
- give greater support to product development partnerships creating drugs, vaccines and microbicides;
- support research into the social, economic and political determinants of health and into ways to give all people the opportunity to be healthy.

Low- and middle-income countries should:

- commit greater resources to health research – at least achieving the target that an amount equal to 2% of government expenditure on health is allocated for research and for strengthening research capacity;
- engage with stakeholders, including researchers and communities, in setting research priorities based on health needs, using a broad definition of health;
- develop both funding streams and policy environments that foster capacity building across all aspects of research for health;
- develop and strengthen national health research systems that ensure that research capacities are effectively utilized on priority research and that results are translated into policy and action;
- support the development of innovation systems that will enable new industries to produce the products needed to address endemic diseases and conditions.

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