

Monitoring Financial Flows for Health Research

2004

Acknowledgements

The work of the Monitoring Financial Flows for Health Research Project (Phase II) presented in this report builds on earlier work in Phase I of the project. Mary Anne Burke and Andrés de Francisco have main editorial responsibility for the report. Contributors to the report include: Chapters 1 and 4, Stephen Matlin as main author, with Andrés de Francisco and Mary Anne Burke; Chapter 2, Mary Anne Burke as main author, with the support of Yuri Heymann and Alison Young for preparation of data, Caryn Miller as author of the section on International Health Research, and Gregor Wolbring as author of the feature on Nanotechnology; Chapter 3, Colin Mathers and Andrés de Francisco as co-authors.

Consultants commissioned by the Global Forum to provide technical analysis, assist in preparation of drafts, and gather relevant data include: Rodolfo Barrere, Walter Gulbinat, Yuri Heymann, Caryn Miller, Gregor Wolbring and Alison Young. Jane Foy was responsible for editing the content, Susan Jupp co-ordinated the publication and John Warriner oversaw the administration.

In addition, we would like to thank Ritu Sadana, Andrew Kennedy, Catherine Michaud, Boris Azais, Paul De Lay, Roy Widdus and Sylvie Olifson for their technical advice and guidance. We would also like to thank Carole Heilman, Irene Glowinski and Logan R. Thornton, NIH NIAID; Jane Rowley and Robert Hecht, IAVI; Shea Fialdini and Rebecca Weber, the Bill and Melinda Gates Foundation; Craig Lissner, HRP; Richard Miller, NIH/FIC; Sylvia Bennett, NIH/OD; David Carr, Wellcome Trust; Joar Svanemyr, NORAD; Bente Ilsoe, Danida; Miyuki Parris, World Bank; Anna Karaoglou, EC; Lana Dakan, Packard Foundation; Fabio Zicker and Erik Blas, TDR; Olivier Fontaine and Cathy Wolfheim, WHO/CAH; Tikki Pang and staff, WHO/RPC; Lisa Devasquez, USAID; Viveka Persson, SAREC; Gerit van Ark, and Anneke Burger, ZonMw; Osamu Kunii, MOFA, Japan; Rob Ives, IDRC; Bo Stenson, UNICEF/GAVI; Sylvia de Haan, COHRED; J.L. Castro, IUATLD; John Chalker, INRUD; Tanja Linde, Bernard van Leer Foundation; Sue West, Sir Halley Stewart Trust; A.Pucie, FNIH; Jill Conley, Howard Hughes Medical Research Institute; Charlanne Burke and Charles Gardner, Rockefeller Foundation; staff at the Foundation Center in New York and Washington, D.C.; staff at the European Foundation Center, Brussels; staff at USAID Library and OECD Documents for their assistance in tracking down and providing data.

The views expressed in this document are the sole responsibility of the Global Forum for Health Research Secretariat.

Mary Anne Burke
Health Analyst/Statistician
Global Forum for Health Research

Andrés de Francisco
Deputy Executive Director
Global Forum for Health Research

Foreword

In September 2000, 189 nations adopted the United Nations Millennium Declaration affirming the right of every human being to development and set goals for the achievement of those rights. Four of the eight Millennium Development Goals (MDGs) specifically address major health issues – malnutrition, maternal and child mortality, and specific infectious diseases. The remaining goals also have a significant health component, given the strong link between health and development.

At current rates of progress, it seems certain that the MDGs will not be achieved by the target date of 2015. In the health sector, one important reason for this under-performance is that current efforts – to improve the capacity and functioning of health systems and services and to ensure that they bring existing knowledge and health technologies to the benefit of people in every country – are simply too little, or at least inadequately shared. A second important reason is that there are still major gaps in our knowledge and in the adequacy of the tools available to improve health and reduce health inequities – gaps that are themselves a reflection of past failures of health research to adequately address the health problems of a large proportion of the world's population.

Inequities in health and health research – many of which derive from biases based on factors such as gender, ability, race and social class – must be eliminated if the MDGs are ever to be met – and with them the compelling needs of most of the world's people. New priorities are needed in allocating research funding to address the urgent health needs of the world's poor, marginalized and disadvantaged, and for research in and by low- and middle-income countries. Resources

must be found and changes in health R&D priorities shifted to support more research on:

- Development of new tools (e.g., drugs, vaccines, diagnostics and change of societal structures) for combating persistent infectious diseases and the growing burden of noncommunicable diseases in low- and middle-income countries.
- Interventions that incorporate equity in delivery and access and their optimum use in local conditions.
- Health systems and policies to increase the efficiency and availability of health delivery systems (e.g., health services and human resources, community involvement, health promotion and disease prevention campaigns that are appropriate to the economic and social circumstances in diverse countries and communities);
- The social, physical, spiritual and mental determinants and co-requisites of health for the poor and marginalized.
- Understanding the determinants, exposures and risk factors associated with poor health and diseases, and their transmission and treatment, including knowledge about pathways to target poor populations and interventions to reduce risk factors.
- Effective health promotion, prevention and treatment strategies to control noncommunicable diseases and injuries.
- Reducing gaps in health systems around delivery, availability and accessibility for health services.
- The health impact of changing patterns in the use of land and environmental resources, particularly for the health of poor and marginalized populations, such as indigenous peoples.
- The health impact of unsustainable global policies and practices that contribute to growing inequities in income; access to public goods and environmental resources,

including water, sanitation and housing; and access to decision-making and governance of the health research agenda.

It is clear that gaps in our knowledge must be filled through research efforts to bring about real improvements in the health of the world's poor and to reduce inequities in health and health research.

Against this background, it is evident that a detailed understanding is needed of what the world is spending on which areas of health research; where these finances come from;

how they are being used; and the extent to which they are directed to addressing *real* priorities in global health. This study of financial flows by the Global Forum for Health Research is presented as a contribution to answering these questions. It is hoped that by shedding light on how the world's health research resources are being used, important gaps will be exposed and action galvanized to close them – namely, by leveraging global health research in a way that genuinely improves *global* health, i.e. the health of the many – the 90 per cent – not just the few.

Professor Stephen Matlin, D.Sc.
Executive Director,
Global Forum for Health Research

Contents

Acknowledgements	ii
Foreword	iii
List of charts	vii
List of tables	viii
Executive Summary	ix
Chapter 1 Introduction	1
1.1 Why track resources for health research?	3
1.2 Health research	5
1.3 Naming the “10/90 gap”	6
1.4 Health research in a complex world	8
1.5 Objectives of the 2004 assessment	10
Chapter 2 Global Funding and Flows	11
2.1 Total global spending on health R&D	13
2.1.1 Measuring global investments	14
2.1.2 Analysing the growth in global investments	16
2.2 Sources of funds and sectors of performance	18
2.2.1 Funding sources	18
2.2.2 Performance sectors	19
2.2.3 Public funding	22
2.2.4 Private funding	26
2.2.5 Foundations and development cooperation	37
2.3 Financial flows for international research by HIC investors	38
2.3.1 Official development assistance (ODA)	40
2.3.2 Multilateral organizations	43
2.3.3 National research institutions	46
2.3.4 Partnerships, initiatives and other not-for-profit NGOs	49
Chapter 3 The Global Burden of Disease	53
3.1 Introduction	55
3.2 Mortality figures	55
3.2.1 Age-specific mortality	56
3.2.2 Causes of death	57
3.2.3 Trends in mortality over time	58
3.3 Burden of disease	59
3.3.1 Disability-adjusted life years (DALY)	59
3.3.2 Comparison of disease-burden patterns	60
3.3.3 Trends in burden of disease over time	62
3.3.4 Risk factors	64
3.4 Discussion and conclusions	66

Chapter 4	Focusing Research to Improve Global Health	69
4.1	A changing world	71
4.1.1	Sources of funding	71
4.1.2	Burden of disease	74
4.2	Implications for the future	76
4.2.1	Measuring the “10/90 gap”	76
4.2.2	Attention to neglected areas of health research	77
4.2.3	Attention to specific health research needs of Africa	80
4.2.4	Special areas requiring attention	80
4.3	The way forward	86
Appendices		
Appendix 1	Concepts and Definitions	89
Appendix 2	Methodology	101
Appendix 3	WHO Member States by geographical region and income level	109

List of charts

Executive Summary

- 1 Rises in total global expenditures on health R&D 1986-2001
- 2 Health R&D as a proportion of total national non-defence R&D

Chapter 2

- 2.1 Estimates for total health R&D expenditure, US\$ billion
- 2.2 Graphic representation of health research funding
- 2.3 Growth in health research expenditure by sectors of performance
- 2.4 Annual health R&D expenditure growth for LMIC
- 2.5 Annual health R&D expenditures growth for HIC
- 2.6 Sources of funds and sectors of performance for health research, 2001
- 2.7 Global distribution of public and private health R&D expenditures, 2001
- 2.8 Health R&D and national R&D as a % of GDP
- 2.9 Strength of investments in health R&D
- 2.10 Public funding of health R&D as a % of public health expenditure and GDP, 2001
- 2.11 Gap between actual and 2 per cent target for public expenditure on health research in LMIC: 2001 estimates
- 2.12 Basic research by pharmaceutical companies, as % of total R&D and in US\$ millions, 1999
- 2.13 Trends in pharmaceutical R&D by US companies, in \$US millions
- 2.14 R&D as a percentage of sales and in \$US millions, PhRMA member companies, 2002
- 2.15 R&D as a % of sales, PhRMA member companies (US), 2002
- 2.16 ODA resource flows for health research
- 2.17 International activities funding, National Institutes of Health (US), 1998-2003, US\$ millions
- 2.18 NIAID funding in Infectious & parasitic diseases, 1998-2003

Chapter 3

- 3.1 Mortality conditions by level of income, 2002 estimates
- 3.2 Age distribution of mortality in China and Africa, 2002
- 3.3 Trends in causes of death for children aged under five, low- and middle-income countries, 1990 and 2002
- 3.4 Burden of disease by major cause groups and country groups, 2002
- 3.5 Comparison of groups of burden of disease in the world, China and Africa
- 3.6 Trends in cause distribution of burden of disease (DALYs) in Africa and in other low- and middle- income countries, 1990 to 2002
- 3.7 Burden of disease by major cause groups and country groups, 2000

Chapter 4

- 4.1 Global health research expenditures, 1986-2001.
- 4.2 Global health research expenditures by sector, 1998 and 2001
- 4.3 Global investment in HIV/AIDS vaccine R&D, 2002, by source of funding
- 4.4 Global burden of disease estimates relating to Millennium Development Goals 4, 5 and 6
- 4.5 Contributions of co-sponsors to HRP, 1992–2001

List of tables

Chapter 2

- 2.1 Estimated global total health R&D funding 2001 (in current US\$ billion) compared with 1998
- 2.2 Public funding of health R&D in HIC, 2001 and 1998
- 2.3 Private for-profit health R&D expenditures by funders in US\$ millions, 2001
- 2.4 Top 10 foundations by giving for health
- 2.5 International health research expenditures, US\$ millions, 2001
- 2.6 Summary of resource flows data for selected ODA agencies in US\$ millions, 2001
- 2.7 Summary financial data for selected multilateral institutions, 2001

Chapter 3

- 3.1 Leading causes of death by income level, 2002
- 3.2 Leading causes of burden of disease by income level, 2002

Chapter 4

- 4.1 FDA new molecular entity (NME) approvals
- 4.2 Rates of disease burden by disease group and country income in 2002, measured by DALYs per 100,000 population
- 4.3 Global research effort for three types of diseases

Highlights

- 2.1 Genomics research and the 10/90 Gap
- 2.2 Future shock? Flagging NBIC technologies

Executive Summary

Introduction

Good health – in the holistic WHO definition of physical, mental and social well-being – is the ultimate goal of both individuals and societies. But despite the importance of health research – creating the new knowledge and technologies that are responsible for much of the gain in lifespan and health quality seen in the last century – the tracking of global expenditures for health research is a new field. The 1990 Commission on Health Research for Development made the first estimates of worldwide spending on health R&D (US\$30.0 billion) and in analysing the flows of resources described what became known as the “10/90 gap” – capturing the inequality revealed in their estimate that less than 10 per cent of the global budget for health R&D was being spent on 90 per cent of the world’s health problems. The expression has passed into widespread use as a shorthand for the continuing under-investment in health research for the needs of developing countries. It has served as a rallying call in the effort to galvanize governments, foundations and development agencies to pay more attention to these needs.

The Commission recommended a mechanism for monitoring and analysing global funding and, in 1998, the Global Forum for Health Research was created. It also recommended that governments in low- and middle-income countries (LMIC) allocate at least 2 per cent of the national health budget to “essential” national health research and that 5 per cent of funding from high-income countries go to health research and research capacity strengthening in LMIC.

Since the benchmark 1990 estimate, few new estimates of global resource flows for health research have been made: in 1996 by the WHO Ad Hoc Committee (US\$55.8 billion) and by the first Global Forum report in 2001 (US\$73.5 billion).

Current context

This second Global Forum assessment set out to see if growth in funding levels was continuing; whether the share of spending from public, private and not-for-profit sources had changed; whether LMIC contributions had increased; how well health problems affecting LMIC and poor populations were being addressed; and the extent to which global health inequities had been reduced.

The current report also takes place in the context of the UN Millennium Development Goals (MDGs), the most important collective commitment ever made by the nations of the world to tackle the poverty, compromised health and deprivation suffered by a large proportion of the world’s population.¹ Four of the eight MDGs specifically address malnutrition, child mortality, maternal health and infectious diseases.

Somewhere in all of this is the implicit understanding that health research will generate global public goods. At the same time, research can be highly specific or contextualized to the local or regional level. This has consequences for decisions about: who sets priorities and what research is conducted; where the research is done and by whom; who funds it; who will use and benefit from the research products.

¹ UN, 2000. *UN Millennium Declaration*. Available at: www.developmentgoals.org

This report also takes place in a complex and fast-changing world:

- In the 1990s, health resources were squeezed by declines in Official Development Assistance (ODA), the impact of structural adjustment programmes, and global economic malaise and downturns in some regions.
- Disease patterns are changing globally, challenging the capacity of national and global health research. Since 1970, 32 new diseases have appeared in human beings – HIV/AIDS being the most devastating – and drug-resistant varieties of old infectious diseases have been surfacing. Increasingly, low- and middle-income countries are experiencing multiple burdens as levels of noncommunicable diseases, HIV/AIDS and injuries mount alongside the existing burden of infectious diseases.
- The pharmaceutical industry, which funds almost half of global health R&D, has undergone changes as well. For example, there are many fewer large players; and the cost of bringing a new drug to market has escalated (one estimate puts the full cost at more than US\$800 million) prompting companies to go for ‘blockbuster’ drugs that justify such large investments with attractive financial returns. This raises concerns that drugs that are largely needed for LMIC “markets” will simply not be developed.

The big picture

As indicated above, the big picture on global health R&D has several important facets, including how much is being spent by whom, where, on what and for whose benefit. This report finds that global spending more than tripled between 1990 and 2001. This is, in part, due to rising costs but also undoubtedly represents a stronger commitment to and recognition of the importance of health research. An estimated US\$105.9 billion was spent globally on health research in 2001 (see

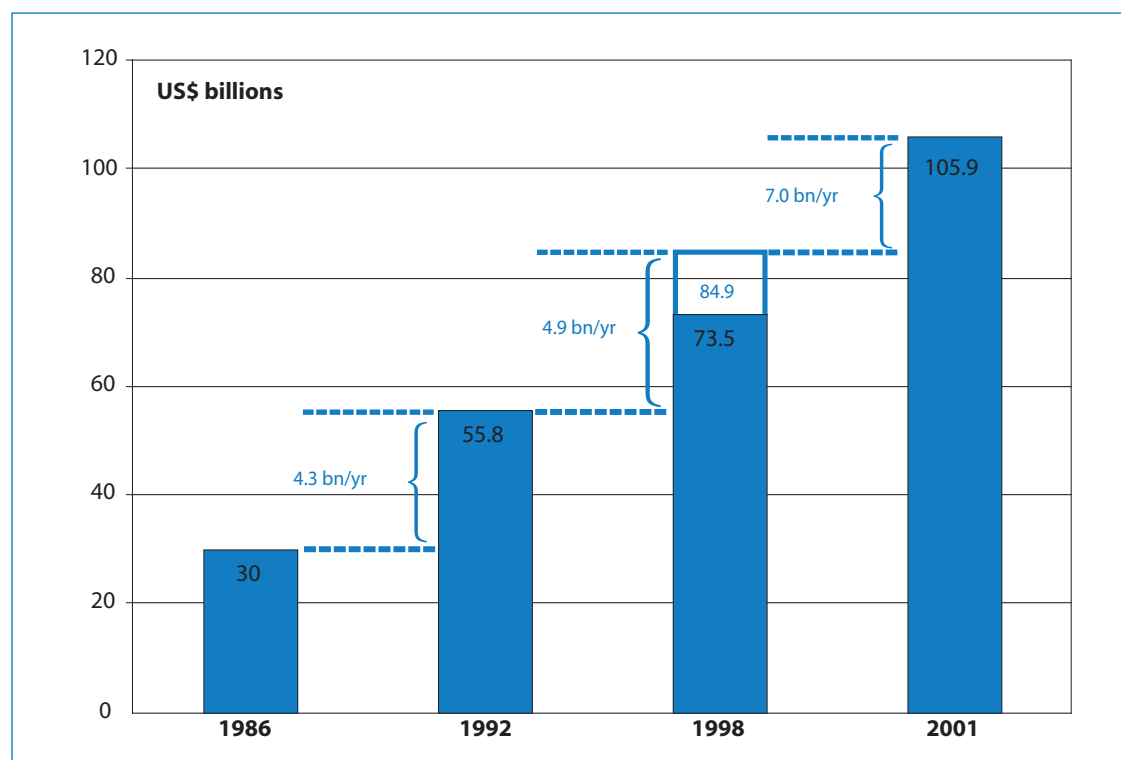
Chart 1); significantly, it represents 3.5 per cent of all health expenditures worldwide, up from 2.6 per cent in 1998.

The vast majority of R&D spending is done by high-income countries in high-income countries, aiming to generate products tailored to healthcare markets of high-income countries; a relatively small share is financed by low- and middle-income countries and carried out in these countries; an even smaller share is funded by high-income countries *but* carried out in and for the primary benefit of low- and middle-income countries.

Arguably, outcomes of health research in HIC have a trickle-down effect on LMIC, but often these outputs do not address the most pressing health issues in low- and middle-income countries; or they may be too expensive or high maintenance (e.g., technologically complex, cold-chain dependent) for LMIC health care systems to support; or, most inappropriately, LMIC health care systems may take on older HIC-generated solutions that serve a disproportionately low share of health issues in these countries at a disproportionately high price. There is a case for low- and middle-income countries to increase their investments in health R&D. However, reducing the “10/90 gap” – especially in the MDG timetable – requires a substantive growth in HIC financing of LMIC health priorities.

Globally, the lion’s share of health R&D funding continues to be roughly split between the public and private sectors – largely government and the pharmaceutical industry – in both HIC and LMIC. In 2001, public spending was an estimated US\$46.6 billion: US\$44.1 billion in HIC and US\$2.5 billion in LMIC. Private-sector spending was US\$59.3 billion, of which US\$51.2 billion came from for-profit companies and, significantly, US\$8.1 billion from not-for-profit organizations. Overall, R&D expenditure grew 24 per cent

Chart 1 Rises in total global expenditures on health R&D 1986-2001



in high-income countries and 23 per cent in low- and middle-income countries between 1998 and 2001.

The private for-profit sector is the largest investor globally, accounting for 49 per cent of funds for health research in high-income countries and 32 per cent in low- and middle-income countries. Governments are next, accounting for 43 per cent of funds in HIC and 59 per cent in LMIC. The private not-for-profit sector (private universities, foundations and charities) supplies 8 per cent of funding in high-income countries and 9 per cent in low- and middle-income countries – a relatively small but still significant wedge in terms of leveraging reduction of the “10/90 gap”.

Global investments in health R&D are heavily dominated by just a few countries – not unexpectedly given their long-standing economic strength. The United States alone accounts for 49 per cent of global expenditures, followed by Japan (13 per cent), United Kingdom (7 per cent), Germany (6 per cent) and France (5 per cent).

In a more sophisticated analysis, this report looks at four dimensions of research spending: national R&D as a percentage of GDP; national *health* R&D as a percentage of GDP; national health R&D as a percentage of national health expenditures; and national health R&D as a percentage of total R&D. The analysis finds, for example, that Sweden

scores very high in both overall R&D and health R&D. Denmark, France, Switzerland, the UK and the United States also have strong investments in both areas. Finland, Germany, Iceland, Japan and Korea do well in overall R&D but relatively less so in health R&D than other high-income countries. In general, low- and middle-income countries demonstrate comparatively low investments in R&D relative to GDP.

Another way of viewing this axis of analysis is presented in Chart 2: looking at health R&D as a proportion of total national non-defence research spending. Among HICs, this proportion varies greatly (e.g. USA, Japan) while among LMICs for which we have data it falls around 10 per cent (e.g. Czech Republic, India). Moreover, as this report shows, only four low- and middle-income countries have met the Commission recommendation of allocating 2 per cent of health spending to R&D: Brazil, Cuba, India and Mexico. Importantly, this analysis raises the same question for each country, though the answers may all be different: how meaningful is a health R&D investment of 2 per cent of the health budget if a country is under-investing in health?

Specific findings

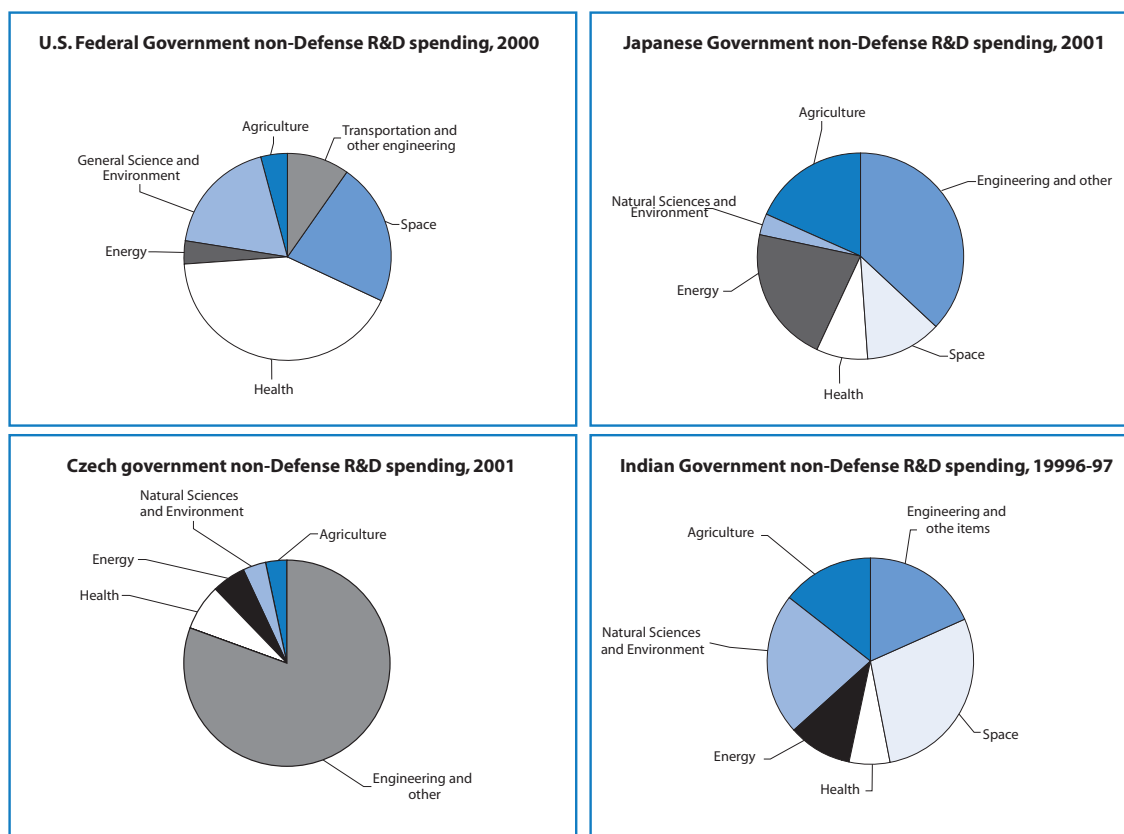
- The biggest actors in the private for-profit sector are multinational pharmaceutical companies. However, there is now explosive growth in investments in genomics research and the newly convergent nano- and related technologies. Predictions are that expenditures in nanotechnology will soon outstrip investments to date in genomics and biotechnology. These biosciences offer enormous potential – and equally large challenges in ensuring global health inequities do not grow even greater. As noted earlier, there are factors that inhibit corporate investment in LMIC health concerns, but a few significant

developments have taken place. The pharmaceutical industry is engaging in donation programmes and partnerships to make drugs available for neglected diseases or geographical regions. There are also prospects in LMIC economies (e.g., Brazil, China, India, South Africa) for drug companies to find attractive markets at levels of US\$10-US\$100 million rather than the US\$1.0 billion sought in high-income countries. This could improve the chances of new drugs being developed for neglected diseases in both local and global settings.

- Official development aid (ODA) fell sharply after 1990 and reached an all-time low in 1997 at just 0.22 per cent of the combined national income of donor countries. In 2001-02, the trend reversed, resulting in a 7.2 per cent real increase in ODA. Health ODA rose from US\$1.6 billion in 1998 to US\$2.7 billion in 2001 of which an estimated US\$400.0 million went to health R&D. Further increases in overall ODA are projected through 2006, setting the stage for increases in both ODA and health R&D.
- National research institutions in industrialized countries are continuing to expand their role in international health research, although it is unclear how much they are strengthening the research capacity of low- and middle-income countries. Most prominent is the National Institutes of Health (NIH) in the United States with a 2003 budget of US\$27.1 billion, up from US\$23.3 billion in 2002 and US\$11.9 billion in 1996.

NIH also funds research on infections and parasitic diseases through its National Institute of Allergy and Infectious Diseases (NIAID). Actual dollar expenditures for these diseases have more than tripled since 1998, but the NIAID share of total NIH spending has declined steadily since 1988. Further, since 2001, biodefence funding has approached half the NIAID budget.

Chart 2 Health R&D as a proportion of total national non-defence R&D



- More countries now report on their health research expenditures, and from the growing body of information it is clear that national research institutions in LMICs have improved their financial contribution to health research and research capacity strengthening.
- In the past decade, a plethora of initiatives, partnerships and other NGO agents involved in international health research has emerged. Some of these entities – like the International AIDS Vaccine Initiative (IAVI) and the Global Alliance for Vaccines and Immunization

(GAVI) – have become large well-funded organizations. Others such as MMV have evolved as public-private partnerships and taken on the legal framework of a foundation. Still others, like the Global Forum for Health Research and the Council on Health Research for Development (COHRED), have taken on roles as catalysts and advocacy organizations. These “third agents” in the global R&D environment can play diverse, important roles such as drawing public attention to neglected health issues, influencing the decision-making environment

at all levels or providing an alternative mode for harnessing public and private funding.

- Foundations, among private not-for-profit funders, are playing a growing financial role in health R&D and in shaping research agendas and, in some cases, focusing on the “10/90 gap”. The Bill and Melinda Gates Foundation in the United States was by far the top foundation in health giving at US\$518.9 million in 2002, focusing on diseases of highest burden worldwide. Support for HIV/AIDS prevention, treatment and research nearly doubled from US\$156.0 million in 2000 to US\$307.6 million in 2001, largely through grants from the Gates Foundation. Foundations have the strongest role and strongest history in western nations. For some of them, giving levels are strongly tied to returns on investment in the financial and stock markets.
- From a burden of disease perspective, the notion that the world is divided conveniently into two distinct parts – HIC most challenged by noncommunicable diseases and LMIC fighting infectious and parasitic diseases – is out of date and no longer tenable. High-income countries are also experiencing new waves of infectious diseases, such as SARS and HIV/AIDS, and many low- and middle-income countries are now faced with substantial health loss associated with noncommunicable diseases and injuries. For the LMIC as a whole, the burden of disease due to noncommunicable diseases (collectively referred to as Group II) and injuries (Group III) is now as high as that for the Group I combination of communicable diseases and maternal, perinatal and nutritional conditions. For China, Group II accounts for two thirds of the disease burden. However, a very different pattern emerges in sub-Saharan Africa, where Group I still accounts for three quarters of the burden of disease – reflecting especially the impact of HIV/AIDS, tuberculosis and malaria and

emphasising the importance of looking beyond highly aggregated averages to improve the focus on the key gaps and needs in each country or region.

Looking ahead

It is clear that the “10/90 gap” persists, that there is continuing under-investment in health research for the needs of developing countries. While an accurate quantitative measure of the actual size of the gap, as a global aggregate, is not practicable, a sustained, deeper and more intensive analysis of individual components of the gap is more vital than ever.

In keeping with its mandate, the Global Forum for Health Research will combine this in-depth analysis with its continued efforts to track and publicize global resource flows for health research. The Global Forum will use this approach to focus attention and leverage increased health research resources for the emerging priorities:

- the burden of disease trends which demonstrate the need to reinforce the global fight against infectious diseases and to strengthen efforts to stem the rising tide of death and disability due to non-communicable diseases and injuries in LMICs;
- the distinctive regional variations such as the intolerably high burden of communicable diseases and maternal, perinatal and nutritional conditions in sub-Saharan Africa;
- the central importance to development generally and to the MDGs in particular of addressing the needs of young people, including the high levels of child mortality in some regions and the globally neglected area of sexual and reproductive health;
- cross-cutting issues like poverty and equity; biases in health research, policies and practices that result in disadvantage on the basis of gender, ability, race, social class, age, and geographic region, among others;

strengthening and utilization of research capacity in LMICs.

By focusing more attention at the level of specific problem areas, examining in detail what needs to be done and by whom, the

Global Forum for Health Research can further increase the effectiveness with which it calls attention to the vital importance of harnessing health research to improve global health, and thereby accelerate the pace at which the “10/90 gap” is closed.

Chapter 1

Introduction

1.1 Why track resources for health research?

Tracking global expenditures for health research is a comparatively recent phenomenon. The first estimates of a global total (US\$30 billion) were published by the Commission on Health Research for Development¹ in 1990. Since then, few new estimates have been made—by the WHO Ad Hoc Committee² in 1996 (US\$55.8 billion) and by the Global Forum for Health Research³ in 2001 (US\$73.5 billion).

Within the global envelope of spending, the studies to date have contained information on the varying contributions of different sectors (e.g., public funds, private sector investments and contributions from not-for-profit organizations); the breakdown of these sources (e.g., contributions from high-income (HIC) and low-and middle-income countries (LMIC)); the share of spending in or for the benefit of low-and middle-income countries (e.g., research on diseases, such as malaria, that predominantly affect LMIC populations).

What purpose does this information serve? Its value can be seen from several perspectives:

- **Economic:** The ‘health industry’ is one of the largest economic sectors in the world, accounting for some eight per cent of global GDP and running to US\$trillions every year. The products and services that this money buys – including diagnosis, treatment, counselling and care as well as disease prevention and health promotion – are in great demand throughout the world. The health services sector is among the largest employers in many countries.
- **Health:** In the past 100 years, people living in high-income countries have come to expect to live 20 or 30 years longer than their great-grandparents. It is hard to over-estimate the scope and impact of this achievement in terms of human accomplishment. As part of this health revolution, significant gains in lifespan have also been made even in the poorest countries and regions – at least before the HIV/AIDS pandemic.

Health research is fundamental to the functioning of this “industry” – providing the basis of knowledge and technology for introducing new products and services, as well as understanding the efficiency and effectiveness of existing ones, and intelligencing information on the needs and demands of the “consumer”.

It is clearly important to know what the world is spending on health research – by whom, when, where and how – in order to support a critical intelligence and analysis of whether (in market parlance) we are getting the best return on investment. It is also clear, as research builds, that compromised health can visit an enormous drag, and even devastation, on economies. The huge long-term impact of HIV/AIDS on the economies of most-affected countries and the crisis hit of US\$billions associated with the SARS outbreak in 2003 illustrate the substantial economic implications that can flow from health and health investments.

A major part of the increase can be attributed to health care improvements (even after discounting the effects of increases in other important factors such as wealth and education), which have derived in large measure from new knowledge and technologies that have helped to reduce or eliminate many diseases and prevent or treat others. However, the job is not yet complete and, indeed, will never be.

The low levels of burden of disease due to infectious conditions that are now a characteristic of high-income countries is a mark of success: it can be done. But the challenges keep coming: increasing mortality in low-income and transition countries; the revival of old enemies like tuberculosis and antibiotic-resistant bacterial infections, and the emergence of new communicable and lifestyle diseases like SARS and HIV/AIDS; and the rise of noncommunicable diseases/conditions globally, including diabetes, lung cancer and obesity. No matter how “well” or “better” we are doing, health challenges await – and arise.

- **Human rights:** Arguably, “good health” is the apex of human desire: TO BE WELL. Access to good social, mental, physical, medical and spiritual health is a basic human right, claimed in the UN Declaration on Human Rights⁴ (1948) and confirmed since in a long series of international conventions and treaties. Importantly, the 1989 Convention on the Rights of the Child, stakes the claim of every child to the “best attainable standard of health.” Arguably, all human rights bend to this goal: the right to a name and a nationality; the right to cultural and political freedom; the right to safety; the

right to adequate food and shelter; the right to expression and participation; the right to be an individual and a member of a community; and the right to make a living. These are all, to some degree, manifestations of the WHO definition of health as not merely the absence of disease but the realization of physical, psychological and social well-being. Notably, the relationship between health and money is uneasy: persons in high-income countries might say that money cannot compensate for poor health; persons in low-income countries might say that good health cannot be had without money. These seemingly contrary perspectives, in effect, describe the “10/90 gap”.

- **Development:** Human development, certainly as measured by the United Nations Development Programme (UNDP), is an expression of three critical indicators: education, income and life expectancy. The latter is a blunt measure of health and the other two are widely recognized not only as facets of health but as determinants of health. Another dimension of development used to be expressed by dividing the world into two: the developed world and the developing world. With the convergence of a number of diverse elements – the rise of a human rights paradigm, the ascendancy of globalization over superpower rivalry, and the growing consensus that the world is not divisible but rather begs approaches that are more participatory and, indeed, work to reduce inequities of all kinds – it is no longer possible to keep these two worlds apart and the gaps between them only become more striking.

1.2 Health research

Health research is a process for obtaining systematic knowledge and technology that can be used to improve the health of individuals or groups and to reduce inequities in health. This definition carries several important consequences:

- In referring to both knowledge and technology, it encompasses a wide spectrum of activities including:
 - Fundamental research on health conditions, including, among other things: basic research to increase knowledge about questions of scientific significance; strategic research to increase knowledge and understanding of a health problem, with a view to eventually solving or reducing the impact of the problem; intervention development and evaluation, including research on the development of new products; public health interventions and personal health service interventions;
 - research on exposures, risk factors and socio-economic determinants and behaviour;
 - research on health systems;
 - research on health care delivery;
 - research capacity strengthening.
- In linking research activities to their ultimate purpose – improving health and reducing health inequities – it recognizes that the spectrum of research extends from the laboratory to the community and individual.
- It, therefore, conceptualizes health research as including:
 - biomedical research to create new products such as drugs, vaccines, diagnostics and appliances;
 - health policy and systems research;
 - research on ethics of health research;
 - social sciences and behavioural research; and
 - operational research.

(These have alternatively been grouped as the disciplines of biomedical sciences, population sciences and health policy sciences¹).

- The objective of benefiting the health of individuals and groups brings with it the requirement that there is human participation as subjects in various stages of the research, carrying with it the requirement for strict ethical codes, standards and systems of regulation.
- It is implicit, in the references to both what is created and the individuals or groups whose health will benefit, that some aspects of health research (such as product creation) will generate global public goods, while other research may be highly contextualised and of direct relevance on a more localized regional, national or sub-national scale. This has consequences for decisions about:
 - who might appropriately set priorities for what research is conducted;
 - where the research may be most appropriately conducted and by whom;
 - who might/should fund it;
 - who will use the research products; and
 - how the individual or group will gain access to and derive benefit from the research products.

In this report, the Global Forum adopts this broad definition of health research as the basis for discussions.

1.3 Naming the “10/90 gap”

The issue of massive under-investment in health research for the needs of low- and middle-income countries was first explicitly described in 1990 by the Commission on Health Research for Development.¹ Based on data for 1987, the Commission estimated that only about five per cent of global annual resources for health research (totalling about US\$30 billion in 1986) were being devoted to 90 per cent of the world's health problems. Of the US\$30 billion expended, more than half (US\$17 billion) came from public sources and the rest from the private sector. The 5 per cent (US\$1.6 billion) devoted directly to health research addressing the primary needs of low- and middle-income countries came from both high-income countries (58 per cent) and low- and middle-income countries (42 per cent) with three quarters of latter contributions arising from just a few countries: Argentina, Brazil, China (including Taiwan), India, Mexico, Saudi Arabia and South Korea.

The Commission recommended that governments in low- and middle-income countries should allocate at least 2 per cent of national health budget for essential national health research and that 5 per cent of external contributions to the health sector be allocated to health research and research capacity strengthening.

A further analysis of resources for health research was presented in the 1996 Report of the WHO Ad Hoc Committee on Health Research Relating to Future Intervention Options.² The Ad Hoc Committee estimated that in 1992 health research globally amounted to US\$55.8 billion, representing just 3.4 per cent of global health expenditure. Of the total, US\$ 28.1 billion (50.4 per cent) came from the public sector, US\$24.7 billion (44.3 per cent) from the private sector, and US\$3.0 billion (5.4 per cent) from the private

not-for-profit sector. Most of the public sector investment was derived from the governments of high-income countries, with the United States being responsible for US\$13.6 billion (50.4 per cent) and all low- and middle-income countries combined contributing US\$1.2 billion (2.2 per cent). Among high-income countries, about half (Austria, Denmark, Germany, Italy, Japan, the Netherlands, Norway, Portugal, Sweden and United States) allocated more than 2 per cent of public health expenditures to health research, with the largest share in the United States (5 per cent) and the smallest in Spain (0.7 per cent).

In estimating the use of this research funding for R&D on health problems in low- and middle-income countries, the Ad Hoc Committee used two different approaches:

Method A:

Examining the causes of disease for which 95 per cent or more of the global burden of disease (GBD) falls in low- and middle-income countries, and extrapolating from the largest single source of public funding (the National Institutes of Health in the United States), it was estimated that approximately 5 per cent (US\$1.3 billion) of all public sector R&D funds would ultimately benefit low- and middle-income countries. It was assumed that the private sector investment for this purpose would be about the same magnitude. This provided a total of US\$2.6 billion from the established market economies for R&D on diseases for which the majority of the burden lies in low- and middle-income countries.

Method B:

This estimation included:

- All public funds allocated to health R&D in low- and middle-income countries.

- Public funds in high-income countries that support R&D on tropical diseases and vaccines directly relevant to low- and middle-income countries.
- All R&D conducted in high-income countries on any health problem when it involves close collaborations with LMIC institutions or individual scientists.

Using this approach, the Ad Hoc Committee estimated that US\$2.4 billion (4.3 per cent of global health R&D) was spent specifically to address a range of health problems pertinent to low- and middle-income countries.

These estimates were complemented by additional analysis of spending patterns on specific diseases. In particular, the Ad Hoc Committee reported that for three leading conditions in developing countries – pneumonia, diarrhoeal diseases and tuberculosis (TB) – which collectively accounted for almost one fifth of global disease burden, R&D spending amounted to just US\$133 million, or 0.2 per cent of the world's total health R&D expenditure.

The Ad Hoc Committee concluded that there was a severe imbalance of resources away from the needs of low- and middle-income populations, suggesting two failures of the international health research community: first, to allocate its efforts in a rational manner to improve health; and second, to convince investors and potential investors of the benefits of investing in research for health. The 1996 Committee Report suggested: “Although there are many factors to consider when judging priorities for R&D, there is little doubt that better information on the balance

between investments and disease burden would provide a highly provocative aid to decision-makers.”

One of the proposals the Committee made was the creation of a Forum for Investors in International Health R&D that would provide a mechanism to enable review of global health needs, advocacy for health research to convince governments and other investors of its benefits, and analysis of the health needs of countries and regions with the aims of identifying existing effort and filling important gaps in global health research, particularly those that affect low- and middle-income populations.

As a result, the Global Forum for Health Research was established in 1998 with a mission to help reduce inequities in health research and the allocation of health research expenditures. It conducted a new assessment of global resources for health research in 2001 and found that of the US\$73.5 billion spent in the most recent year for which data were then available (1998), half came from the public sector (47 per cent from high-income and transition countries; 3 per cent from low- and middle-income countries), 42 per cent from the private sector and 8 per cent from the not-for-profit sector. The assessment noted that none of the developing countries studied was meeting the 1990 Commission's recommendation to spend as much as 2 per cent of the national health budget on health research, but a number of countries, including India and several in the Latin American/Caribbean region were spending more than one per cent, with Brazil and Cuba closest to the 2 per cent target.

1.4 Health research in a complex world

The need for conducting a new assessment of worldwide spending on research and development in the health field has been made urgent by several global developments in recent years. These have created a strong interest that spans the economic, political, developmental and public interest domains and the fields of health and science and technology.

The decline in Official Development Assistance (ODA) during the 1990s, combined with economic downturns in some regions in the second half of the decade and the impact of structural adjustment programmes on resources for the health sector, have all led to severe constraints on resources and threats to the capacities of health system – and concerns about the resulting impacts on population health. Health research is often regarded as a luxury and may be one of the first areas to suffer cuts in response to such pressures.

Disease patterns are changing globally, with many of the most profound changes occurring in low- and middle-income countries. Increasingly, many are experiencing multiple burdens as levels of noncommunicable diseases, HIV/AIDS and injuries mount alongside the existing burden of infectious diseases. At the same time, there is an increasing globalization of health problems, with high-income countries facing the resurgence of drug-resistant varieties of old infectious diseases and threats from new ones. Since 1970, 32 new diseases have appeared in human beings – including dengue fever, Legionnaire's Disease, hepatitis C, HIV, SARS and several other viral infections. These rapid changes have led to concerns about the extent to which health research at global and national levels is adequately resourced and appropriately focused.

Some notable changes in the sources and uses of resources for health research have taken place in the last few years. On the positive side, major increases have been made in funding for the NIH in the United States, and the Bill and Melinda Gates Foundation has made substantial donations to health research. New entities, in the shape of public-private partnerships for health, have been created, especially in the late 1990s, and about a score of these are focused on developing new products (drugs, vaccines, diagnostics) to meet the needs of low- and middle-income countries. On the negative side, other sources of private giving have been adversely affected by sharp falls in stock markets in the early part of the new century. How are these changes affecting the prospects of reducing global health gaps?

Major consolidations within the pharmaceutical industry have been proceeding in recent years, with amalgamations and take-overs among the world's leading companies involved in R&D, resulting in fewer large players now competing internationally. During this period, the cost of creating a new medicinal agent and bringing it into general clinical use has continued to escalate. Recent estimates⁵ now put this at over US\$800.0 million (half of which goes to opportunity costs of the capital invested). The large companies have increasingly sought billion-dollar/year 'blockbuster' drugs that justify such large investments with attractive financial returns. This leads to worries that drugs that are largely needed for markets in low- and middle-income countries will simply not be developed.

At the same time, there has been a move towards drug discovery being 'out-sourced' to smaller, creative enterprises whose innovations are then bought up or licensed by larger companies, and towards the

establishment of generic drug manufacturing companies in LMIC countries that are able to meet the Good Manufacturing Practice (GMP) standards required for international marketing of drugs.

There are some prospects that combinations of scientific innovation and manufacturing capabilities in some of LMIC economies (e.g., Brazil, China, India, South Africa) could lead to industries that would find attractive markets at levels of US\$10-US\$100 million rather than US\$1.0 billion predicated in high-income countries. This could improve the chances of new drugs being developed for neglected diseases in both local and global settings.

A further development in the pharmaceutical industry that has important implications for health in LMIC is the trend towards engaging in donation programmes and other partnerships to make drugs available for neglected diseases or geographical regions. A landmark was the agreement between Merck and WHO in which the company made the drug ivermectin (Mectizan) available *free* for the treatment of African river blindness. This move has had a profound effect on the treatment of the disease and has been responsible for averting large amounts of blindness in Africa. The challenges encountered in ensuring delivery of and effective treatment with the drug also highlighted the need for functioning health systems and local capacities to conduct applied research, such as systems and operational research, on factors influencing effectiveness and efficiency of service delivery. With the recent rapid growth in the number of public-private partnerships for health that are aiming to create or improve access to drugs for neglected diseases, these challenges will be of increasing significance.

The Millennium Development Goals (MDGs), agreed upon by the world's governments at the Millennium Summit (UN, 2000), represent the most important collective commitment ever made to tackle the poverty, compromised health and deprivation suffered by a large proportion of the world's population.⁶ Four of the eight MDGs specifically address major health issues relating to malnutrition, child mortality, maternal health and specific infectious diseases. All of the remaining goals address issues that have health impacts, including poverty, education, gender equality, the environment, and international partnerships for development. Recent assessments indicate that many of the goals, which include 18 specific targets, will not be met, with Africa falling furthest behind. It is clear that, to achieve the MDGs, it is not only necessary to intensify and accelerate actions to scale up existing efforts and apply available tools, but also to generate new knowledge and technologies. To what extent are the resources and priorities for health research geared to supporting this agenda?

Since 1990, there have also been very significant developments on the scientific front, including advances in: mapping genomes of different species; technologies for manipulating atomic and molecular entities; combinatorial technologies for creating vastly increased numbers of candidate drugs for screening; and genetical engineering and cloning. These bioscience advances offer enormous potential for improving human health – and equally large challenges in ensuring that disadvantaged populations can benefit from them and that global health inequities do not grow even larger.

1.5 Objectives of the 2004 assessment

Previous estimates of global health research spending indicated a rise from about US\$30.0 billion in 1987 to about US\$73.5 billion in 1998 – an average annual rate of increase of around US\$4 billion per year over that period. This 2004 assessment was designed to examine whether such increases have continued into the 21st century; whether the proportions of spending from public,

private and not-for-profit sources have changed; whether the contributions of low- and middle-income countries to health research have increased; the extent to which health problems affecting predominantly poor populations and low- and middle-income countries are being adequately addressed; and the extent to which global health inequities have been reduced.

¹ Commission on Health Research for Development, 1990. *Health Research: Essential Link to Equity in Development*. Oxford University Press, New York.

² Report of the WHO Ad Hoc Committee on Health Research Relating to Future Intervention Options, 1996. *Investing in Health Research and Development*. World Health Organization, Geneva.

³ Global Forum for Health Research, 2001. *Monitoring Financial Flows for Health Research*. Global Forum for Health Research, Geneva.

⁴ UN Declaration on Human Rights, 1948.

⁵ According to the Tufts Center for the Study of Drug Development (<http://csdd.tufts.edu/NewsEvents/>), the fully capitalized cost to develop a new drug, including studies conducted after receiving regulatory approval, averages US\$ 897 million.

⁶ UN, 2000. *UN Millennium Declaration*. Available at: www.developmentgoals.org

Chapter 2

Global Funding and Flows

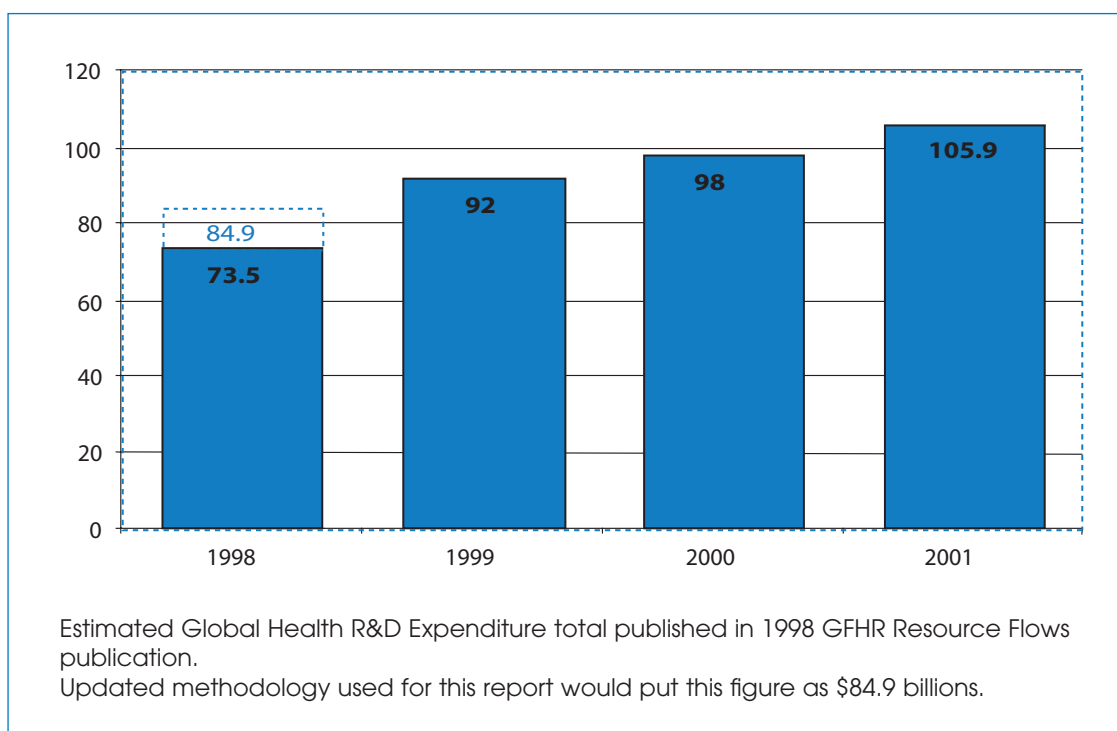
Global Funding and Flows

2.1 Total global spending on health R&D

In 2001, an estimated US\$105.9 billion was spent globally on health research and development, up from US\$73.5 billion in 1998 (see Chart 2.1). These expenditures represent

3.5 per cent of total estimated national health expenditures worldwide, up from 2.6 per cent in 1998.¹

Chart 2.1 Estimates for total health R&D expenditure, US\$ billion



Source: Global Forum estimates based on OECD data

Chart 2.2 illustrates how these global expenditures play out in a “10/90” perspective. The vast majority of R&D spending is done by high-income countries (HIC) for high-income countries (Area A); a relatively small share is financed by low- and middle-income countries (LMIC) and carried out in these

countries (Area B). The even smaller area of overlap (AB) is of particular importance for correcting “the 10/90 gap”: it describes R&D funded mainly by high-income countries *but* carried out in and for the primary benefit of low- and middle-income countries.

Chart 2.2 Graphic representation of health research funding¹



2.1.1 Measuring global investments

Estimating the global investment in health R&D is far from a precise science. The total basically includes the largest known contributors. The R&D efforts of many low- and middle-income countries are still substantially undercounted or unaccounted. Teasing out this information is important. It will not add significantly to the global total but it will increase understanding of what is going on in the parts of the world where health is most compromised. Better systems for reporting and collecting data, and improved methodologies for analysis will help this knowledge grow.

Indeed, some of the growth in global R&D investments described in Chart 2.1 can be attributed to money "found" since the 2001 *Financial Flows* report. However, it is clear that there has also been real growth between 1998 and 2001. Increases can be ascribed as below:

- More complete data for 1998 and adjustments in estimation methodology account for US\$11.43 billion of the increase. Most of the adjustment was in the private for-profit sector – US\$10.07 billion.

There was also an increase of US\$1.48 billion in the public sector and a decrease of US\$0.13 billion for the private not-for-profit sector.

- Real increases (not adjusted for inflation and currency fluctuations) in expenditures in the private for-profit sector of US\$10.66 billion.
- Real increases (unadjusted) in public-sector expenditures of US\$8.14 billion.
- Real increases (unadjusted) in private not-for-profit sector expenditures of US\$2.19 billion (see Table 2.1).

Stronger investments in health research come from both the public and private sectors in both high-income and low- to middle-income countries. Public expenditures were an estimated US\$46.6 billion – US\$44.1 billion in high-income countries and US\$2.5 billion in low- and middle-income countries. The private sector accounted for another US\$59.3 billion. Private-sector expenditures were split between for-profit companies (US\$51.2 billion) and not-for-profit organizations (US\$8.1 billion) (see Table 2.1).

Table 2.1

Estimated global total health R&D funding 2001 (in current US\$ billion)
compared with 1998

	2001		1998 published		1998 adjusted	
	\$	%	\$	%	\$	%
Total	105.9	100	73.5	100	84.9	100
Total Public Sector	46.6	44	37	50	38.5	45
Total Private Sector	59.3	56	36.5	50	46.4	55
Total Private for Profit ⁽¹⁾	51.2	48	30.5	41	40.6	48
Total Private Not for Profit	8.1	8	6	8	5.9	7
<i>HIC</i>						
Public Sector	44.1	42	34.5	47	36.2	43
Private for Profit Sector	49.9	47			40	47
Domestic Pharmaceuticals ⁽²⁾	44.1	42			35	41
Foreign Pharmaceuticals ⁽²⁾	5.8	5			5	6
Private Not-for-Profit ⁽³⁾	7.7	7			5.6	7
<i>Total HIC</i>	<i>101.6</i>	<i>96</i>			<i>81.8</i>	<i>96</i>
<i>LMIC</i>						
Public Sector	2.5	2.4	2.5	3.40	2.3	2.7
Public Sector Domestic	2.0	1.9			1.8	2.1
Public Funding from foreign ODA ⁽⁴⁾	0.4	0.4			0.4	0.5
Public Funding for International Research ⁽⁴⁾	0.07	0.1			0.07	0.1
Private for Profit Sector						
Foreign and Domestic Pharmaceuticals	1.35	1.3			0.98	1.2
Domestic Private Not-for-Profit	0.08	0.1			0.08	0.1
Foreign Private Not-for-Profit ⁽⁴⁾	0.3	0.3			0.2	0.3
<i>Total LMIC</i>	<i>4.3</i>	<i>4.0</i>			<i>3.5</i>	<i>4.2</i>

Source: Global Forum estimates based on OECD database, national surveys, pharmaceutical associations and other publications

¹ The effect of the changes in methods and sources of data for the pharmaceutical industry results in an increase of \$10.1 billion in 1998.

² Foreign pharmaceutical R&D stands for R&D expenditure outside the United States by U.S.-owned PhRMA member companies and R&D conducted abroad by the U.S. 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.

³ Private non-profit includes \$3.1 billion estimated for private General University Fund (GUF) in 2001, and \$2.5 billion in 1998.

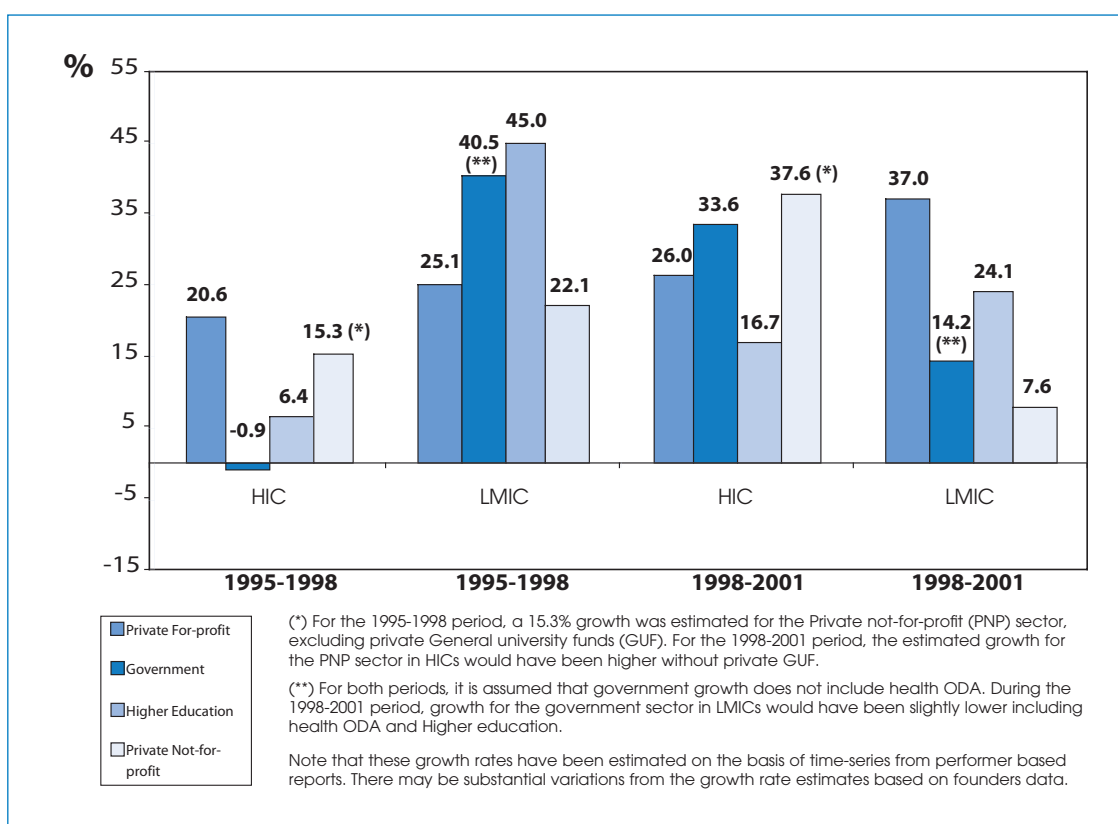
⁴ International research, foreign PNP and foreign ODA are rough estimates.

2.1.2 Analysing the growth in global investments

Overall, the growth in R&D expenditure was marginally greater in high-income countries (24 per cent) than in low- to middle-income countries (23 per cent) over the period 1998-

2001. Most of the growth in high-income countries came from the public sector and private not-for-profit sectors. In low- and middle-income countries, the growth was in the private for-profit and higher education sectors (see Chart 2.3).

Chart 2.3 Growth in health research expenditure by sectors of performance



Source: Global Forum estimates from time series extracted from the OECD database

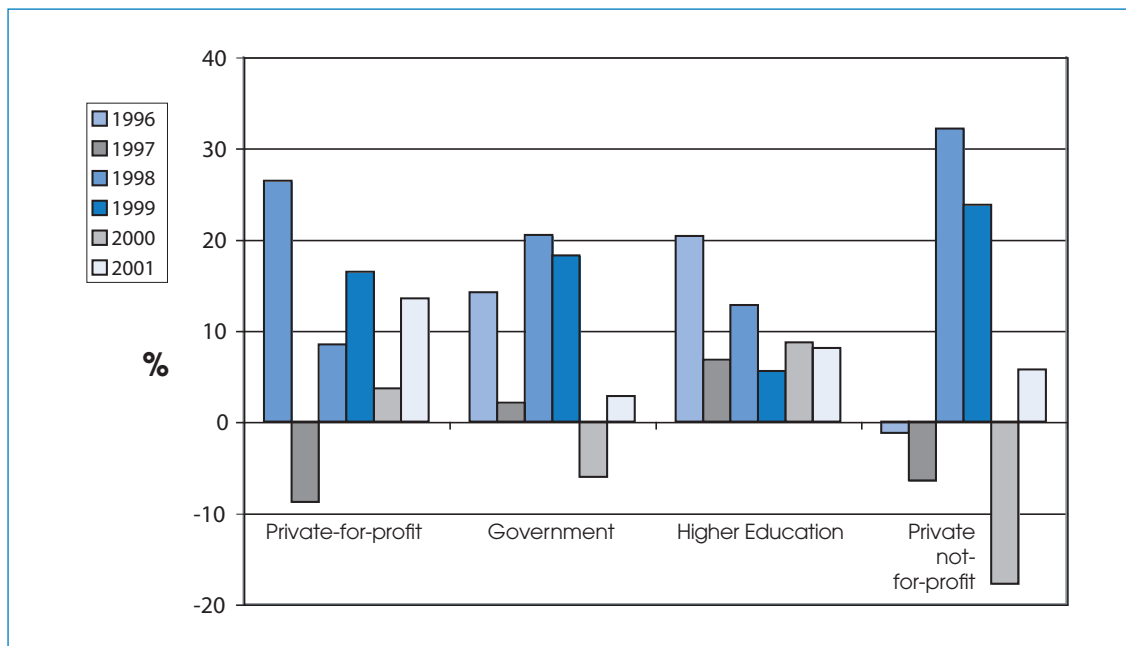
Annual R&D expenditures tend to be more volatile in low- and middle-income countries. (In the period 1995-1998, they showed greater percentage growth than did high-income countries.) This is because even small amounts of additional money can yield large percentage increases (see Chart 2.4). As well, much financing comes from a variety of sources

abroad (mostly through ODA and the private not-for-profit sector) and is, therefore, subject to change – and, significantly, sometimes in a sudden and/or uncoordinated way. In other words, currently low- and middle-income countries do not have control over a large share of health R&D expenditures in their countries.

For example, ODA and NGO grants have been relatively reliable capital flows to LMIC, but private flows fell sharply in the early 1980s reflecting the collapse in international bank lending. Private flows revived in the 1990s, but they have not recovered to earlier levels when measured as a proportion of the Gross

National Income (GNI) of DAC member countries. Although grant making by some asset-based foundations declined during the economic downturn of 2000-01, so far the impact on international funding appears minimal.

Chart 2.4 Annual health R&D expenditures growth for LMIC

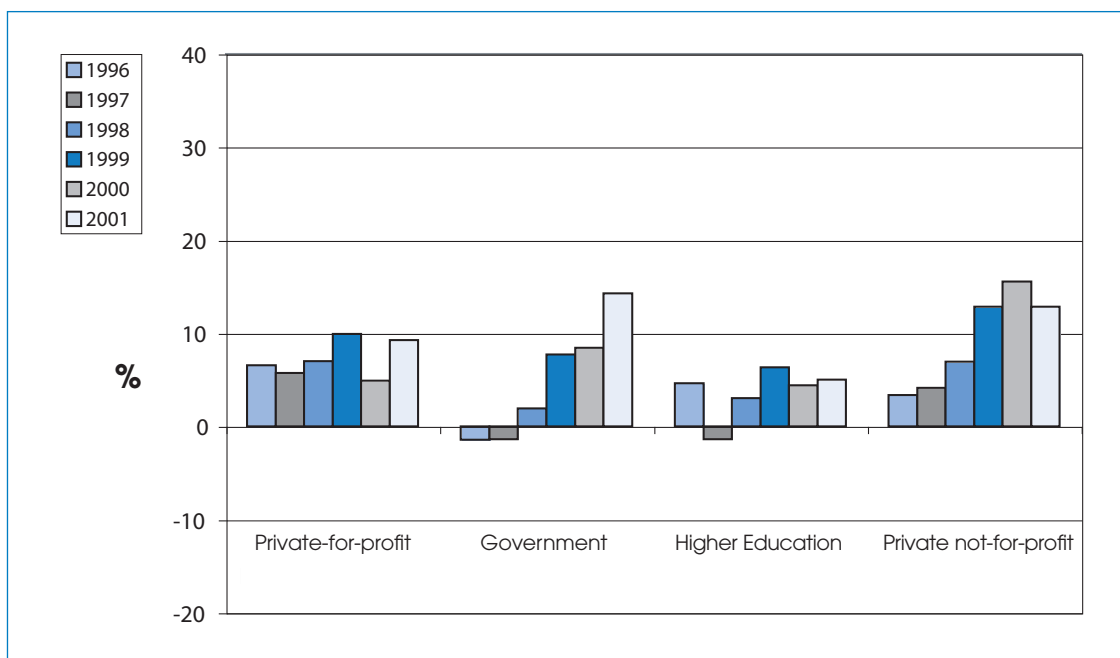


Source: Global Forum estimates based on OECD

In high-income countries, growth in annual R&D expenditures has been fairly steady over recent years. Government expenditures dropped in the years 1996-97, but then

recovered with 2001 showing the biggest increase of the period, in part due to rising levels of health ODA (see Chart 2.5).

Chart 2.5 Annual health R&D expenditures growth for HIC



Source: Global Forum estimates based on OECD

2.2 Sources of funds and sectors of performance

2.2.1 Funding sources

Funding for health research in any country typically comes from four types of sources:

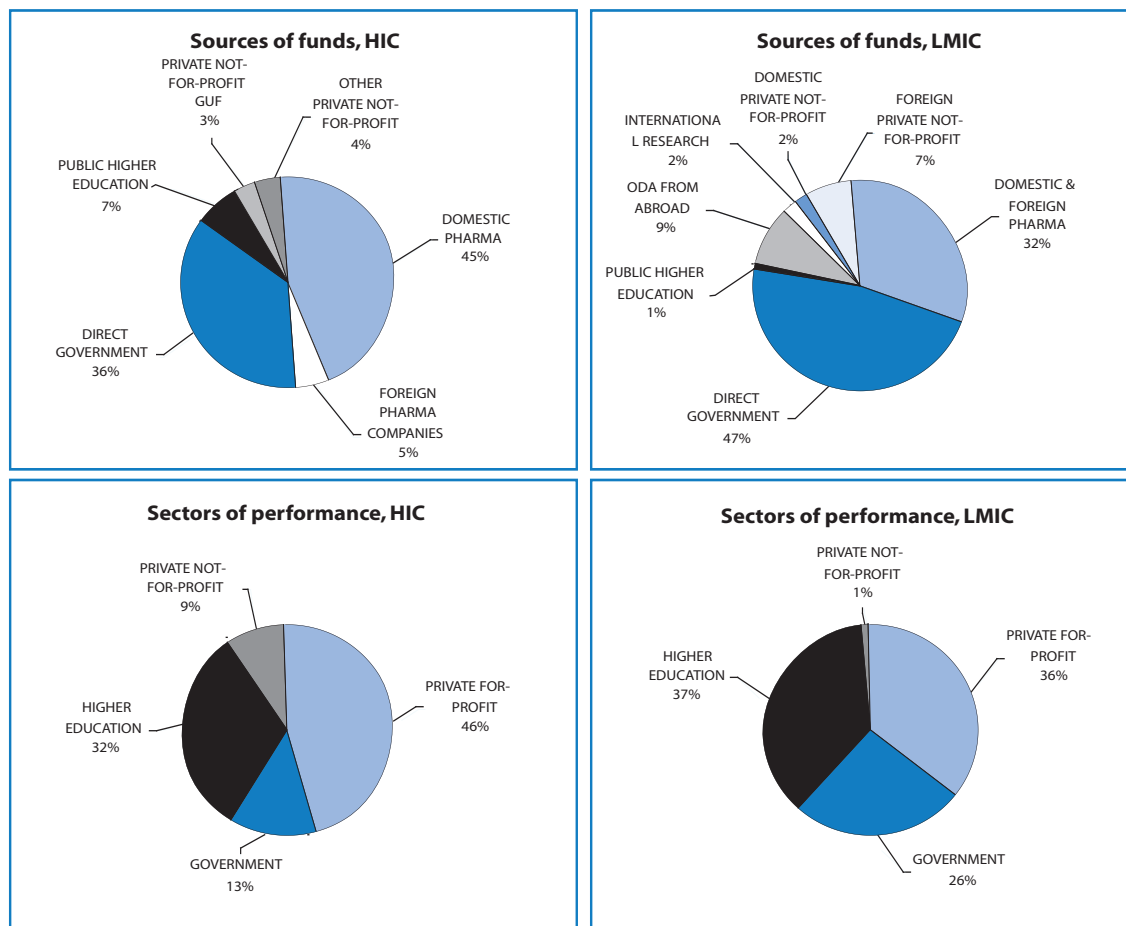
- private for-profit sector;
- public sector;
- private not-for-profit sector; and
- various public and private non-domestic sources.

The private for-profit sector is the largest investor globally, accounting for 49 per cent of funds for health research in high-income countries and 32 per cent in low- and middle-income countries. Private companies based in high-income countries usually invest in their home country, but, as in the case of pharmaceutical companies, they also invest in both other high-income countries and to a lesser extent in low- and middle-income countries.

Governments are the next-largest funders, accounting for 43 per cent of overall funds in high-income countries. Governments support health research through their allocations to ODA, higher education, science and technology, R&D, trade, public health and medicine. In low- and middle-income countries 59 per cent of overall research funds come from governments. This includes money they receive from non-domestic sources such as ODA accounting for 9 per cent of total funds and research institutes in high-income countries contributing 2 per cent (see Chart 2.6).

The private not-for-profit sector includes private universities, foundations and charities. It pulls roughly the same funding weight in high-income countries (8 per cent) and low- and middle-income countries (9 per cent).

Chart 2.6 Sources of funds and sectors of performance for health research, 2001



Source: Global Forum estimates based on OECD database; Pharmaceutical Associations; the Foundation Center; and surveys

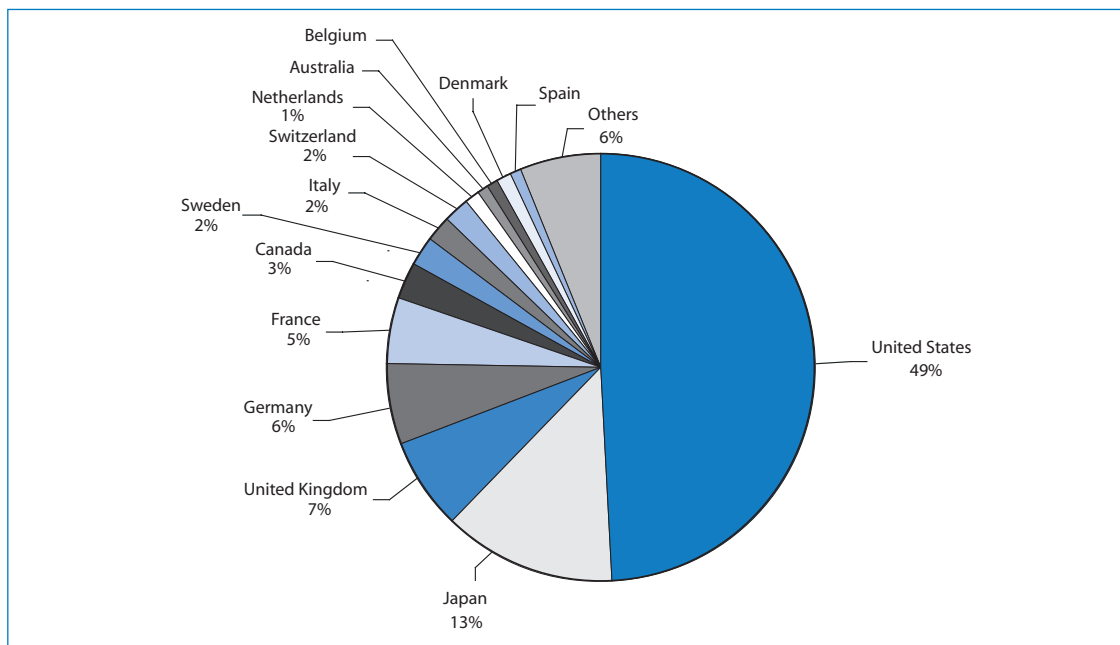
2.2.2 Performance sectors

Health R&D tends to be carried out by the same four sectors in both high-income and low- and middle-income countries (see Chart 2.6). In high-income countries, roughly equivalent amounts of research are carried out by the public (45 per cent) and private for-profit sectors (46 per cent). Research funded by the private not-for-profit sector accounts for the remaining nine per cent, and is carried out by independent researchers in universities. In low- and middle-income countries, most research is carried out within

the public sector (63 per cent), pointing to the potential for development of the private research sector (36 per cent) in these countries.

Global investments in health R&D are heavily dominated by just a few countries – not unexpectedly given their long-standing economic strength (see Chart 2.7). The United States alone accounts for 49 per cent of global expenditures, followed by Japan (13 per cent), United Kingdom (7 per cent), Germany (6 per cent) and France (5 per cent).

Chart 2.7 Global distribution of public and private health R&D expenditures, 2001



Source: Global Forum estimates based on data from OECD

More interestingly, Global Forum estimates indicate that countries other than the above investing significantly in health R&D when a more complex measure than absolute dollars is used. This analysis considers four dimensions:

- 1) national R&D expenditure as a percentage of GDP;
- 2) national health R&D as a percentage of GDP;
- 3) national health R&D as a percentage of national health expenditures; and
- 4) national health R&D 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 health R&D. Scores for a number of countries are plotted on Chart 2.8 and Chart 2.9.

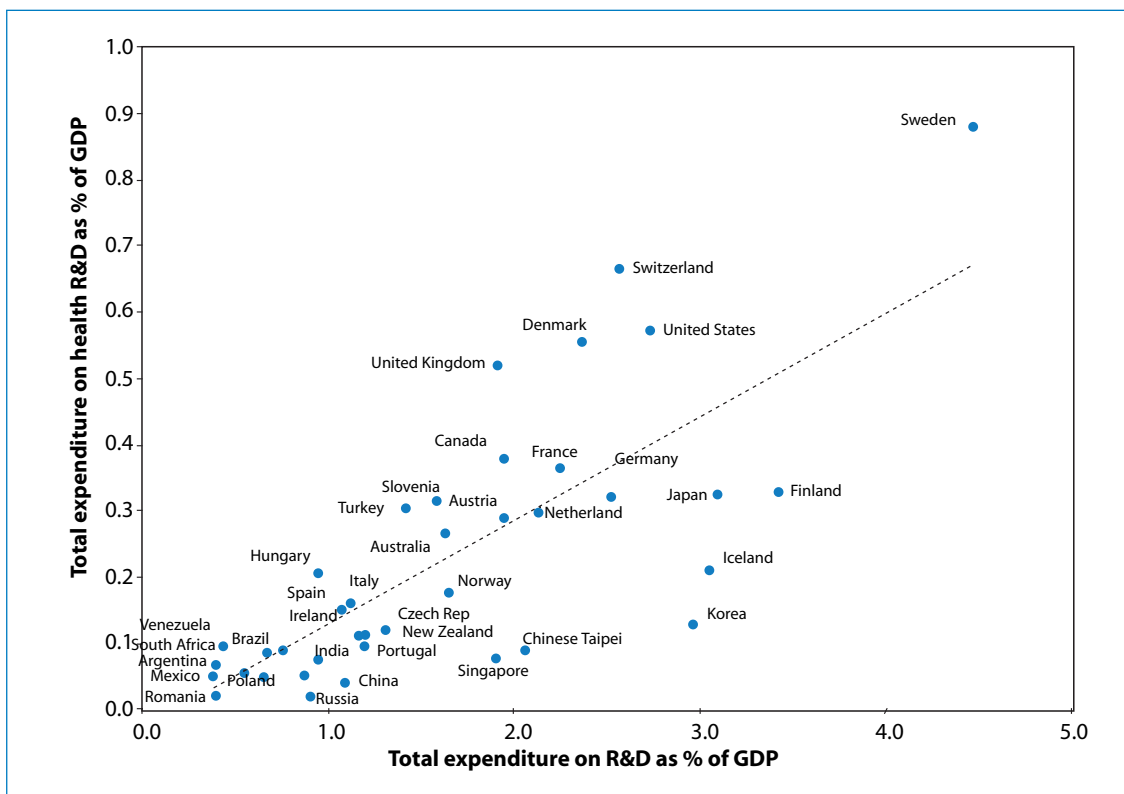
In Chart 2.8, the further the score is from the vertical axis, the larger the investment in R&D as a proportion of total GDP. The higher up the vertical axis, the larger the investment in health R&D as a proportion of GDP. For example, Sweden scores very high in both overall R&D and health R&D. (The optimal position on the scatter graph is as far up and to the right as possible.) Denmark, Switzerland, the UK and the United States also have strong investments in both areas. Finland, Germany, Iceland, Japan and Korea do well in overall R&D but relatively less so in health R&D than other high-income countries.

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, Brazil, Mexico, Poland and South

Africa, have relatively higher investments in health R&D 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 health R&D. An appropriate policy goal for all countries is to shift their scores into the upper-right quarter of the graph.

Chart 2.8 Health R&D and national R&D as a % of GDP



Sources: Global Forum estimates based on data from the WHO, the OECD, other publications
GDP data from the World Bank Group

Chart 2.9 looks at investments in health R&D 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 health R&D relative to the size of their health sectors. The further away the score is from the vertical axis, the higher the investment in health R&D as a proportion of total R&D. Once again, Sweden has the highest relative investment in health research. Denmark, Switzerland and the

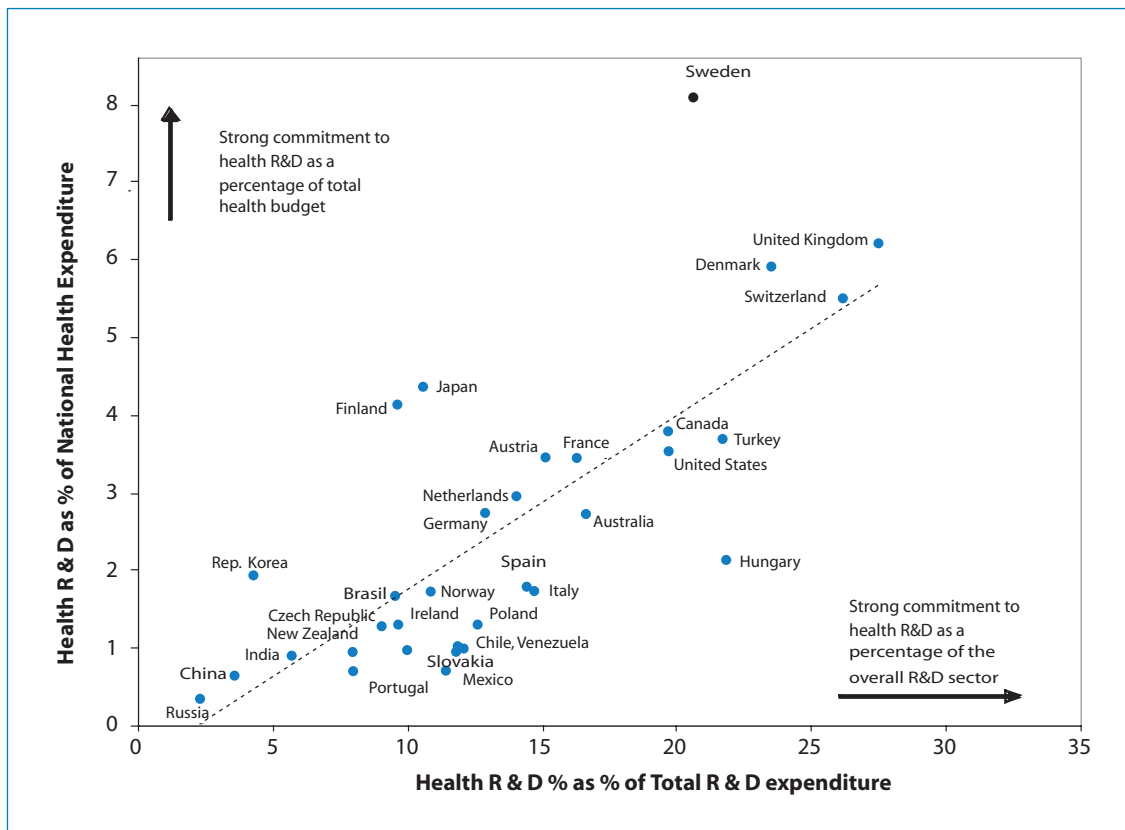
United Kingdom, also show high investments in health research relative to the size of their health and overall R&D sectors. The relatively low score of the United States reflects an emphasis on private-sector investments in health.

Below the diagonal, Latin American countries and transition countries of the former Soviet bloc whose economies are recovering have relatively higher scores on health R&D as a

proportion of overall R&D than countries above the line like China, India, Korea and Russia. Illustrative of a transition country experiencing economic recovery, Hungary spends the same share of its R&D on health as many of the G7 countries²; but as a share of overall health expenditures its health R&D

is more in line with Brazil and Korea. As its economy expands, Hungary will be able to move further into the upper right quarter of the figure. Unfortunately, many low- and middle-income countries could not be plotted due to lack of data.

Chart 2.9 Strength of investments in health R&D



Source: Global Forum estimates based on data from WHO

2.2.3 Public funding

Though the private for-profit sector is the largest contributor to global expenditures on health R&D, this report looks first at public-sector funding because States bear the primary responsibility for the health and rights of their citizens. Governments are also signatories to international commitments on health.

High-income countries

Governments in high-income countries contributed US\$44.1 billion to health R&D in 2001, up from US\$36.2 billion reported in 1998 (see Table 2.2), excluding foreign ODA. The United States government was the biggest spender at US\$28.6 billion and accounted for more than half of the total in these countries. Japan followed with US\$2.5 billion, Germany

US\$2.0 billion, France US\$2.45 billion, the United Kingdom US\$1.69 billion, Italy US\$1.2 billion and Canada US\$1.0 billion. Together, the G7 countries invested more

than 87 per cent of publicly funded health R&D in high-income countries. Together, all other high-income countries added another US\$3.93 billion.

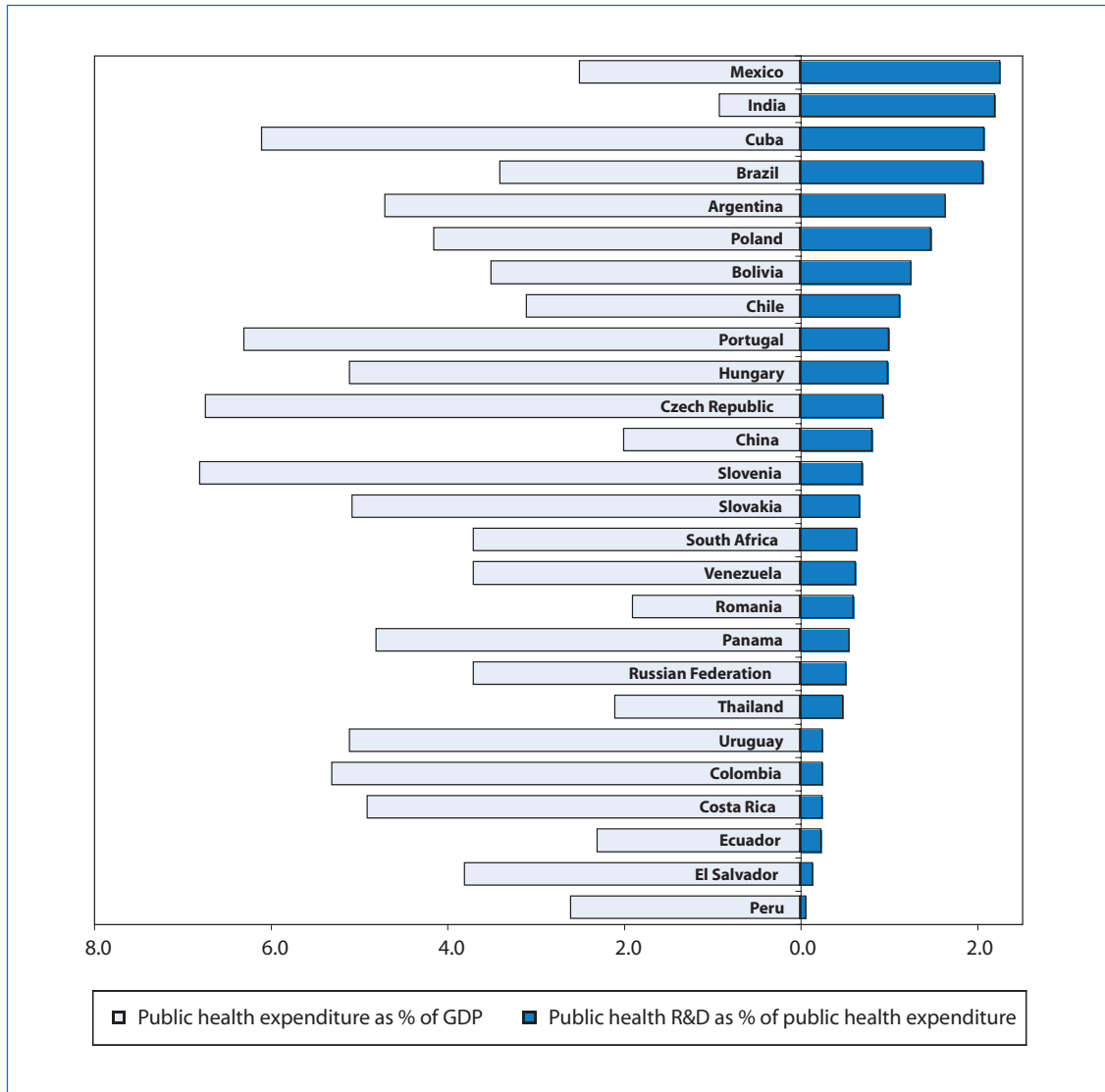
Table 2.2

Public funding of health R&D in HIC, 2001 and 1998

	2001 Current Million US\$	1998 Million US\$	2001 as % GDP	2001 as % public expenditures on health
Funder Reported				
United States	28600	19527	0.28	4.9
Germany	2297	2393	0.12	2.3
France	2448	2242	0.19	2.6
United Kingdom	1692	1789	0.12	2
Italy	1218	–	0.11	1.9
Netherlands	605	542	0.16	2.9
Sweden	369	458	0.18	2.8
Austria	408	375	0.22	3.9
Spain	367	302	0.06	1.2
Denmark	204	223	0.13	1.9
Finland	200	201	0.17	3.3
Portugal	63	–	0.06	1
Greece	35	45	0.03	0.7
New Zealand	20	38	0.04	0.6
Ireland	23	16	0.02	0.4
Korea	169	–	0.04	1.5
Iceland	7	–	0.1	1.3
Taiwan	181	–	0.06	–
Belgium	117	–	0.05	0.8
Israel	179	–	0.16	–
Performer reported				
Japan	2952	2896	0.07	1.2
Canada	980	754	0.14	2.2
Australia	553	506	0.15	2.5
Norway	205	205	0.12	1.9
Switzerland	250	–	0.1	1.7
TOTAL	44139	32510		

Source: Global Forum for Health Research estimates based on data from Eurostat (annual); OECD (annual); and national publications.

Chart 2.10 Public funding of health R&D as a % of public health expenditure and GDP, 2001



Sources: Public health expenditure estimates from WHO, UNDP and selected publications; Health R&D estimates based on OECD and nation surveys.

Low- and middle-income countries

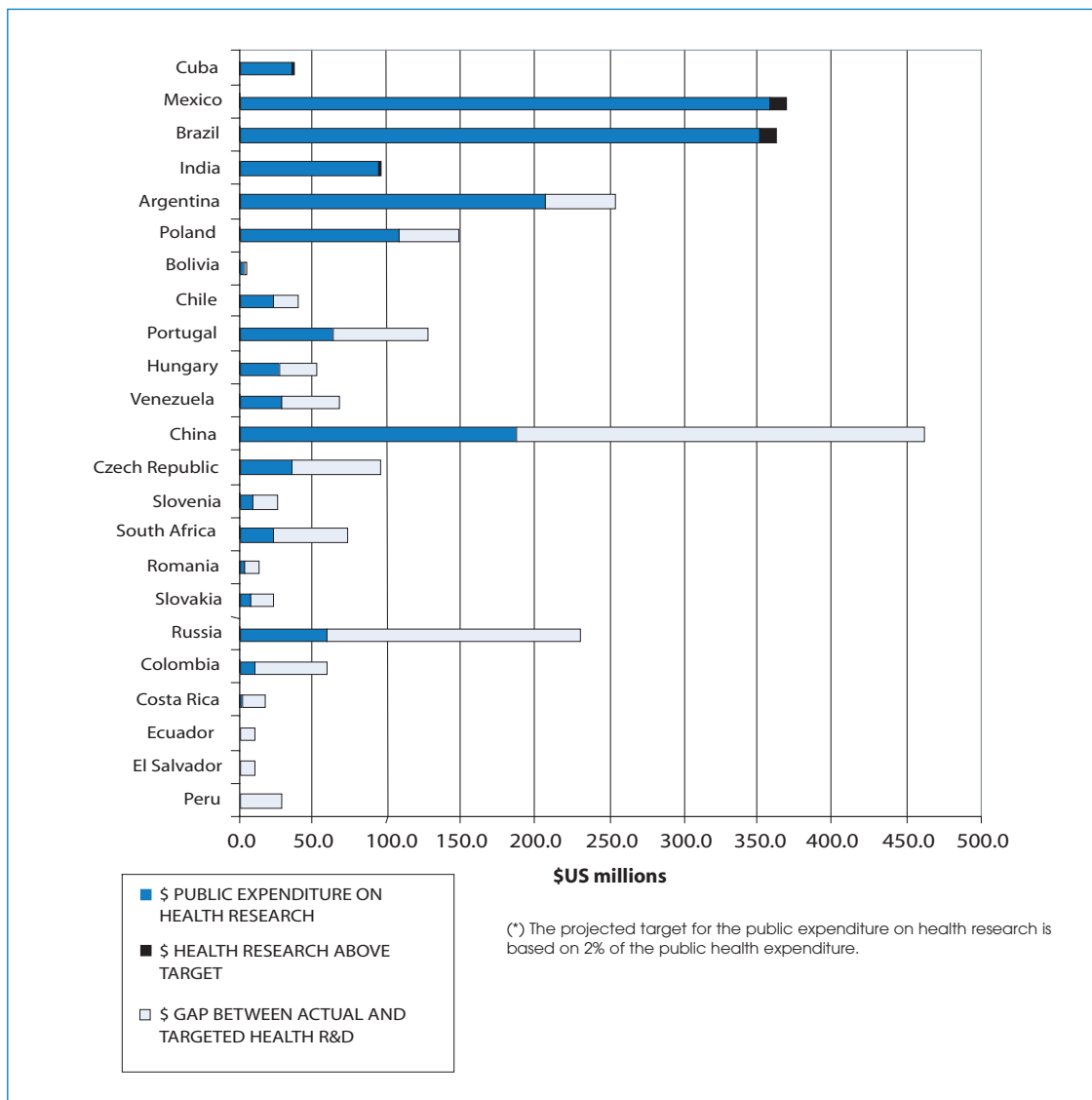
Governments in low- and middle-income countries – for which data are available – spent a minimum of US\$2.5 billion on health R&D in 2001. This figure equals the US\$2.5 billion cited in the 2001 *Financial Flows* report, but is higher than the adjusted figure for 1998 of US\$2.3 billion. As more countries report on health research expenditures and the quality of reporting improves, further adjustments will be in order.

Few low- and middle-income countries collect and report data on expenditures on health research. Nonetheless, health research is being funded by many governments, notably many Central and Eastern European countries, some of which report to OECD; and countries in Central/South America and the Caribbean, including Brazil, Argentina, Brazil, Costa Rica, Cuba, Ecuador, El Salvador, Mexico, Trinidad and Tobago.³

Health R&D efforts in low- and middle-income countries are still relatively scant, despite recent growth in the sector. Given the gross mismatch between health R&D and health needs in these countries (“the 10/90 gap”), the 1990 Commission on Health Research for Development recommended that governments in low- and middle-income countries allocate at least two per cent of national health expenditures for research. Among LMIC, only Mexico, Cuba, Brazil and India have met this level (see Chart 2.10).

Even a goal of two per cent may look almost unattainable to some lower income countries. However, as indicated earlier, the actual dollar amount needed to reduce the health research gap is smaller than it may seem (see Chart 2.11). This is especially the case in countries that are under-investing in their health sectors. That said, it is reasonable for the poorest of countries to concentrate health resources on delivering services and focus any research on operational issues such as targeting.

Chart 2.11 Gap between actual and 2 per cent target* for public expenditure on health research in LMIC: 2001 estimates



Sources: Health R&D: Global Forum estimates based on OECD, RICYT, national surveys. Public health expenditures: WHO and UNDP estimates

2.2.4 Private funding

Private for-profit financing

The private for-profit sector spent 49 per cent of total global health R&D expenditures in 2001, investing US\$51.2 billion, up from US\$40.6 billion in 1998 (adjusted figure as noted earlier). The biggest actors in the private for-profit sector are multinational

pharmaceutical companies and, to a lesser extent, biotechnology and medical instrument companies. That could change in the next few years given the explosive growth in investments in genomics research (Highlight 2.1) and the newly convergent NBIC technologies (Highlight 2.2).

Highlight 2.1

Genomics research and the “10/90 Gap”

The human gene code is the object of intense – and increasingly successful – research and investment. The sequencing of genes and the development of related therapies and technologies has become a major and accelerating thrust of research efforts in recent years.

The for-profit sector (pharmaceutical, biotechnology and genomics start-ups) is the biggest funder of genomics and most of that funding goes to private sector researchers in the United States. The top six genomics firms are U.S.-based, and 76 per cent of publicly traded and 71 per cent of privately held genomics companies are U.S.-based.*

Unquestionably, genomics is big business with big money and big health issues at stake. There is a huge amount of R&D money dedicated to genomics. Private spending on genomics is likely more than US\$1.0 billion annually and could be as high as US\$1.5-2.0 billion, based on estimates of the World Survey of Funding for Genomics.

The World Survey also tried to get at the more sophisticated aspects of genomics and the implications for “the 10/90 gap”. In economies that are both knowledge-driven and private-sector-driven, the powerful secrets of genes are being treated as intellectual property that is largely privately owned, and largely owned by companies in the United States. The drive in genomics research seems less about creating raw sequence information that can be readily shared, but about creating patentable data sets for profit. This commodification of genomics is unlikely to beget a balanced distribution of benefits among the world’s population. In other words, without explicit attention at the international level, the initial technological fruits of genomics are likely to consist primarily of therapeutic and diagnostic applications for conditions affecting large populations in rich countries. According to the World Survey “[e]ven more than for biomedical research in general, the skew of research funding is heavily toward the developed economies with large pharmaceutical markets”.

There are exceptions where genomics research is being done in and for the benefit of low- and middle-income countries. Notable are collaborative efforts between researchers in Africa, Latin America, the Middle East and Asia, and major genomics laboratories in the U.S. and Europe. These include projects to investigate the genetics of major diseases like malaria and cholera, and neglected diseases like Chaga’s disease, schistosomiasis and river blindness.

There is also a modest but growing literature on impact on developing countries of patenting DNA. The World Survey captures talk of “biocolonialism”, “bioimperialism” and even “biopiracy.” It goes on to say: “Renewed attention to uses of genomics could also shed light on how the data and technologies can benefit populations other than those living in developed economies who have highly prevalent conditions. Such attention will, however, require organization and a strategy for mediating a productive discussion.”

Source:

* “World Survey of Funding for Genomics Research”, Final Report to the Global Forum for Health Research and World Health Organization, 2000. Robert Cook-Degan, Carmie Chan and Amber Johnson.

Highlight 2.2

Future shock? Flagging NBIC technologies

NBIC technologies – nano/bio/info/cogno – capture the convergence of the most powerful frontiers in science at the atomic or molecular scale. Nanotechnology or nanoscience enables a new paradigm of science where technologies converge at the nanoscale, namely: nanoscience, biotechnology and biomedicine; information technology; and cognitive science, including neuro engineering.

The popular image of NBIC technologies would be something like a computer chip that is implanted in the brain and downloads information on any subject instantaneously from a global database. More imminently, NBIC technologies are expected to have applications in the environment, energy, water, weapons and other military applications, globalization, agriculture, space exploration, extending life, enhancing human performances and health.

Nanomedicine

Nanomedicine¹ refers to medical intervention at the molecular scale for curing disease or repairing damaged tissues, such as bone, muscle, or nerve. The U.S. National Institutes of Health recently unveiled a “Roadmap for Nanomedicine” for the next 10 years.² The International Journal of Pharmaceutics has announced that it will add a regular section on pharmaceutical nanotechnology. Products have already been developed in three areas: bioanalysis; drug delivery and therapeutics; biosensors and medical devices such as nanotubes, nanowires, nanopore structures for single-molecule detection, and tissue-engineered material such as nanobones.³

Leading medical applications include material technologies for use as medical-device coatings and diagnostic contrast agents, and nanoscale devices for biodetection and drug-delivery applications. The ability to manipulate living matter at the nanoscale could also inspire biology-based approaches to technology development and fabrication. For example, medical researchers envisage an ability to synthesize new molecules, direct the self-assembly of individual biomolecules, or create molecular-scale tools for in vivo sensing, diagnostics, analysis, therapy design, and drug delivery. Nanobiotechnology opportunities also span food, cosmetics, energy, and electronics applications.⁴

Nanobiotechnology

M.C. Roco, Executive Director of the U.S. National Nanotechnology Initiative (NNI), says 25 per cent of NNI funding will be in Nanobiotechnology. Since 1999, venture capitalists alone have devoted more than US\$450 million to nanobiotechnology.⁵ Since 1998, nanobiotechnology⁶ venture deals have gone 54 per cent to drug discovery, 5 per cent for drug delivery, 37 per cent for diagnostics and 4 per cent for biopharmaceuticals.⁷ The distribution of venture capital for nanotechnology in the period 1998-2003 saw 52 per cent spent on nanobiotechnology, 12 per cent on material sciences, 32 per cent on nanodevices and 4 per cent on nanotools.⁸ The U.S. National Science Foundation (NSF) estimates that half of all drugs will be made with nanotechnology by 2010.⁹

Maturation of the Nanotechnology Industry

In general, nanotechnology is fast emerging as a leading area for R&D investments. According to the “2004 European NanoBusiness Survey”, 90 per cent of companies believe nanotechnology will have an influence on their businesses; 55 per cent forecast an impact within three years; 84 per cent believe nanotechnology will have a significant effect on their competitiveness.¹⁰ The NanoBusiness Alliance and NSF estimate that the total market impact of nanotechnology worldwide will reach US\$1.0 trillion by 2015 and create 800,000 to 2,000,000 new jobs.¹¹ One indication of the maturation of the

nanotechnology field is the increase in publications. In 1987, the scientific literature included about 200 “nano” references; by the end of 2001, some 7,700 “nano” citations for the year; and in just the first six months of 2002, more than 6,000 citations.¹² Furthermore, the numbers of patents has increased significantly.¹³

Financing

A 2004 report by Lux Research Inc. tallies global spending on nanotechnology at more than US\$8.6 billion.¹⁴ Government spending is reckoned to account for more than US\$4.6 billion: US\$1.6 billion (35 per cent) in North America; US\$1.6 billion (35 per cent) in Asia; US\$1.3 billion (28 per cent) in Europe; and US\$133 million (two per cent) in the rest of the world. Meanwhile, corporations will spend an estimated US\$3.8 billion on nanotechnology R&D: US\$1.7 billion (46 per cent) by North American companies; US\$1.4 billion (36 per cent) by Asian companies; US\$650 million (17 per cent) by European companies; and less than US\$40 million (one per cent) in the rest of the world.

According to Lux Research, in 2004 the U.S. government will spend nearly twice as much on nanotechnology as it did on the Human Genome Project (HGP) in its peak year.¹⁵ Projections say expenditures in nanotechnology will soon outstrip investments to date in genomics and biotechnology. Lux also reports that 2004 will be the last year that governments outspend corporations on nanotechnology as activity shifts from basic research to applications. Worldwide more than 4,000 companies and research institutes are working in nanotechnology.¹⁶

NBIC, the “10/90 gap” and the definition of health

As with each emerging technology, questions need to be asked about how much money will be devoted to medicine – in this case nanomedicine – and what will the impact be on health research, health care and, ultimately, health. Initial observations indicate that the potential impacts of NBIC technologies on human health are so enormous that they shift the very definition of health. NBIC applications will not only ‘fix people’ but be able to improve existing abilities and enable the acquisition of new ones.

This ‘cycling up’ makes it difficult to distinguish between “therapies towards the norm” and “therapies exceeding the norm”—which leads to “improved” norms. As a result, the concept of health is evolving from one of “normative functioning” to “optimum functioning.” These shifts perpetuate health and health

Estimated government nanotechnology R&D expenditures in 1997-2004 (in \$ millions/year)

Région	1997	1998	1999	2000	2001	2002	2003	2004***
W. Europe	126	151	179	200	~225	~400	~650	~900
Japan	120	135	157	245	~465	~720	~800	~900
USA*	116**	190**	255**	270**	465**	697**	862**	~960
Others	70	83	96	110	~380	~550	~800	~900
Total	432	559	687	825	1535	2367	3112	3660
(% of 1997)	(100%)	(129%)	(159%)	(191%)	(355%)	(547%)	(720%)	(847%)

Notes: “W. Europe” includes countries in EU (15) and Switzerland; the rate of exchange \$1=1 Euro until 2002; = 0.9 Euro in 2003, and = 0.8 Euro in 2004; Japan rate of exchange \$1 = 120 yen until 2002, = 110 yen in 2003, = 105 yen in 2004; “Others” include Australia, Canada, China, Eastern Europe, FSU, Israel, Korea, Taiwan and other countries with nanotechnology R&D; (*) A financial year begins in USA on October 1 of the previous calendar year, six months before in most other countries (**) denotes the actual budget recorded at the end of the respective fiscal year; (***) – preliminary data Estimates use the nanotechnology definition as defined in the NNI (this definition does not include MEMS microelectronics or general research on materials), and include the publicly reported government spending.

research systems that serve the affluent—the individuals who can afford the “therapies.” They contribute to an increased concentration of scarce health and health research resources in the affluent world, away from the health needs of the world's poor majority.

Given the exponential growth to date in the NBIC industry, which has health as one of its targets, and projections for even larger growth over the next few years, an urgent and open policy discussion is needed about nano applications, how they will be used and for whose benefit.

Note: This highlight was contributed by Dr Gregor Wolbring¹⁸

- ¹ Nanomedicine Taxonomy, by Neil Gordon & Uri Sagman Canadian NanoBusiness Alliance [http://www.regenerativemedicine.ca/nanomed/Nanomedicine%20Taxonomy%20\(Feb%202003\).PDF](http://www.regenerativemedicine.ca/nanomed/Nanomedicine%20Taxonomy%20(Feb%202003).PDF)
- ² “Roadmap for Nanomedicine,” National Institutes of Health, United States; <http://nihroadmap.nih.gov/nanomedicine/index.asp>
- ³ Commercializing Nanotechnology. Mazzola L. Nature Biotechnology, 2003 Oct; 21(10):1137-43.
- ⁴ SRI Consulting Business Intelligence Nanobiotechnology <http://www.sric-bi.com/Explorer/NB.shtml#viewpoints> see also Commercializing nanotechnology. Mazzola L. Nat Biotechnol. 2003 Oct;21(10):1137-43; and http://www.nsf.gov/home/crssprgm/nano/nanotechbriefs03_10_03.pdf and some Nanotechnology product see http://www.etcgroup.org/documents/nanoproducts_EPA.pdf and http://www.nanovip.com/directory/Products_and_applications/index.php
- ⁵ ETC Group News Release Thursday, March 25, 2004, Jazzing up Jasmine: Atomically Modified Rice in Asia? <http://www.etcgroup.org/documents/NRatomrice1.pdf>; the European Nanobusiness Association put the numbers at 6 billion Euro a year <http://www.nanoeurope.org/files/European%20Nanotech%20Funding.pdf> ; for further webpages dealing with Nanotechnology funding see The Institute for Nanotechnology, Nanotechnology in Asia Pacific March 2004 http://www.nano.org.uk/Reports2004/AP_Sample.pdf; Invest in Taiwan, Nanotechnology Turning Today's Nanoscience Discoveries into Tomorrow's High Tech Realities <http://investintaiwan.nat.gov.tw/en/opp/nanotech.html>; Responses to questionnaire on nanotechnology for different countries. Country identified in url <http://www.nanotec.org.uk/evidence/Brazil.htm>; <http://www.nanotec.org.uk/evidence/Canada.htm>; <http://www.nanotec.org.uk/evidence/Germany.htm>; <http://www.nanotec.org.uk/evidence/USA.pdf>; <http://www.nanotec.org.uk/evidence/Poland.htm>; <http://www.nanotec.org.uk/evidence/Singapore.htm>; <http://www.nanotec.org.uk/evidence/Netherlands.htm>; European Nanobusiness Association It's Ours to Lose: An analysis of European Commission Spending <http://www.nanoeurope.org/files/European%20Nanotech%20Funding.pdf>
- ⁶ http://www.imakenews.com/evoxpopuli/e_article000254769.cfm
- ⁷ “Investing in nanotechnology,” Paull R, Wolfe J, Hebert P, Sinkula M Nature Biotechnology, 2003 Oct; 21(10): 1144-7 Figure 3a)
- ⁸ Investing in nanotechnology. Paull R, Wolfe J, Hebert P, Sinkula M Nat Biotechnol. 2003 Oct;21(10):1144-7 Figure 3b)
- ⁹ The Nanotech Report 2004 (TNR 2004) <https://www.globalsalespartners.com/lux/#> <http://www.luxresearchinc.com/>
- ¹⁰ The European Nanobusiness Association 2004 <http://www.nanoeurope.org/files/The%202004%20European%20NanoBusiness%20Survey.pdf>
- ¹¹ The Big Down 2003 ETC Group page 47 <http://www.etcgroup.org/documents/TheBigDown.pdf>
- ¹² The Big Down 2003 ETC group page 39 <http://www.etcgroup.org/documents/TheBigDown.pdf>
- ¹³ The Nanotech Report 2004 (TNR 2004) <https://www.globalsalespartners.com/lux/#> <http://www.luxresearchinc.com/>
- ¹⁴ The Nanotech Report 2004 (TNR 2004) <https://www.globalsalespartners.com/lux/#> <http://www.luxresearchinc.com/>
- ¹⁵ The Nanotech Report 2004 (TNR 2004) <https://www.globalsalespartners.com/lux/#> <http://www.luxresearchinc.com/>
- ¹⁶ Helmut Kaiser Consultancy, Tübingen. <http://www.hkc22.com/nanomarkets.html>
- ¹⁷ Questionnaire International Dialogue on Responsible R&D of Nanotechnology Reply by: Dr. M.C. Roco Senior Advisor for Nanotechnology at NSF; Chair NSTC/NSET USA June 12, 2004 1. Nanotechnology R&D programs in USA http://www.nsf.gov/home/crssprgm/nano/mcr_04-0616_usandresnano_meridian_3.pdf
- ¹⁸ Gregor Wolbring is a member of the Canadian Commission for UNESCO; a Biochemist in the Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of Calgary; Adjunct Assistant Professor for bioethical issues at University of Calgary and University of Alberta; a consultant for bioethics, disability and governance of science and technology issues. Web: <http://www.bioethicsanddisability.org>

Virtually all (97.4 per cent) of the expenditures of the private for-profit sector were made by high-income countries. China accounted for 0.5 per cent and the rest of the low-

and middle-income countries made up the remaining 2.6 per cent of the global total (see Table 2.3).

Table 2.3

Private for-profit health R&D expenditures by funders in US\$ millions, 2001

Global Total	\$51,230	100%
USA	22,009	43.0%
Japan	7,878	15.4%
United Kingdom	2,981	5.8%
Germany	3,538	6.9%
France	2,194	4.3%
Switzerland	1,387	2.7%
Sweden	1,325	2.6%
Canada	1,122	2.2%
Other HIC	7,452	14.5%
Total HIC	\$49,885	97.4%
China	262	0.5%
India	141	0.3%
Transition	182	0.4%
Other LMIC	760	1.5%
Total LMIC	\$1,345	2.6%

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

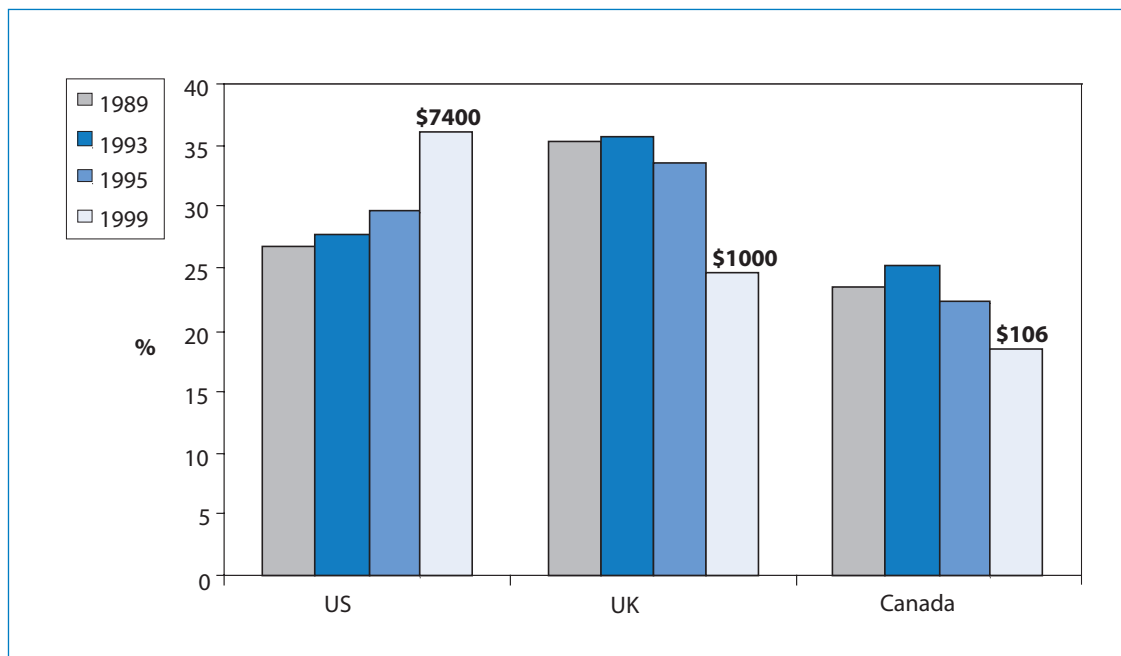
Note: The estimates for the United States private-for-profit R&D funding is lower than the US\$23,502 million figures provided for U.S. domestic pharmaceuticals as a sector due to research performed in the private sector that is funded by non-private sources.

Of the US\$49.9 billion spent by the private for-profit sector on health research in high-income countries in 2001, US\$44.1 billion was spent by domestic pharmaceutical companies in high-income countries and US\$5.8 billion was spent outside the United States by US-owned PhRMA member firms. This follows a trend, beginning in the 1990s, to concentrate the research activities of

pharmaceutical companies in the United States.

Further, basic research has grown as a share of pharmaceutical R&D in the United States (from 26 per cent in 1989 to 36 per cent in 1999) while decreasing in the United Kingdom (from 35 to 25 per cent in the same 10-year period) and Canada (from 25 per cent to 18 per cent) (see Chart 2.12).

Chart 2.12 Basic research by pharmaceutical companies, as % of total R&D and in US\$ millions, 1999



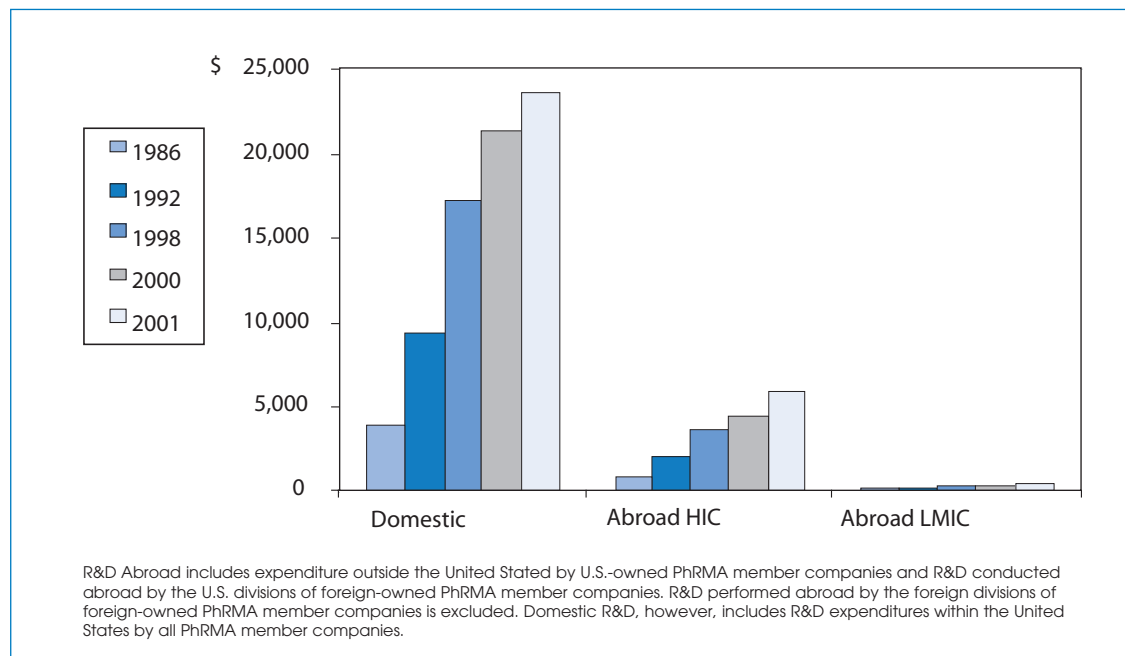
Source: A Comparison of Pharmaceutical Research and Development Spending in Canada and Selected Countries (2002), PMPRB

This concentration of pharmaceutical research in the United States, is reflected in spending patterns of members of the Pharmaceutical Research and Manufacturing Association of America (PhRMA). R&D expenditure by PhRMA member companies was estimated at US\$31.0 billion in 2002. Just one per cent of that amount (US\$297.0 million) was spent on R&D in low- and middle-income countries.

In contrast, PhRMA companies spent US\$5.0 billion in other high-income countries.

Domestic R&D expenditure by U.S.-owned pharmaceutical companies has also been growing steadily for some years, primarily within the United States and other high-income countries – e.g., from US\$17.1 billion in 1998 to US\$23.5 billion in 2001 (see Chart 2.13).

Chart 2.13 Trends in pharmaceutical R&D by US companies, in US\$ millions

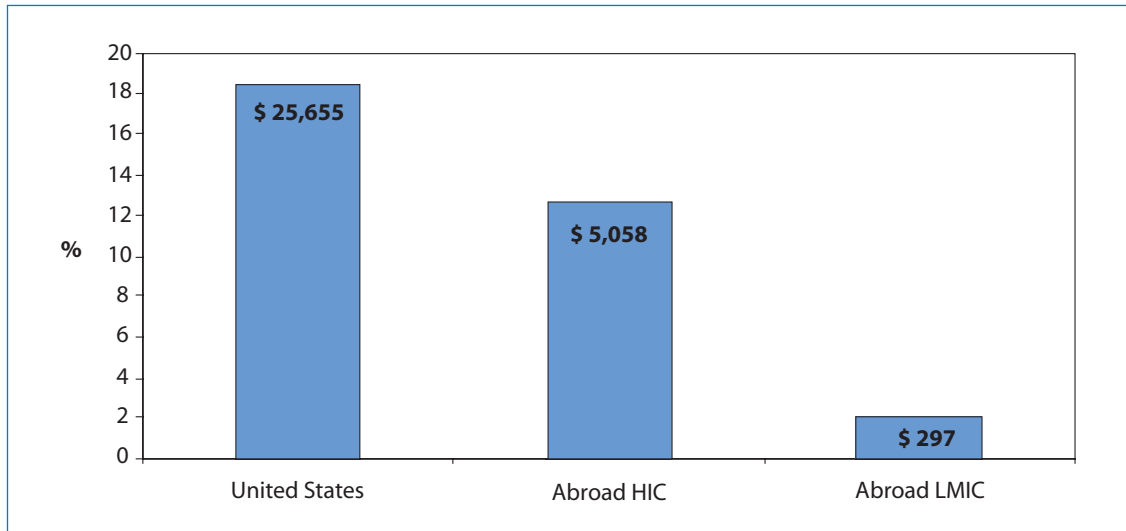


Source: Pharmaceutical Industry Profile 2004, PhRMA

Investment in R&D as a share of pharmaceutical sales is also very high within the United States, and to a lesser extent in other high-income countries; in contrast, investment to sales ratios in low- and middle-income countries are quite low. Domestic R&D by American pharmaceutical companies was US\$25.6 billion in 2002, the equivalent of 18 per cent of domestic sales (see Chart 2.14). R&D abroad by U.S.-owned

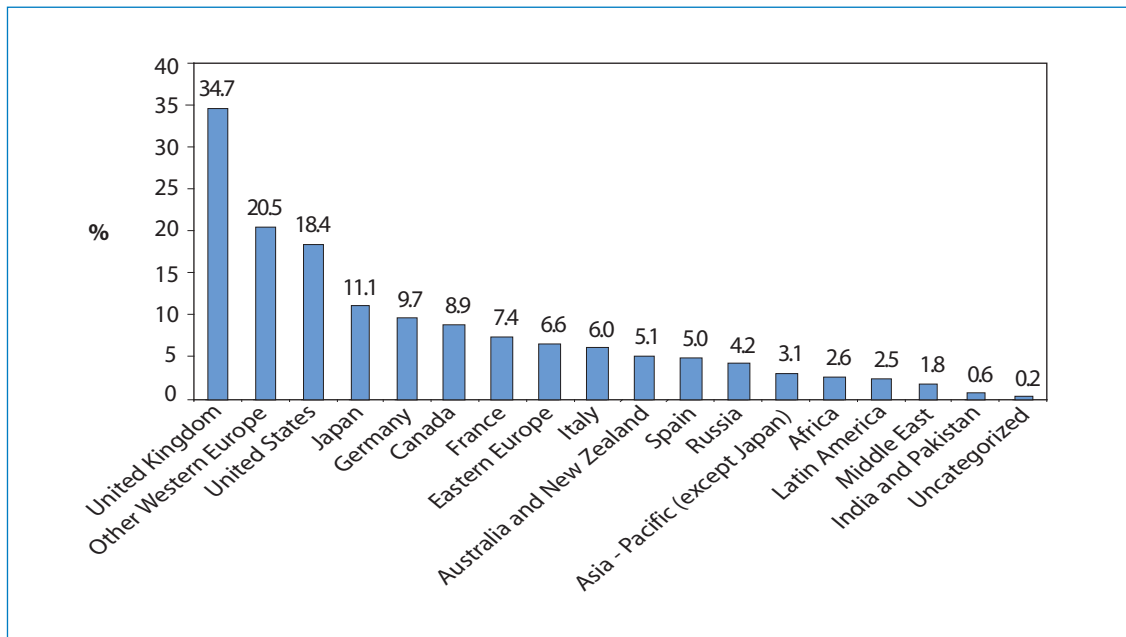
pharmaceutical companies was estimated at 13 per cent of sales in high-income countries and just two per cent of sales in low- and middle-income countries. In fact, the highest ratio is 35 per cent in the United Kingdom; ranges from 5 to 21 per cent in Europe; three per cent in Africa, two per cent in Latin America and one per cent in India/Pakistan (see Chart 2.15).

Chart 2.14 R&D as a percentage of sales and in US\$ millions, PhRMA member companies, 2002



Source: Pharmaceutical Industry Profile 2004, PhRMA

Chart 2.15 R&D as a % of sales, PhRMA member companies (US), 2002



Source: Pharmaceutical Industry Profile 2004, PhRMA

The ratio of R&D to domestic pharmaceutical sales is very high for Swiss-owned (103 per cent), Danish-owned (79 per cent) and Swedish-owned (44 per cent) companies. These high ratios may reflect a situation where domestic sales are quite small compared to international sales. U.S.-based pharmaceutical companies spend about 35% of their funds on Phase 1-Phase 3, 20% on phase 4 and product approval, with another 34 per cent allocated for basic and pre-clinical research, and 11% undesignated. Equivalent data for Europe and Asia were not identified.

Private not-for-profit financing

The private not-for-profit sector has an increasingly strong commitment to health R&D – estimated at close to US\$8.0 billion in 2001, up from US\$6.0 billion in 1998. Almost all of this funding (US\$7.7 billion) came from private foundations and universities in high-income countries for health R&D carried out in these countries. In contrast, in 2001, just US\$0.08 billion was spent in low- and middle-income countries and financed by domestic private foundations and universities (roughly the same amount estimated for 1988). Foreign foundations and universities also financed health R&D in low- and middle-income countries, an estimated US\$0.15 billion in 2001, up from an estimated US\$0.11 billion in 1998.

Foundations are making an ever-increasing contribution to health research at both national and international levels. In recent years, Foundations have contributed on estimated US\$3.0 billion annually to international and development activities, more than half this amount originating in the United States. These expenditures are usually made through multilateral agencies or domestic institutions, rather than directly. Foundation expenditures on international and development activities are part of the OECD-DAC estimates for NGOs, which are roughly US\$7.0 billion annually. Private flows, however, are under-

reported. Foundations are not simply giving away funds – they 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 government and the market.⁴

These entities are building up their roles by forming associations and networks: The Foundation Center in the United States maintains a foundation data base and tracks resource flow information; the Association of Medical Research Charities in the United Kingdom sets standards for peer review; the Charities Aid Foundation issues annual reports on charity trends in Britain; the European Foundation Center (EFC) represents 143 foundations; Grupo de Institutos, Fundacoes e Empresas (GIFE) in Brazil; and the Third Sector Foundation of Turkey (TUSEV).

The United States and United Kingdom have the most complete data for the third sector at the country level, so the data in this report are primarily from those two countries. Regional organizations such as the EFC in Brussels have the potential to contribute data from more countries in the future. OECD has also indicated interest in obtaining improved data from the private sector – including foundations and trusts – so this may stimulate the collection of additional data at the country level.

In general, endowments of asset-based foundations and trusts experienced unprecedented returns from investments in the 1990s, resulting in increased asset values and increased expenditures for grants, generally peaking in 2001. The decline in financial markets starting in 2000 has been followed by a decline in asset values and grant making. The value of assets declined followed by decreases in grant making. Recovery of asset values and grant making is already taking place as the economic climate continues to improve.

United States

Between 1990 and 2000, total giving by US-based foundations more than tripled from US\$8.8 billion to US\$27.6 billion. In the same period, international giving by US-based foundations almost quadrupled from US\$0.8 billion to US\$3.1 billion. The number of foundations nearly doubled – from 32,401 in 1990 to 56,582 in 2000. An estimated US\$1.8 billion can be attributed

to health giving by US-based foundations in 2001.⁵ The impact of the financial markets is reflected in lower expenditures in 2002 (see Table 2.4). Health as a category experienced a 15 per cent decline in foundation grant dollars between 2001 and 2002 but grant dollars for health research rose from 8.5 to 10.6 per cent, so that it was the only sub-category of health to show positive growth (up 1.3 per cent in 2002).

Table 2.4
Top 10 foundations by giving for health*

	2001		2002
Bill and Melinda Gates Foundation	\$470,751,526	Bill and Melinda Gates Foundation	\$518,917,755
Robert Wood Johnson Foundation	469,357,867	Robert Wood Johnson Foundation	432,327,603
David and Lucille Packard Foundation	321,855,474	California Endowment	160,963,943
Theodore and Vada Stanley Foundation	193,888,270	Avon Foundation	78,047,321
California Endowment	144,795,398	Starr Foundation	68,996,000
Whitaker Foundation	78,535,715	Whitaker Foundation	55,663,725
Starr Foundation	48,766,000	Ford Foundation	40,131,259
Ford Foundation	44,165,668	David and Lucille Packard Foundation	39,673,765
Duke Endowment	43,657,849	Duke Endowment	38,793,557
John A. Hartford Foundation	33,433,658	Rockefeller Foundation	28,808,830

* includes health research

Source: Foundation Giving Trends 2003 and 2004, The Foundation Center, New York

By grant dollars, the Gates Foundation was by far the top foundation in health-giving at US\$518.9 million in 2002, focusing on diseases of highest burden worldwide. The Robert Wood Johnson (RWJ) Foundation ranked second at US\$423.3 million but its activities are confined to the United States.

Support for HIV/AIDS prevention, treatment and research nearly doubled from US\$156.0

million in 2000 to US\$307.6 million in 2001, largely through grants from the Gates Foundation. Allocations for mental health research more than doubled in 2001, largely due to a US\$186.3 million grant from the Theodore and Vada Stanley Foundation to the Stanley Medical Research Institute. Private foundations created with proceeds from the sales of not-for-profit health care entities to for-profit corporations awarded

US\$320.8 million through grants – 9.1 per cent for research, including 1.7 per cent for medical research. Of the 96 largest grants awarded in 2001 by US-based foundations, 14 were predominantly health oriented and at least eight include research. About half of the recipients of foundation giving in 2002 were universities; others included government, other trusts and foundations, and community groups.

United Kingdom

Most charity funding for research goes to universities and medical schools – an estimated 74 per cent in 2004, up from 58.5 per cent in 1990/91. Charities are the single-most important source of funding for research in universities and they support approximately one third of medical research in the United Kingdom (or 13 per cent of total R&D).⁶ Charity sector contributions for medical research have grown from UK£138.0 million in 1987/88 to an estimated UK£500.0 million in 2004. Six charities account for 83 per cent of charity sector contributions but only three have international programmes: Wellcome Trust, Cancer Research UK and the Leukemia Research Fund.

In 2001/02 large academic and scientific trusts accounted for one quarter of grant-making dollars and almost half of foundation assets. The value of those assets grew from 1996 to 2001 and then fell by more than 20 per cent in 2001/02, echoed by a fall in grant levels by 14 per cent in real terms – victim to a weak global economy.

Japan

A lengthy bout of reduced economic performance has stunted the relatively young foundation sector in Japan. In 1999, only two new foundations were established compared to 56 in 1990. Total annual grant-spending by 140 foundations peaked in 1993 at 230.0 Yen-100 million falling to 161.0 Yen-100 million by 1999.⁷ Low interest rates on savings accounts

hampered many foundations that drew their main funding resources from interest on bank deposits.

LMIC

In many low- and middle-income countries, the private not-for-profit sector is non-existent. Where it does exist, non-profits like foundations focus on national issues. In some countries, there has been an effort to encourage the development of the private not-for-profit sector. In some, private entities funded by foundations from abroad or that operate through international partnerships have been set up. The legal and fiscal environment can be a key obstacle to the development of the third sector. There is a need for proper regulations to ensure the status of foundations, the right of association, incentives for philanthropy such as deductibles on corporate income or tax-exemptions on donations, as well as processes to facilitate the registration of new foundations and not-for-profit organizations.

2.2.5 Foundations and development cooperation

Foundations have shifted their areas of interest over the years in parallel with, and sometimes in advance of, shifts in ODA agency priorities. For example, social action and environment have been significant areas of interest for foundations for at least 30 years, whereas ODA agencies have increased their involvement in these areas only over the last 15 years. On the other hand, ODA agencies have led the way towards broader approaches to reproductive health, while many foundations remained focused on narrow vertical approaches such as family planning. To some extent this may be because foundations are filling a gap left by the public sector.

Foundation work over the past decade has emphasized promotion of democracy, social participation and peace-building. However, recent new initiatives involve agricultural

crop and disease research and health and infectious diseases, marking a decisive return of foundation interest to LMIC. The United States' contribution to health and health research has been led by the Gates Foundation which has formed partnerships with USAID and other bilateral aid agencies as well as multilateral agencies administering ODA. Whereas Japan has a large official aid program, the resources available to foundations are small, especially due to low interest rates and investment returns in Japan over the last years. Therefore, foundations concentrate on filling the gaps of ODA programs. In Europe, foundations participate actively with ODA agencies especially where they have long-term mutual interests (e.g., the Wellcome Trust and DFID in malaria).

The most successful foundation initiatives in low- and middle-income countries share these characteristics:

- They have been long-term programmes, sustained for 15-25 years.

- Their planning has combined vision and sound scientific understanding.
- Projection implementation has been participatory and built upon trust and respect with local authorities, technical staff and populations.
- Initiatives were bold and involved accepting a risk of failure.

ODA agencies have limits to the extent to which they can take on these approaches as they are public agencies, responsible to the taxpayer for results within a shorter time frame than foundations. However, there are some lessons learned from the best foundation projects that bilateral agencies might consider:

- Tap the best scientific advice early in the development of new programmes.
- Bring more rigour to the assessment of projects aimed at behavioural change and the social sciences through evaluation.
- Improve knowledge of foundation activities that could be extended by ODA agencies.

2.3 Financial flows for international research by HIC investors⁸

International health research is defined here as research funded by high-income countries that is carried out:

- abroad, including in other high-income countries and in low- and middle-income countries;
- domestically, but addressing important global health issues.

The total value of international health research for 2001 is estimated at US\$6 billion.

Of this, an estimated US\$1.1 billion flows from high-income countries to low- and middle-income countries to fund research undertaken in these countries (see Table 2.5). This flow represents about one per cent of the estimated US\$101.6 billion spent on health R&D in high-income countries and about one quarter of the US\$4.3 billion total health R&D expenditures of low- and middle-income countries.

Table 2.5**International health research expenditures, US\$ millions, 2001**

	Total International Health Research	Financial Flows from HICs to fund Health Research in LMICs
ODA	3,328	401
Bilateral agencies	1,806	222
Multilateral agencies	1,464	179
World Bank*	58,3	n/a
Foundations	980	304
Research Institutes	1,986	74
Private for-profit Companies	n/a	345
TOTAL	6,294	1,124

*There may be additional spending from other Development Banks, but the amount is unknown

Note: International research often includes research performed in HIC that addresses diseases of poverty. Hence, the estimated amount expended in the LMIC may be much lower.

Sources: Global Forum estimates based on data from OECD, foundations, research institutes and pharmaceutical associations

The flow of funds from high-income countries to low- and middle-income countries happens in a variety of ways. Some funds are direct transfers for specific research in low- and middle-income countries by development aid programmes, the non-profit sector, and research institutions in high-income countries. Other funds are pooled through multilateral agencies and secondary investors. Funding may be provided as contracts or grants.

Sources of funding are:

- official development assistance agencies (ODA);
- multilateral agencies;

- foundations;
- research institutes;
- NGOs, including partnerships and initiatives; and
- private for-profit companies.

Research funded by money flowing from high-income countries to low- and middle-income countries covers a broad range of health R&D: epidemiology, etiology and pathogenesis; social science research, health policy and systems research; clinical research and operations research; and research capacity strengthening (RCS).

The estimates provided above are the best available to date. Unfortunately, information on private sector investments in international health and specifically on money flowing to LMIC is not readily available. It is hoped that this report will motivate private sector companies to provide such data in the future. Also, it is difficult to estimate the amount of money spent on international research that actually flows for research in low- and middle-income countries. Nonetheless, the picture of resource flows from HIC investors to international health R&D does shed some light on work being done on health problems pertaining to low- and middle-income countries. Details of investments by selected organizations follow.

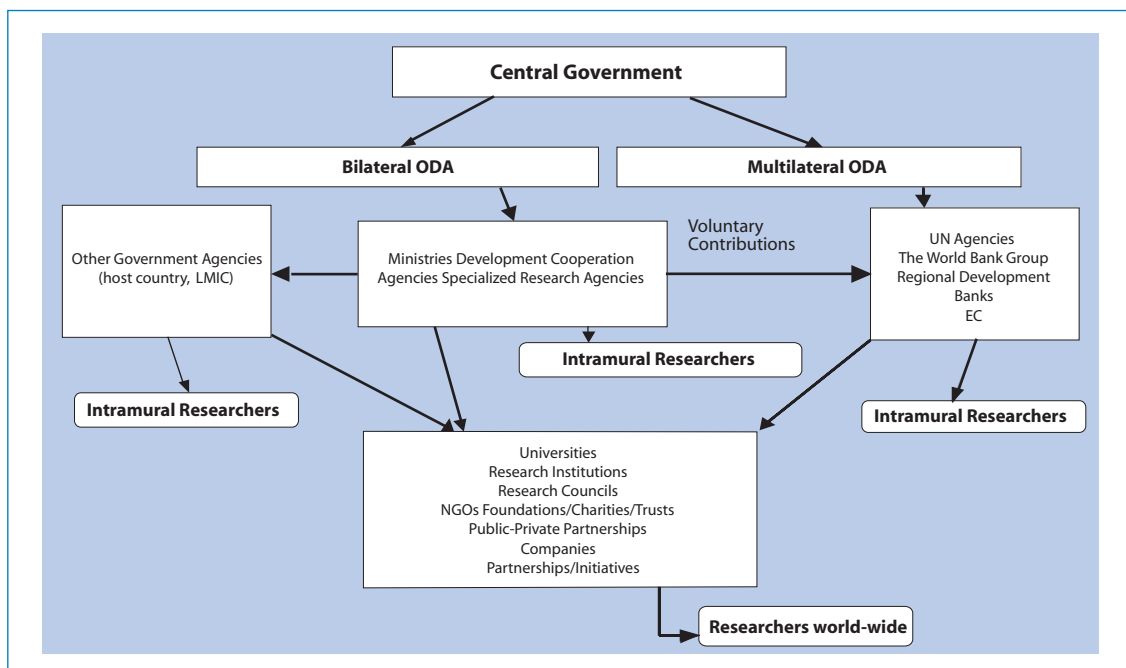
Primary investors are organizations that receive direct allocations from national governments or generate their own funds for health research. *Secondary investors* receive grant funds from primary investors. Primary

investor agencies and organizations may transfer funds laterally to other primary investors and vertically to secondary investors, making resource flows difficult to track. Organizations have very diverse mandates, modes of operation and priorities – with implications for how they define and track data, making international comparisons difficult.

2.3.1 Official development assistance (ODA)

Official development assistance (ODA) is an important source of health and health research funding for developing countries (bilateral ODA) and multilateral institutions (multilateral ODA). At a supra-national level, ODA financial flows are monitored by the Development Assistance Committee (DAC) of OECD. ODA is administered by countries in a variety of ways through specialized development cooperation or development aid agencies (see Chart 2.16).

Chart 2.16 ODA resource flows for health research



After maintaining a steady level through the 1980s, aid to LMIC fell sharply with the dissolution of the Soviet bloc and the end of superpower rivalry in LMIC. By 1997, aid reached an all-time low of 0.22 per cent of donors combined national income. In 2001-2002, the trend reversed, resulting in a 7 per cent real increase in ODA. Health ODA rose from US\$1.6 billion in 1998 to US\$2.7 billion in 2001 of which an estimated US\$400.0 million went to health R&D. Further increases in overall ODA are projected through 2006, setting the stage for increases in both ODA and health R&D.

ODA health research implemented in low- and middle-income countries includes mainly non-basic research such as operational research, capacity strengthening, health policy research, clinical and large-scale field trials, development of tools and methodologies to be used in low-income settings, and socio-economic research. However, ODA implemented through secondary investors may support a wider range of research, including biomedical research. Resource flows for selected ODA agencies for which health research data were obtained are summarized in Table 2.6.

Table 2.6
Summary of resource flows data for selected ODA agencies in US\$ millions, 2001

	ODA US\$ millions	Institution	Health US\$ millions	Health Research, Estimates US\$ millions
USA	11'429	USAID	1'474	96
UK	4'579	DFID	316	23.5
France	4'198	IRD	210	5.7
Norway	1'346	NORAD	183	2.2
Canada	1'533	CIDA/IDRC	112	4.4
Sweden	1'666	Sida/SAREC	63	12.3
Denmark	1'634	Danida	59	5.1

Source: Annual Reports, OECD, institutional financial reporting, personal communication

Research as a percentage of health ODA increased for some ODA agencies between 1998 and 2001 and fell for others. Of the six agencies supporting both research and operational programs from ODA and whose data were made available, four (USAID, DFID, Sida/SAREC, and Danida) met the goal established by the 1990 Commission on Health Research to allocate at least five per cent of their health ODA to research. Since ODA is disbursed to numerous agencies in some countries, the percentage provided is not

equivalent to five per cent total ODA for a country.)

Denmark

Development cooperation is very centralized and compact, with one government entity (MOFA/Danida) directly responsible for most ODA funds. In 2001, from total ODA of DKK12,800 million, DKK247.0 million were allocated for research.⁹ More than 40 per cent of total research funding was allocated to global research that is largely

channeled through multilateral/international organizations.¹⁰

In 2001, US\$163.0 million – or 3.6 per cent of net ODA – was allocated for health and population. Support for health research included DKK31.0 million for tropical disease research at the Danish Bilharziasis Laboratory (DBL), DKK23.0 million for bilateral support to health research through ENRECA and Council for Development research projects, and DKK42.0 million for global research mainly executed through multilateral institutions.¹² Disease-specific allocations and percentages of research monies made available to LMIC researchers were not available.

Sweden

The majority of ODA is administered by the Swedish International Development Agency (Sida). In 2001, 3.8 per cent of ODA was allocated for health and population and in 2002 that percentage rose significantly to 8.4 per cent as ODA rose from US\$1.7 billion to US\$1.8 billion.¹³ In 2001, from the Sida budget of SEK11.9 billion, SEK775.0 million was allocated for research administered by the Department of Research Cooperation, SAREC.¹⁴ In 2001, health research constituted SEK126.5 million of the total for research (17 per cent).¹⁵ Since 1999, the amount of funds for health research has shown modest increases; disease control constitutes the largest sub-sector with 39 per cent of funds, while sexual health and rights is the second-largest sub-sector.

United Kingdom

Net ODA disbursements (2001 prices and exchange rates) rose from US\$3.4 billion in 1993 to US\$4.6 billion in 2002. The main executing agency for British aid is the Department for International Development (DFID). Multilateral and bilateral assistance are seen as a continuum and thus not subject to arbitrary allocations. Multilateral

disbursements have been about 40 per cent of ODA mainly due to contributions to the European Commission (EC) (20-25 per cent of total ODA). Sector allocation of ODA has been driven by the Millennium Development Goals (MDGs), resulting in an increased focus on health and education: 6.9 per cent of bilateral ODA was committed to health in 2001 and that percentage rose to 11.5 per cent in 2002. In 2001/02, DFID spent UK£146.6 million (just over US\$200.0 million) on research and development, up from UK£104.0 million in 1998/99. Health research expenditures for 2001/02 were about UK£16.3 million (US\$23.5 million), up 16 per cent since 1998 in UK£ but unchanged in US dollars.¹⁶

United States

In 2002, 98 per cent of ODA was distributed to eight government agencies with USAID receiving the largest portion (50 per cent). In 2002, the United States increased its commitment to development cooperation with the launch of the Millennium Challenge Account that will increase 2002 ODA levels by about 50 per cent by 2006.¹⁷

From 1998/99 to 2000/01, USAID health budgets rose each year – US\$1.1 billion to US\$1.4 billion – as overall funding levels fell.¹⁸ Funding for infectious diseases increased steadily, while HIV/AIDS funding more than tripled over the three-year period. Research levels dropped significantly in 1999 compared to 1998, but rose by 66 per cent from 1999 to 2001. Of the US\$1.4 billion health budget in 2001, an estimated seven per cent or US\$96.0 million is attributable to health research funded by the Bureau for Global Health and does not include research funded by Regional Bureaus or field missions.¹⁹ Priority health research includes: population, maternal health, infant and child health, HIV/AIDS, and infectious diseases.

Canada

Canadian ODA declined steeply from 0.45 per cent of GNI at the beginning of the 1990s to 0.22 per cent in 2001. In 2002, the government set a goal of increasing the ODA/GNI ratio to about 0.35 per cent by the end of the decade.²⁰ The Canadian International Development Agency (CIDA) plays the lead role for development assistance programme implementation (managing 79 per cent of international assistance in 2000). The International Development Research Centre (IDRC) plays the lead role for research related to development. The IDRC budget for 2000/01 was CD\$91.0 million, with CD\$60.0 million from the Canadian Parliament representing about 60 per cent of total revenues.²¹ Other revenues derived from external resource mobilization, including funding from CIDA, other donor agencies and the private sector. After significant declines in overall ODA through 2000, health research has been restored close to early 1990 levels in absolute terms. In 2003/04, health research disbursements were CD\$9.5 million, with provisional forecasts for 2004/05 of CD\$12.0 million. Health research has also increased as a share of the IDRC research budget, rising from 6.7 per cent in 1999/00 to 13.6 per cent in 2002/03.²²

France

ODA net disbursements (at 2001 prices and exchange rates) declined from US\$6.7 billion in 1993 to US\$4.2 billion in 2001. Five per cent of ODA was allocated for health and population in 2001, up from 3.2 per cent in 1998. ODA rose by 22 per cent in real terms in 2002 but the allocation for health and population declined to 4.2 per cent.²³ Allocations from the government to the public Institute for Research and Development (IRD, formerly ORSTOM) declined from US\$175.0 million in 1998 to US\$148.0 million in 2001 but increased in 2002 and again in 2003 to a

level of US\$190.0 million. Of the total IRD budget of about US\$160.0 million, 91 per cent came as institutional funds from government and nine per cent from other sources – largely other government ministries and the EU. Nearly half of IRD funds are spent in France.²⁴

Norway

The Ministry of Foreign Affairs plays the lead role in administering ODA and directly manages bilateral and multilateral ODA while the Norwegian Agency for Development Cooperation (NORAD) manages the support to NGOs, civil society and development research.²⁵ Norwegian ODA levels have been fairly stable over the past decade. However, in 2000, Norwegian ODA decreased by 9.6 per cent, mainly due to exchange rate fluctuations, and in 2002, ODA increased by 13 per cent in real terms to US\$1.7 billion. In 2001, 11.9 per cent of Norway's bilateral budget was spent on health. General medical research increased enormously from NOK 4.2 million in 2000 to NOK18.7 million in 2001, and sharply again to NOK24.7 million in 2002 before decreasing slightly in 2003.

2.3.2 Multilateral organizations

Multilateral organizations are international institutions with governmental representation. They include multilateral banks, UN agencies, and regional groupings such as the EU. They receive funds from governments, non-governmental sources and the for-profit sector. A contribution is defined as multilateral if it is pooled with other contributions and disbursed at the discretion of the agency. These secondary investors provide support for health research through loans, grants and contracts to universities, research institutes, NGOs and LMIC governments. Resource flows are difficult to understand and document given the size and complexity of the organizations. Resource flows for selected institutions are provided in Table 2.7.

Table 2.7**Summary financial data for selected multilateral institutions, 2001**

	Total *	Health	Estimated Health Research
EC Research INCO***	US\$64.7 million	US\$17.3 million	US\$17.3 million
World Bank	US\$17.3 billion	US\$1.23 billion	US\$58.3million
WHO RPC **	US\$1.0 million	US\$1.0 million	US\$1.0 million
Co-sponsored HRP**	US\$33.3 million	US\$22.8million	US \$22.8million
WHO CAH **	US \$16.5 million	US \$16.5 million	US \$7.2 million
Co-sponsored TDR **	US \$37.0 million	US \$25.0 million	US \$25.0 million

* Income or expenditures for named organization.

** Resource flows for WHO and co-sponsored programmes are based on dividing the biennial budget by two to arrive at figures for 2001.

*** EC resource flows determined by dividing programmes by four.

Source: Annual Reports, financial reports, internal documents and personal communications

European Commission

The majority of international health research is funded through two directorates: Research and Development.²⁶ Only the Research Directorate provided data for this report. Its health budget, within the international scientific cooperation programme, has risen steeply at four-year programme intervals. Under the INCO/DEV Programme 1998-2002, EURO62.0 million was expended for health research, including EURO17.9 million for health systems and policy research. During the course of the programme, the share of funding going to LMIC researchers increased steadily.

The Research Directorate and International Cooperation (INCO) Programme now work under the new EU Sixth Framework Programme (FP6). INCO under FP6 will be allocated about EURO45-50 million for health research projects.²⁷ FP6 encourages the participation of low- and middle-income countries. For the first time, LMIC researchers

will be able to participate in all programs, not just INCO. Under the new programme, international research cooperation activities will be carried out in three areas, totaling EURO710.0 million.

- research in seven priority areas, several of which relate to health – EURO285.0 million;
- international cooperation activities under INCO – EURO315.0 million;
- human resources and mobility, including research training for LMIC researchers in Europe – EURO110.0 million.

WHO/Research Policy and Coordination (RPC)

The RPC budget increased from US\$2.0 million in the 2000-01 biennium to US\$3.5 million in 2002-03. Donors for the two-year period 2000-01 were the governments of Norway, Sweden, Switzerland, the United Kingdom and Rockefeller Foundation. In 2000-01, 34 per cent of the budget was spent on enabling health researchers from LMIC.

In 2002-03, this allocation increased to 62 per cent, primarily because of the Health Research Systems Initiative (HRSA) that has funded a pilot project on in-depth country studies for the testing of data collection tools in 14 low- and middle-income countries.

UNDP/UNFA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP)

HRP is the main instrument in the UN system for research in human reproduction. HRP income has declined dramatically from about US\$46.0 million in the 1992-93 biennium to US\$34.0 million in 1998-99 and finally to US\$27.2 million in 2002-03. Expenditures on research of global relevance, as well as national research and research capacity strengthening have also declined – from US\$25.0 million in 1992-93, to US\$20.0 million in 1998-99 biennium and US\$18.9 million in 2002-03. About one third of its research budget is used to support national research capacity strengthening in reproductive health.

HRP co-sponsors have contributed about one third of the total expenditures over the past 14 years but the absolute amount and its share of the budget have been declining over the past seven years (from US\$8.3 million to US\$4.3 million, and from 41 per cent to 28 per cent of the total budget²⁸). UNDP has not contributed since 1996. The relative share of contributions from Member States has also declined, while the share of contributions from foundations increased from 5 to 22 per cent over the past 12 years.²⁹

WHO/Department of Child and Adolescent Health and Development (CAH)

CAH is responsible for promoting health, growth and development outcomes for the age group from birth to 19 years. Newborn and child health are sub-categories that

address five of top 12 global burden of diseases/conditions:

- respiratory infections;
- HIV/AIDS (paediatric);
- diarrhoeal disease;
- nutritional deficiencies; and
- perinatal/neonatal conditions.

Both the CAH total budget and the budget for child and newborn research rose in the mid-1990s but fell in the 1998-99 biennium to levels of US\$27.8 million for child health activities, US\$6.7 million of which went to R&D. During the 2000-01 biennium, research for newborn and child health rose greatly to US\$14.4 million and the total budget grew to US\$38.0 million. Funding rose again in 2002-03 but should fall in 2004-2005 as some large research grants conclude.

World Bank Group

The World Bank provides research funding through its support for regional and global programmes administered by the Development Grant Facility (DGF) and through its lending programmes (IBRD and IDA) implemented at the country level. In 2001, the World Bank Group provided US\$17.3 billion in loans to client countries, down from US\$28.5 billion in 1998. The health lending budget totaled US\$1.2 billion in 2001, down from US\$2.0 billion in 1998. DGF grants totaled US\$25.4 million, up from US\$20.0 million in 1998.³⁰ Priorities followed the 1997 Population, Health and Nutrition (PHN) Sector Strategy – diseases of the poor (malaria and tuberculosis), family planning reproductive health, HIV/AIDS, malnutrition, health systems and policy research.

It is estimated that funds lent for health research (mainly health policy studies) totaled US\$50.0 million in 2001, with some US\$14.0 million wholly devoted to HIV/AIDS. An additional US\$3.0 million is attributed to the HIV/AIDS, Malaria, STD and Tuberculosis

Project; and US\$2.0 million to the Integrated Early Childhood Project. In 2001, DGF funding for global and regional programmes included at least an estimated US\$8.3 million for health research. About US\$1.0 million was allocated to the Child Health and Nutrition Research Initiative and an equal amount for the Medicines for Malaria Venture (MMV) and the Multilateral Initiative for Malaria (MIM) through the Global Forum for Health Research.

Thus, of the total expenditures of US\$17.3 billion in 2001, US\$1.2 billion can be attributed to health of which an estimated US\$58.3 million was for health research, compared to US \$55.7 million in 1998.³¹

UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR)

This programme focuses on the communicable diseases found mainly in low- and middle-income countries but also increasingly worldwide as globalization grows: malaria, leishmaniasis, filariasis, schistosomiasis, Chagas disease, trypanosomiasis, onchocerciasis, leprosy, tuberculosis and dengue. Over the last five years, public-private partnerships with the objective of producing new tools for application in LMIC countries have received increased attention.

The launch of the TDR strategy for 2000-2005 has resulted in a reversal of a downward trend of income. By 2002-2003, income was 30 per cent higher than in 1998-1999 – US\$67.0 million compared to US\$52.0 million. However, the nature of the income changed as the new funding was designated for specific research projects. As a result the undesignated income of US\$44.0 million for the 1998-99 biennium fell to US\$37.0 million in 2002-03; During the same biennia, TDR operations in low- and middle-income countries fell from US\$24.0 million to US\$18.0 million and total research capacity strengthening slipped from

US\$16.0 million to US\$15.7 million. Research capacity strengthening is mainly funded from undesignated income and so has been affected by the decline in undesignated funding since 1992-93. TDR spends about 30-40 per cent of its research funds in low- and middle-income countries.³²

2.3.3 National research institutions

National research institutions in industrialized countries are continuing to expand their role in international health research, although it is unclear what the magnitude of their contribution is in strengthening the capacity of developing country researchers.

In some cases, there has been a re-organization of the research landscape as in the consolidation of research institutions in Canada to form the Canadian Institutes of Health Research (CIHR) and in the process institutionalizing a global health coordinating office. In 2001, Health Research The Netherlands (Zon) and the Council for Medical and Health Research of NWO (Mw-NWO) merged to form the Netherlands Organization for Health Research and Development (ZonMw) but legal issues preclude research support outside the Netherlands at this time. The U.S. National Institutes of Health (NIH) have institutionalized “internationalism” by having an international coordinator in each Institute. Both NIH and the Centers for Disease Control and Prevention (CDC) have overcome obstacles in expanding their international research.

The level of collaboration among national research institutions appears to be increasing, especially as the health and science issues continue to evolve at a global level. Although some of the collaboration is stimulated by the ever-increasing number of global initiatives and partnerships, there is also considerable institution-to-institution collaboration on issues of mutual interest.

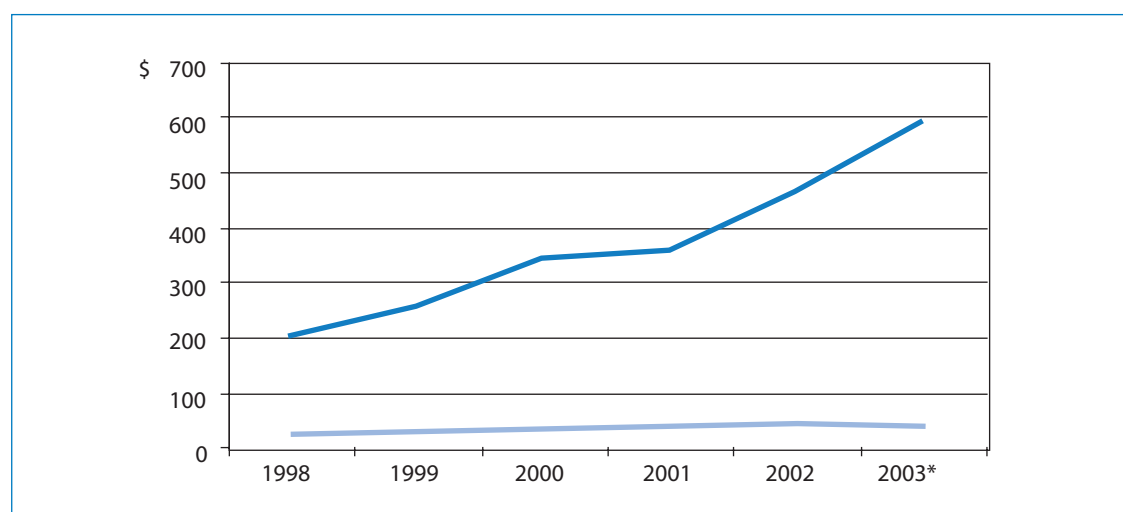
National Institutes of Health, United States

NIH is composed of 27 institutes and centres each with its own broadly defined mission. Appropriations from Congress have risen enormously – at US\$11.9 billion in 1996 and nearly doubling to US\$23.3 billion in 2002. The biggest increase in a single year came in 2003 with a jump to US\$27.1 billion.

In fiscal year 2001, NIH appropriation totaled US\$20.5 billion, of which US\$5.4 billion went to cancer and US\$2.3 billion to cardiovascular

diseases - reflecting the high impact of these diseases in the United States. HIV/AIDS also received a high level of funding at US\$2.7 billion in 2003/04. NIH allocated US\$353.5 million for international activities consisting of grants and contracts to foreign institutions, foreign components of domestic grants, the NIH Visiting Program (foreign scientists working and training at NIH) and training grants primarily for LMIC country scientists (see Chart 2.17). The latter totalled US\$41.5 million in 2001, up from US\$23.3 million in 1998.

Chart 2.17 International activities funding, National Institutes of Health (US), 1998-2003, US\$ millions



*training grants are a subset of the total

The Foundation for the National Institutes for Health (U.S.) supports the mission of the NIH, which is to develop new knowledge through biomedical research. In 2003, the Gates Foundation announced a US\$200 million grant to the foundation to establish the Grand Challenges in Global Health Initiative. The Initiative identified critical scientific challenges in global health and has initiated a programme

to address those challenges. The first grants will be awarded early 2005.

The Fogarty International Center (FIC) is the focal point for international activities within NIH. The Director of FIC also serves as the Associate Director for International Research for the NIH. FIC priorities include biodiversity, ecology of infectious diseases, HIV/AIDS,

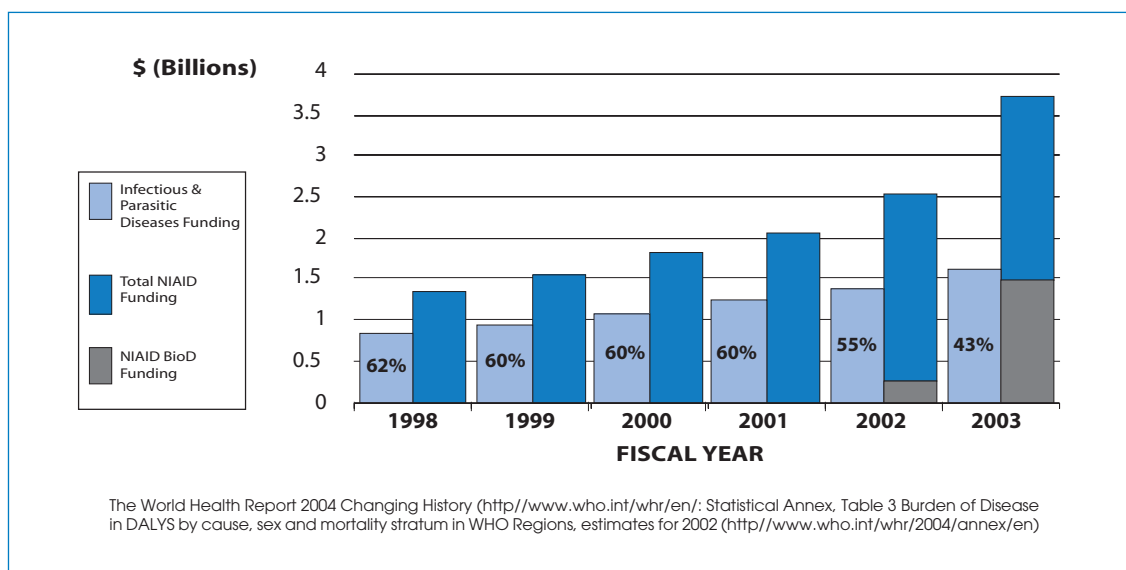
population and health, emerging and re-emerging infectious diseases, malaria, tuberculosis, medical informatics, bioethics, stigma, brain disorders, trauma and injury, and tobacco. Capacity building for biomedical researchers in developing countries is also an important objective for FIC, especially for basic and clinical research. A number of research centers in American universities participate as training centers for LMIC researchers. FIC also operates a research grant program for north/south partnerships and serves as the coordinating point for international activities such as the Disease Control Priority Project.

In fiscal year 2003, the Fogarty centre had international activities totaling US\$63.4 million, more than double the 1998 level of

US\$28.3 million. Training grants constituted a large portion of the international budget – US\$51.2 million in 2003, up from a level of US\$21.2 million in 1998.

NIH also funds research on infections and parasitic diseases through its National Institute of Allergy and Infectious Diseases (NIAID). Actual dollar expenditures on research for these diseases have since 1998, more than tripled but the NIAID share of total NIH spending has declined steadily since 1988. Further, the NIAID share of expenditures on infections and parasitic diseases dropped significantly after 2001 while biodefense funding is approaching half the NIAID budget (see Chart 2.18).

Chart 2.18 NIAID funding in infectious & parasitic diseases (1998-2003)



Medical Research Council, United Kingdom

An annual grant from Parliament provides about 83 per cent of total MRC funding, growing from UK£276.0 million in 1998/99 to UK£423.0 million in 2001/02, an increase of 36 per cent. A level of UK£421.0 million is forecast for 2003-04.³³

In 2001, MRC spent about UK£403.2 million on research. About half of funds is spent intramurally (mostly for basic research), 40 per cent goes to universities and two per cent abroad as contributions to several international biomedical organizations.³⁴ The council is engaged in numerous international research collaborations with other European countries, Canada and the United States. MRC funding for research in developing countries is focused on combating infectious diseases. MRC Laboratories in the Gambia are playing an important role in the understanding of hepatitis, malaria, acute respiratory infections and schistosomiasis, and in the development of effective interventions.

Canadian Institutes for Health Research, Canada

In 2001-02, the first full year of operation for the consolidated CIHR, expenditures totalled CD\$523.0 million of which grants and awards totalled CD\$494.0 million. Since this reorganization of publicly funded research, strategic research increased from 16.2 per cent of expenditures in 2000-01 to 29.5 per cent in 2003-4. CIHR engages in international research through numerous collaborations as well as its own research. For example, agreements with research agencies in Australia and New Zealand focused on indigenous people's health collaborations. In 2001, CIHR initiatives in HIV/AIDS research totaled CD\$12.8 million.³⁵ CIHR has established a new initiative for global health. For 2004-05, Global Health Research Program Development and Planning grants totaling CD\$2.3 million

have been awarded to Canadian institutions with partners in LMIC.³⁶

Howard Hughes Medical Research Institute, United States

In 2004, HHMI spent US\$419.0 million on research by its own investigators and US\$75.0 million on grants for undergraduate, graduate and international education, research and training. Annual grants for international research and education average about US\$10.0 million. Out of 132 scholars receiving grants, 95 are in low- and middle-income countries, representing an estimated 70 per cent of the total international budget.

Netherlands Organization for Health Research and Development, Netherlands

Total expenditures for 2001 were EURO83.0 million, including EURO75.0 million for health research. As ZonMW is not yet allowed to fund non-Dutch researchers outside the Netherlands, its spending for international research totalled only EURO216,000.

National Agency for AIDS Research, France
ANRS receives all of its funds from the government and funding levels have been stable since 1998. Its main role is as a funding agency. In 2002, it distributed its funds to INSERM, CNRS, Institute Pasteur, universities, hospitals and other institutions and public agencies. An increasing share of ANRS funding has gone to HIV/AIDS research in LMIC – up from 13 per cent in 2000 to 21 per cent in 2002.

2.3.4 Partnerships, initiatives and other not-for-profit NGOs

In the past decade, a plethora of initiatives, partnerships and other NGO agents involved in international health research has emerged. Some of these entities – like the International AIDS Vaccine Initiative (IAVI) and the Global Alliance for Vaccines and Immunization (GAVI) – have become large well-funded

organizations. Others such as MMV have evolved as public/private partnerships and taken on the legal framework of a foundation. Still others have taken on roles as catalytic and advocacy organizations and venues for communicating research results rather than funding large research portfolios themselves; these include the Global Forum for Health Research and the Council on Health Research for Development (COHRED). Others serve as networks for organizing and coordinating research but monies are not pooled; instead participating network members each are responsible for supporting their agreed-upon component as in the case of the International Network for the Rational Use of Drugs (INRUD).

- In 2001, total GAVI expenditures were US\$28 million. Beginning in 2002, US\$0.5-\$0.8 million is being spent annually on data quality audits. In 2002 a major study on access to immunization was commissioned; in early 2004 a study on immunization services support was undertaken. An R&D task force laid the foundation for two Accelerated Development and Introduction Plans (ADIPs) – one on pneumococcal vaccines and one on rotavirus vaccines. Each has a long-term budget of US\$30.0 million

with the first disbursements being made in 2003 of US\$2.4 million and US\$4.0 million respectively. Beginning in 2004, vaccine impact studies will be conducted relating to the new vaccine introductions financed by GAVI and the Vaccine Fund.

- Over the past decade, COHRED has made a significant contribution to health and health research in low- and middle-income countries by advocating for essential national health research programmes in these countries and by strengthening the capacity of countries to better prioritize and manage health research resources. In 2001, half of the budget of US\$1.4 million was devoted to activities focused on strengthening capabilities for health research system development in low- and middle-income countries.
- The annual budget of the International Union against Tuberculosis and Lung Disease (IUATLD) is approximately US\$15.0 million. Funding is obtained from national association members representing more than 130 countries, individual members, grants and donations. About eight per cent of the annual budget can be attributed to research and research capacity strengthening.

-
- ¹ *Monitoring Financial Flows for Health Research*, 2001, Global Forum for Health Research. Updated methodology used for the current 2004 report would put this figure at 2.8 per cent.
- ² The G7/G8 currently include: United States, Canada, United Kingdom, France, Germany, Italy, Japan, Russia, the United Kingdom, the United States—and the European Union. Russia was added to make the G8, but because it is not a HIC, the text refers only to the G7 countries.
- ³ Data for Latin American countries are available through The Network on Science and Technology Indicators—Ibero-American and Inter-American (RICYT). [<http://www.ricyt.org/interior/interior.asp?Nivel1=5&Nivel2=1&Idioma=ENG>]
- ⁴ (Helmut Anheier, 2003)
- ⁵ *Foundation Giving Trends*, 2003 Edition, The Foundation Center, New York.
- ⁶ AMRC, 2000.
- ⁷ Japan Foundation Center web site.
- ⁸ For a comprehensive and detailed examination, access the contributing research paper “High-income Country Investors: Financial Flows for International Health Research,” by Caryn Miller at www.globalforumhealth.org
- ⁹ Caryn Miller, personal communication, Danida.
- ¹⁰ Report of the Commission on Development-related Research Funded by Danida.
- ¹¹ Development Co-operation Report 2002.
- ¹² Caryn Miller, personal communication, Danida.
- ¹³ OECD DAC Reports.
- ¹⁴ Personal communication, SAREC.
- ¹⁵ *Facts & Figures 2002 Health Sector*, Sida 2003.
- ¹⁶ *Forward Looks, 2000-2003*.
- ¹⁷ *DAC Journal 2002*, Volume 3, No. 4, OECD.
- ¹⁸ USAID, personal communication.
- ¹⁹ USAID, personal communication.
- ²⁰ *DAC Journal, 2002*, Volume 3, No.4, OECD.
- ²¹ *DAC Journal, 2002*, Volume 3, No. 4
- ²² IDRC personal communication.
- ²³ (*Development Co-operation Reports*, OECD).
- ²⁴ (*IRD Annual Report*).
- ²⁵ personal communication, NORAD
- ²⁶ In the past, the Development Directorate supported policy and operational research closely related to programmes implemented in LMIC countries. It is unclear to what extent this will continue under the Sixth Framework Programme (FP6)—the main EU instrument for funding research in Europe—under which the Research Directorate will implement programmes for specific research activities in support of the Community’s foreign policy and development aid policy.
- ²⁷ Personal communication.
- ²⁸ HRP External Evaluation, 2003.
- ²⁹ HRP External Evaluation, 2003.
- ³⁰ (*Monitoring Financial Flows for Health Research*, 2001 for 1998 data; World Bank financial reports, personal communication for 2001 data).
- ³¹ There may be spending by other development banks but data were not included for this report.
- ³² TDR financial documents and personal communication.
- ³³ *Forward Look*, 2003.
- ³⁴ MRC Annual Report 2001-2
- ³⁵ CIHR Annual Report, 2001-02.
- ³⁶ CIHR web site.

Chapter 3

The Global Burden of Disease

3.1 Introduction

Understanding the relative impacts of different diseases and other health injuries is important to setting priorities for research.¹ In an effort to look at this formula in global context, the concept of “global burden of disease” was developed in a benchmark assessment in 1993 by the Harvard School of Public Health in collaboration with World Bank and WHO. The study was also used to identify causes of disease burden where current knowledge was

inadequate to identify research priorities and support interventions.²

In the GBD framework, this chapter reports 2002 data for two epidemiological indicators:

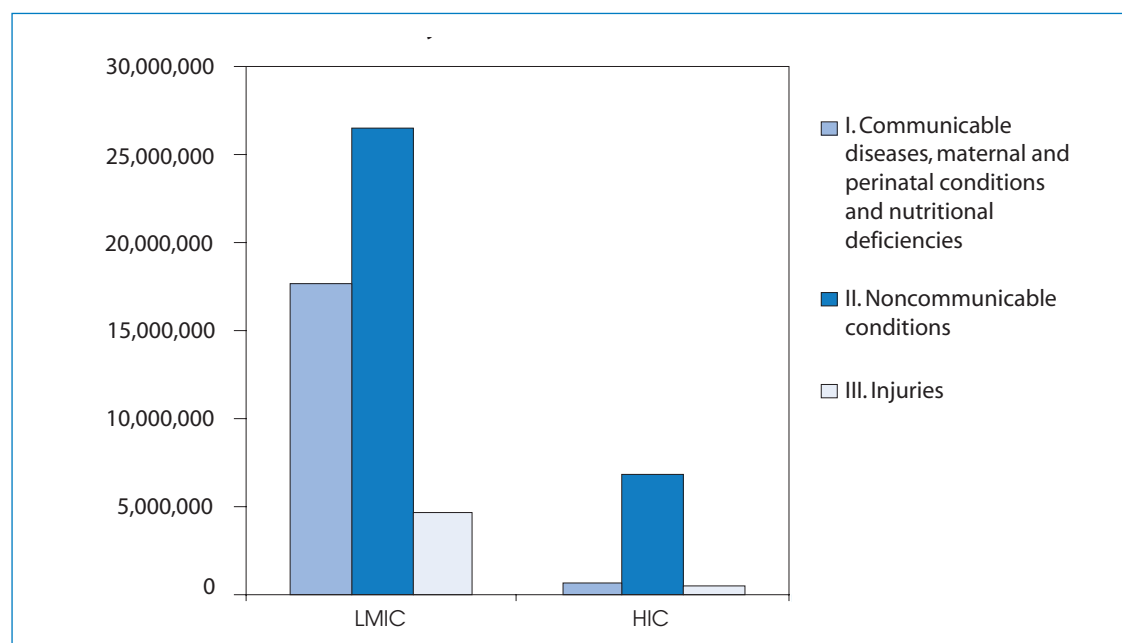
- mortality figures, which refers to the numbers of people who die and the cause of death;
- burden of disease, using the disability adjusted life year (DALY) metric.

3.2 Mortality figures

Almost 57 million persons died in 2002. One in five were children under the age of five. Of these 10.5 million child deaths, 98 per cent

occurred in low- and middle-income countries (see Chart 3.1).

Chart 3.1 Mortality conditions by level of income, 2002 estimates



Source: WHO Burden of Disease estimates, 2002

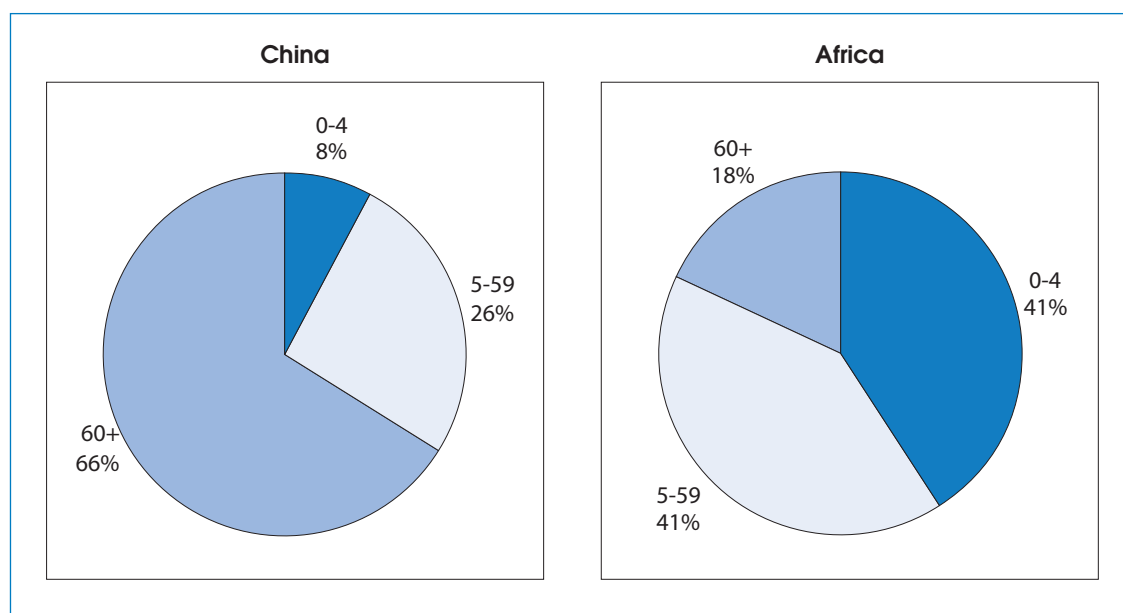
3.2.1 Age-specific mortality

Not unexpectedly, there is a profound mortality divide between high-income countries (HIC) and low- and middle-income countries (LMIC). More than 80 per cent of deaths in high-income countries occur beyond age 60, compared to about 45 per cent in low- and middle-income countries.

However, there is also a significant mortality gap between low-income and middle-income countries. The contrast between middle-

income countries such as China (with more than one sixth of the world's population) and low-income countries in Africa (with one tenth of the global population) illustrates the extreme range in health conditions among LMIC (see Chart 3.2). In China, fewer than one in 10 deaths is a child under five, compared to four in 10 deaths in Africa. At the same time two thirds of people who die in China are older than 60, compared to fewer than one in five in Africa.

Chart 3.2 Age distribution of mortality in China and Africa, 2002



Today nearly all child deaths (97 per cent) occur in low-income countries and almost half of them in 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 as a result of the HIV/AIDS epidemic.

Adult mortality rates have been declining in recent decades in most regions of the world. Life expectancy at age 15 has increased by two to three years for most regions over the last 20 years. The notable exceptions are high-mortality countries in Africa, where life expectancy at age 15 has decreased by nearly seven years between 1980 and 2001, and the transition countries of Eastern Europe, where

life expectancy at age 15 has decreased over the same period by 4.2 years for males and 1.6 years for females.

The probability of premature adult death varies widely among regions. For example, the probability of premature adult death in Africa is much higher – around three times – than that observed in China and some middle-income countries of the Western Pacific region. Even within regions with higher incomes, there are wide variations. Men in some Eastern European transition countries are three to four times more likely to die prematurely than men in high-income countries. Furthermore, male adult mortality in Eastern Europe is much greater than in low- and middle-income countries of the Americas, South-East Asia and the Eastern Mediterranean.

In all regions, male mortality is greater than female and that gender (social) and sex (biological) difference is much greater among adults than children. The study did not examine mortality differentials by other social characteristics such as ability and race. This is an area in need of further study.

3.2.2 Causes of death

The top 10 disease and injury causes of death in the year 2002 are shown in Table 3.1 for high-income countries and for low- and middle-income countries. The countries in each of these groups are listed in APPENDIX 3.

Ischaemic heart disease and cerebrovascular disease (stroke) cause almost one in four deaths worldwide. HIV/AIDS has increased from 0.3 million deaths globally in 1990 to 2.6 million in 2002, representing almost five per cent of global deaths in 2002. 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). Both intentional and

unintentional injuries figure within the top 10 causes of death.

Overall, the 10 leading causes account for 86 per cent of all child deaths. Communicable diseases still represent seven out of the top 10 causes of child deaths and cause about 60 per cent of all child deaths. However, in Latin America and some Asian and Middle Eastern countries, conditions arising in the perinatal period, including birth asphyxia, birth trauma and low birthweight have replaced infectious diseases as the leading causes of death and are now responsible for 21–36 per cent of child deaths. Such a shift in the cause-of-death pattern has not occurred in sub-Saharan Africa, where malaria, lower respiratory infections and diarrhoeal diseases continue to be the leading causes of death in children, accounting for 53 per cent of all deaths. HIV/AIDS is now responsible for a little over 300,000 child deaths in sub-Saharan Africa and nearly seven per cent of all child deaths in the region.

Despite global trends of a declining burden of communicable disease in adults, HIV/AIDS challenges that progress. AIDS-related deaths have become the leading cause of mortality among adults aged 15–59, responsible for more than two million deaths in 2002 or 13 per cent of global deaths in this age group. HIV/AIDS deaths are responsible for the same proportion of deaths as ischaemic heart disease and cerebrovascular disease combined, and 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 among men. Suicide and violence (homicide) are also among the top ten causes of death in adults aged 15–59 years. Together with war/armed conflict, intentional injuries account for nearly one in 10 deaths in this age range globally.

The leading causes of mortality are very different in high-income countries than in low- and middle-income countries (see Table 3.1). While cardiovascular diseases, diabetes, chronic lung disease and four cancers dominate the leading causes of death in high-income countries, accounting for almost half of all deaths, communicable diseases remain responsible for more than half of deaths in sub-Saharan Africa. HIV/AIDS, tuberculosis and malaria together account for more than one in three deaths in sub-Saharan Africa, and

lower respiratory infections, measles and diarrhoea for another one in five deaths. In most other low- and middle-income countries, ischaemic heart disease and cerebrovascular disease are among the leading three or four causes of death, together with infectious and perinatal causes, and in some regions suicide and violence. As discussed below, this order changes when burden of disease, which incorporates measures of both mortality and morbidity, is examined.

Table 3.1
Leading causes of death by income level, 2002

High-income countries		% total deaths	Low- and middle-income countries		% total deaths
1	Cardiovascular diseases	38.1	1	Cardiovascular diseases	27.9
2	Malignant neoplasms	26.2	2	Malignant neoplasms	10.3
3	Neuropsychiatric disorders	5.0	3	Respiratory infections	7.4
4	Respiratory infections	4.3	4	Unintentional injuries	6.6
5	Unintentional injuries	4.1	5	HIV/AIDS	5.6
6	Diabetes mellitus	2.6	6	Perinatal conditions	4.9
7	Intentional injuries	1.9	7	Diarrhoeal diseases	3.6
8	Perinatal conditions	0.4	8	Tuberculosis	3.2
9	HIV/AIDS	0.3	9	Intentional injuries	3.0
10	Nutritional deficiencies	0.2	10	Malaria	2.6

3.2.3 Trends in mortality over time

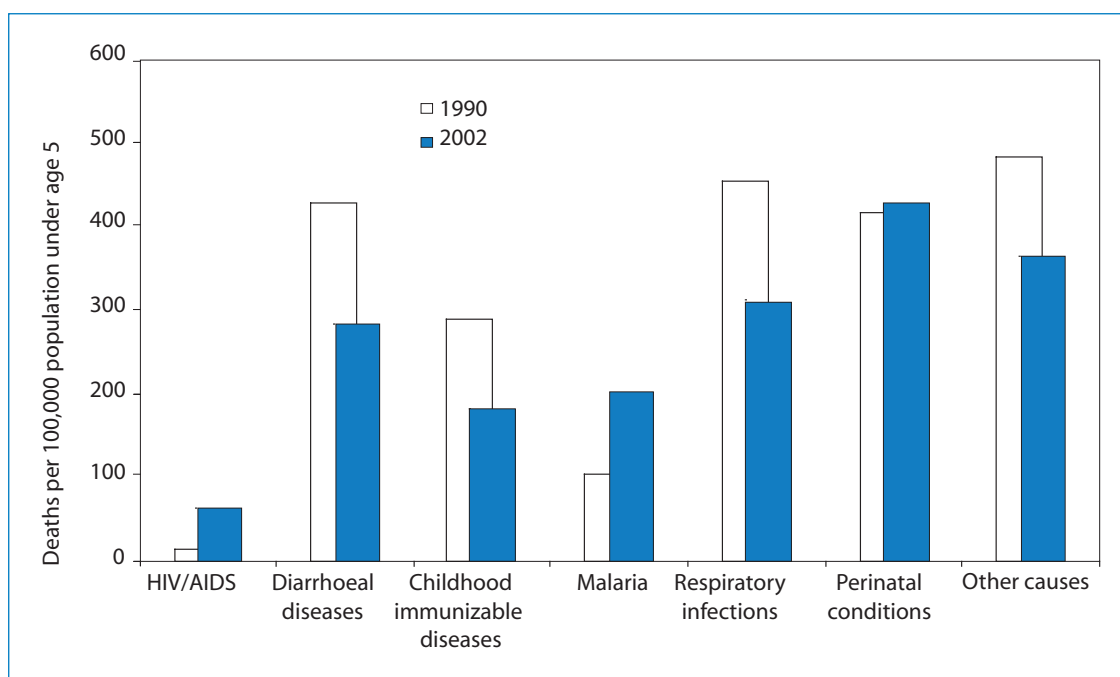
Chart 3.3 compares the distribution of the causes of child deaths under the age of five in 1990 and in 2002 for low- and middle-income countries. Allowing for some uncertainty due to changes in data availability and methods, this figure shows broad improvements in child mortality due to diarrhoeal diseases, childhood

immunizable diseases (particularly measles), and acute respiratory infections. While incidence is thought to have remained stable, global mortality from diarrhoeal diseases has fallen from 2.5 million deaths in 1990 to about 1.6 million deaths in 2002, accounting for 13 per cent of all child deaths under age 15. There has also been a modest decline in deaths

from measles, although globally more than half a million children under five still succumb to the disease every year. Malaria is causing

over one million child deaths every year and has risen to claim nearly 11 per cent of all under-five deaths.

Chart 3.3 Trends in causes of death for children aged under five, low- and middle-income countries, 1990 and 2002



Source: 1990 estimates for all regions except EME from [3], 2002 estimates from [5]

3.3 Burden of disease

3.3.1 Disability adjusted life years (DALY)

The DALY metric combines years of life lost from premature death and years of life lived with disabilities into a single indicator designed to allow the assessment of the total loss of health from different causes (see definition in APPENDIX 1). The 1993 “Global Burden of Disease” study introduced the DALY concept and generated comprehensive and consistent sets of estimates of mortality and morbidity by age, sex and region.

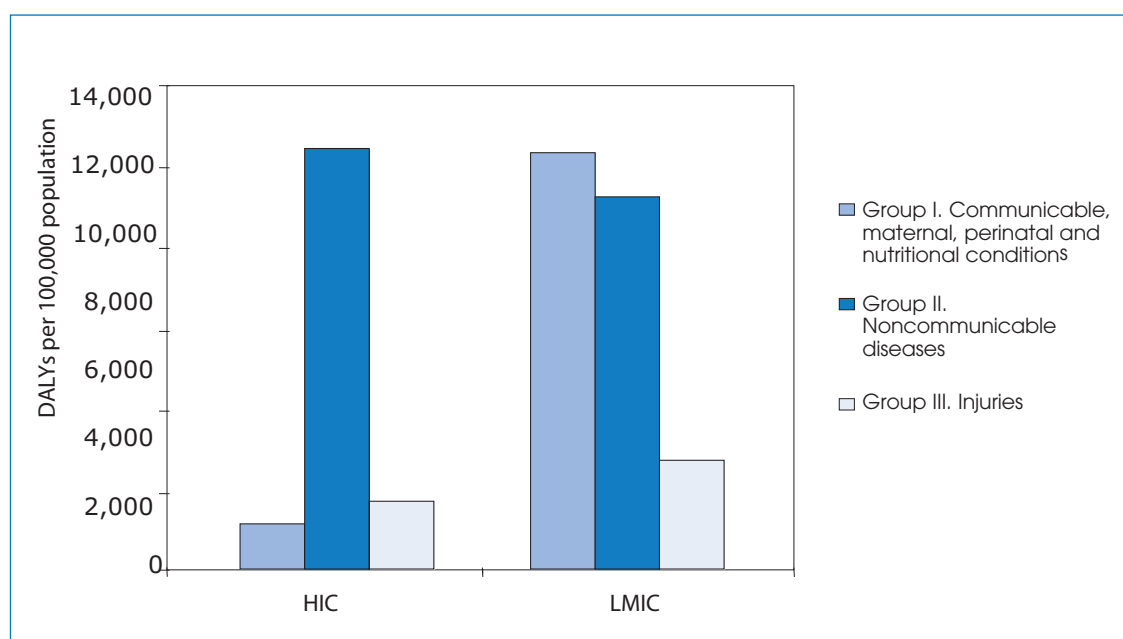
WHO undertook an assessment of GBD for 2002 that is intended to provide an overview of the main causes of burden of disease in low- and middle-income countries as well as major trends since 1990. The data sources and methods used are documented elsewhere⁴ and summary results for 14 regions of the world are published in the World Health Report⁵ and on WHO web site (www.who.int/evidence/bod).

3.3.2 Comparisons of disease burden patterns

Lost years of full health per capita (as measured by the DALY) are higher in low- and middle-income countries than in high-income countries (see Chart 3.4). The rate of burden

of disease is more than four times higher in Africa than in high-income countries, and just over twice as high in India. People in Africa and India make up one third of the world's population and together bore almost half of the total global burden of disease in 2002.

Chart 3.4 Burden of disease by major cause groups and country groups, 2002



High-income countries have a relatively lower disease burden than do low- and middle-income countries (see Chart 3.4). In the former, well-endowed socio-economic environments create better conditions for health and contribute to a predominantly noncommunicable disease epidemiology. LMIC, in turn, have a high rate of disease burden from Group I diseases (communicable, maternal, perinatal and nutritional conditions), as much as nine times higher than do HIC. Contrary to common belief, noncommunicable diseases (Group II) play a key role in disease burden in low- and middle-income countries:

rates of Group II disease burden are as high in these countries as in high-income countries. As such, LMIC countries have high incidence of both Group I and Group II conditions.

Chart 3.5 compares the group causes of disease burden in HIC, in China and in Africa. A high loss of health due to Group I causes (communicable, maternal, perinatal conditions and nutritional deficiencies) characterizes societies that have not gone through the epidemiological transition, while a high loss due to Group II causes (noncommunicable diseases) reflects societies that have. (The

transition refers to the shift from patterns of predominantly Group I conditions to predominantly Group II diseases as a result of social and economic changes in society.) Chart 3.5 shows the balance between Groups I, II and III (injuries) in the world in the year 2002.

The picture for China shows that Group II conditions continue to be responsible for 66 per cent of the burden of disease. The situation in Africa is different: more than 70 per cent of disease burden is due to Group I diseases, of which up to one quarter is due to HIV/AIDS.

Chart 3.5 Comparison of groups of burden of disease in the world, China and Africa

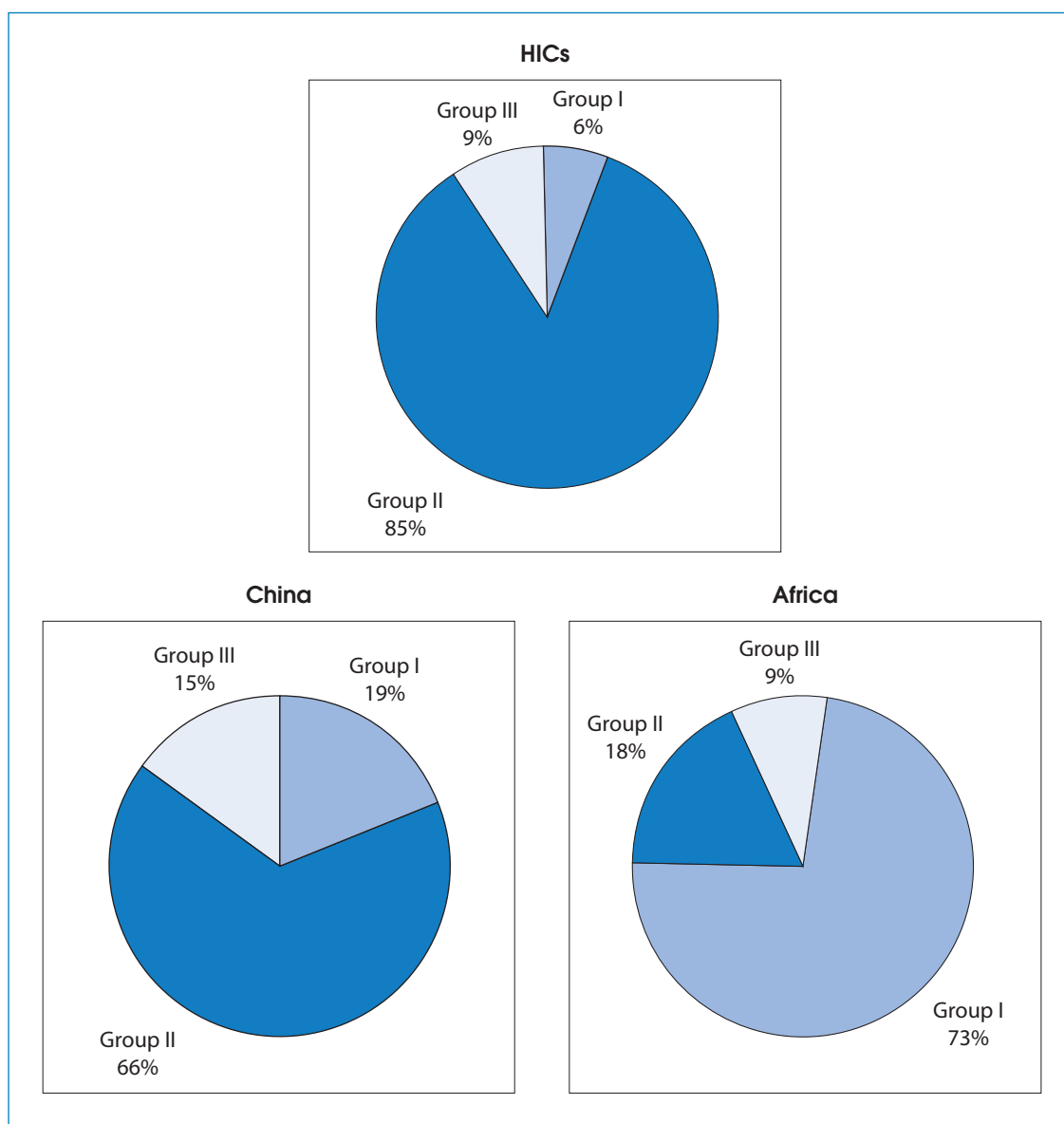


Table 3.2**Leading causes of burden of disease by income level, 2002**

High-income countries		% total DALYs	Low- and medium-income countries		% total DALYs
1	Neuropsychiatric disorders	27.3	1	Neuropsychiatric disorders	11.7
2	Cardiovascular diseases	15.4	2	Cardiovascular diseases	9.5
3	Malignant neoplasms	14.7	3	Unintentional injuries	9.1
4	Unintentional injuries	6.4	4	Perinatal conditions	7.0
5	Intentional injuries	2.7	5	Respiratory infections	6.8
6	Diabetes mellitus	2.6	6	HIV/AIDS	6.1
7	Perinatal conditions	1.2	7	Diarrhoeal diseases	4.5
8	Respiratory infections	1.2	8	Malignant neoplasms	4.2
9	Nutritional deficiencies	0.8	9	Malaria	3.4
10	HIV/AIDS	0.6	10	Intentional injuries	3.3

Neuropsychiatric disorders and cardiovascular disease are the leading causes of burden of disease in both high-income countries and low- and middle-income countries (see Table 3.2). These two conditions account for 43 per cent and 21 per cent of the disease burden in HIC and LMIC respectively. Whereas infectious diseases are not major causes of burden of disease in high-income countries, they still are in low- and middle-income countries, where HIV/AIDS, malaria, diarrhoeal diseases and acute respiratory infections are among the 10 leading causes of burden of disease and account for one fifth of the total burden of disease.

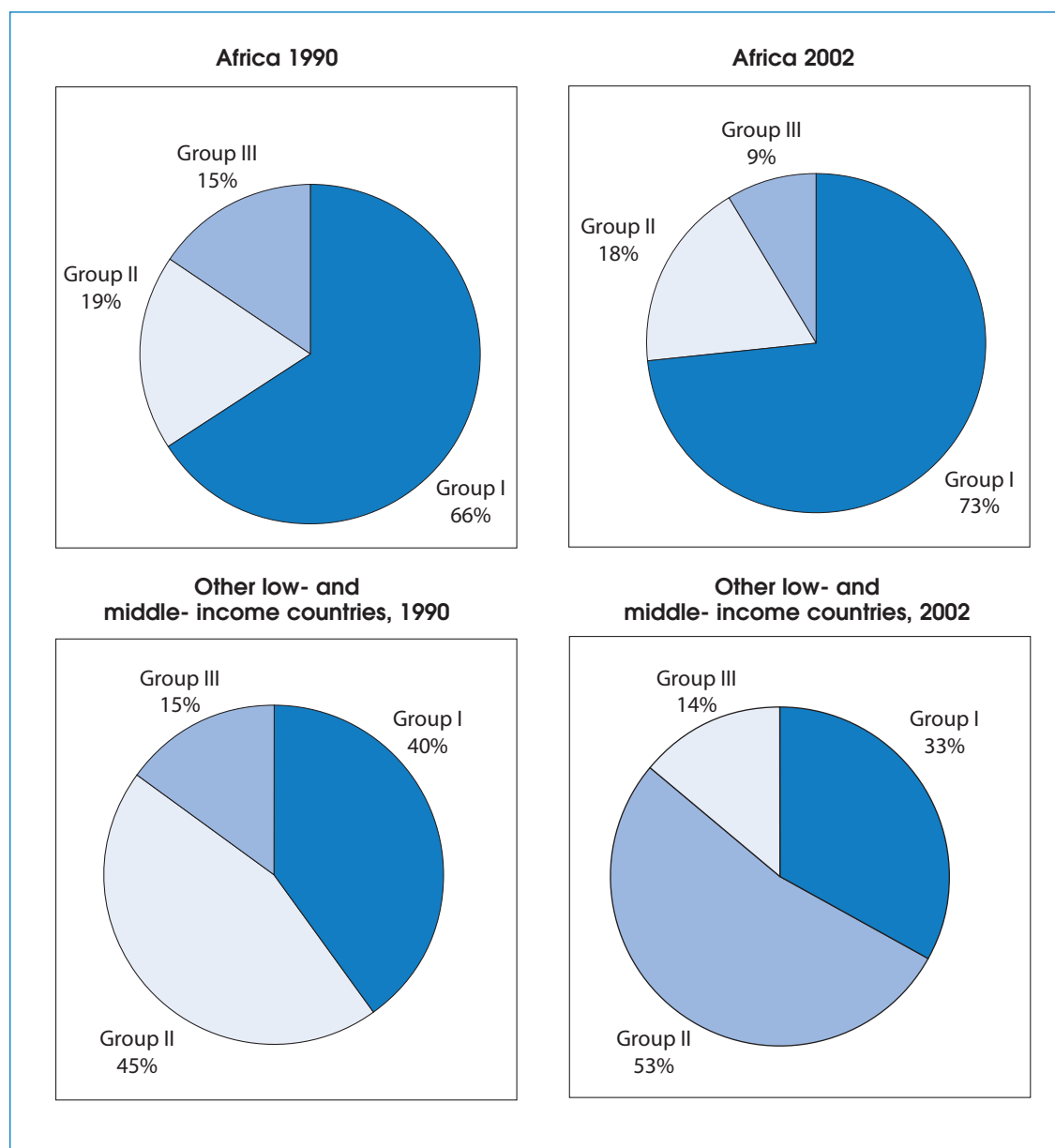
3.3.3 Trends in burden of disease over time

There have been marked changes in epidemiology of disease burden in the past years in low- and middle-income countries. African countries have tended to increase their share of disease burden from Group I diseases.

Conversely, other low- and middle-income countries have increased their relative share from Group II diseases (see Chart 3.6).

HIV/AIDS rose from 0.8 per cent of total disease burden in 1990 to nearly 6 per cent of the burden of disease in 2002, taking its greatest toll in Africa. The overall burden of communicable diseases has fallen somewhat since 1990, reflecting improvements against measles, diarrhoeal diseases and some other infectious diseases. The overall burden of noncommunicable diseases has increased globally. Falls in the burden of cardiovascular diseases in high-income countries – reflecting improvements in risk factor control and in treatment – have been offset by increases in the cardiovascular disease burden in middle-income countries, reflecting population ageing and a shift from communicable to noncommunicable diseases in countries undergoing the epidemiological transition.

Chart 3.6 Trends in cause distribution of burden of disease (DALYs) in Africa and in other low- and middle- income countries, 1990 to 2002



The burden of noncommunicable diseases (Group II) is increasing, accounting for just over half of the global burden of disease in 2002. These diseases account for more than 85 per cent of the burden in high-income

countries and have also exceeded 60 per cent in all other parts of the world except India and Africa. Population ageing and changes in the distribution of risk factors have accelerated the epidemic of noncommunicable disease in

many developing countries. These changes are discussed more in the section on risk factors below.

Globally, neuropsychiatric conditions account for 10 per cent of the disease burden among adults, almost all of this resulting from non-fatal health outcomes. Unipolar depressive disorders are among the leading causes of burden of disease in all regions except sub-Saharan Africa. The proportion of burden of disease attributable to cancer was 17 per cent in high-income countries and five per cent in other regions in 2002. There were an estimated 1.2 million lung cancer deaths in 2002, an increase of nearly 30 per cent in just 11 years, reflecting the emergence of the tobacco epidemic in low- and middle-income countries.

In low- and middle-income countries of Europe and the Americas, around 40 per cent of the entire disease burden among male adults aged 15-44 is attributable to injuries. Globally, road traffic accidents are the second leading cause of burden in that age-sex group, preceded only by HIV/AIDS, and followed by mental depression. In high-income countries, suicides account for the largest share of intentional injury burden, whereas in low- and middle-income countries violence and war are the major sources. The former Soviet Union and other middle-income countries of Europe have rates of injury burden among males approaching those in Africa.

3.3.4 Risk factors

WHO recently undertook 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 (DALY) for health outcomes.⁶ This analysis limited itself to “proximal risk factors” such as smoking and obesity, thereby excluding “distal risk factors” such as poverty and inequity. The

regional distribution of burden of disease attributable to 20 risk factors is summarized here both for high income and for low and middle income countries (see Chart 3.7).

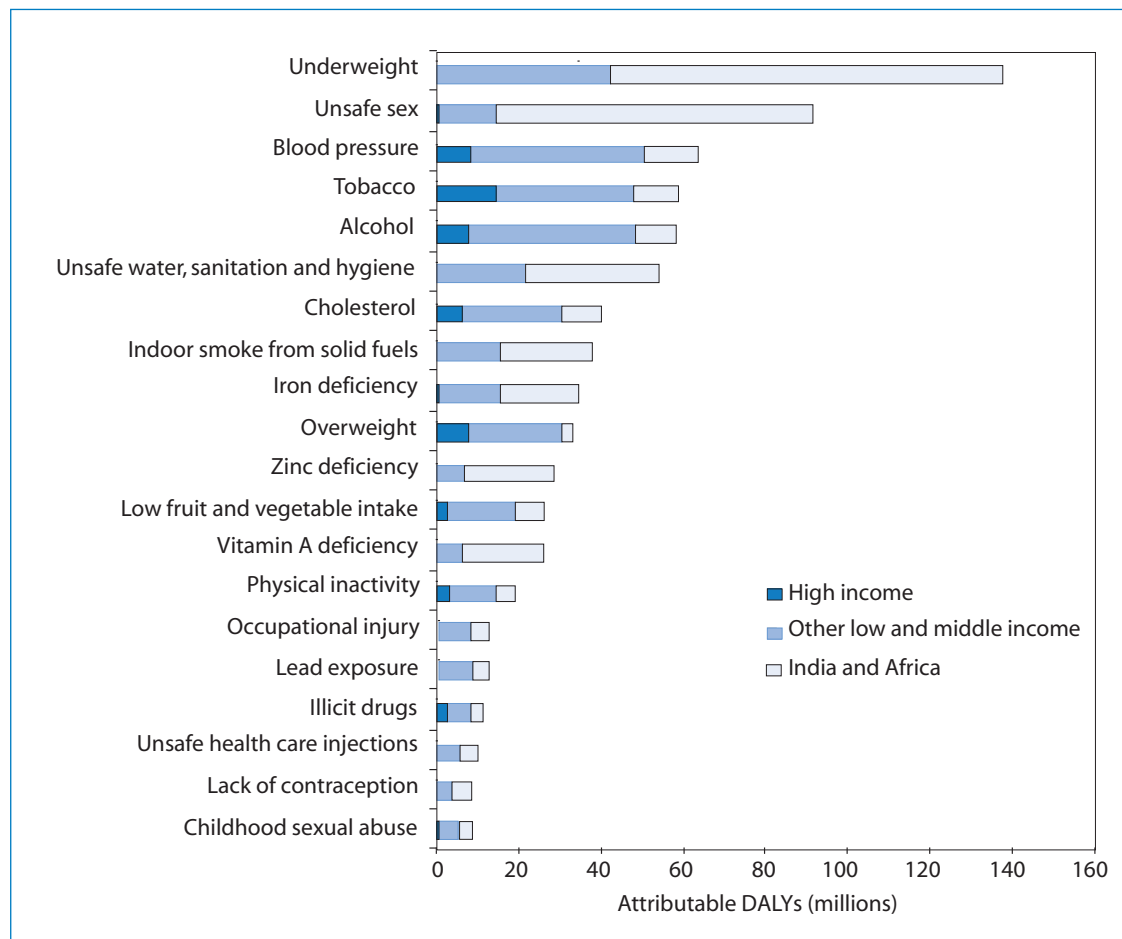
One fifth of the global disease burden can be attributed to the effects of under-nutrition. The five leading global risks causing burden of disease are underweight due to malnutrition unsafe sex, raised blood pressure, tobacco smoking and alcohol. Risks are extraordinarily concentrated in low-income countries, meaning relatively few risks are responsible for a considerable proportion of the burden of disease. For example, almost 15 per cent of the total burden of disease in India and Africa is attributed to underweight and under-nutrition.

The burden from these risks alone exceeds that of the entire burden of disease and injury in high-income countries. Unsafe sex is the second leading risk in low- and middle-income countries, and in Africa accounts for almost one fifth of the disease burden.

For high-income countries, tobacco is the leading risk factor, accounting for 12 per cent of the disease burden. Alcohol and blood pressure combined are responsible for seven to eight years of healthy life lost, with cholesterol and overweight combined accounting for five to six years lost. Low- and middle-income countries now face a double burden of disease from risk factors and diseases of poverty and wide-scale socio-economic inequities, as well as the chronic diseases associated with smoking, overweight, diet and physical inactivity.

Underweight, under-nutrition and unsafe water affect children almost exclusively. The burden from addictive substances, unsafe sex, lack of contraception, risk factors for injury, unsafe injections and child sex abuse occurs almost exclusively among teens and young

Chart 3.7 Burden of disease by major cause groups and country groups, 2000



adults. Nutrition-related, environmental risks and unsafe sex are about equally distributed between the sexes, but four fifths of the burden from addictive substances and 60-90 per cent from occupational risks occurs among men. Women experience more negative health impacts from child sex abuse and lack of contraception.

Almost half (47 per cent) 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 per cent) of global deaths can be attributed

to the leading 10 risk factors and almost one third to the leading five risk factors. These latter 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.

3.4 Discussion and conclusions

Burden of disease analysis provides a comprehensive, comparative overview of the state of population health, and the factors affecting the health of populations. This analysis – despite its limitations inherent biases, e.g., a negative view of disability – helps identify and assess areas of health that demand attention. The 2002 WHO study of global burden of disease, summarized here, is a much expanded effort compared to the original 1990 GBD study; it incorporates much new data and a greater understanding of the limitations of routinely available data sets.

Yet, of great policy consequence, there remains substantial uncertainty about the comparative burden of diseases and injuries in many parts of the world, especially among disadvantaged sub-populations such as disabled persons. Much more research is needed in this area in particular, given the over-representation of disabled people among the world's marginalized poor and the inherent limitation in measuring their health using indicators such as DALYs. By definition, DALYs a) assume a “reduced value” of lives lived with a disability; b) use the term disability interchangeably with ill health; c) assume that living with a disability represents a net drain on society; and d) assume that individuals with a disability suffer an existence that lies somewhere between living and an anticipated premature death.

The burden of disease information presented can be summarized as follows:

- Mortality estimates are higher in low- and middle-income countries than in high-income countries and people in the former die much younger.
- Still, mortality varies greatly among low- and middle-income countries: in China most deaths occur past age 60, but in Africa populations die prematurely and a very large share of them are young children.

- Contrary to popular images, noncommunicable diseases are highly prevalent in LMIC with disease burden rates comparable to those in HIC (e.g., two thirds of the disease burden in China). Conversely, Africa has a pattern of disease burden dominated by infectious diseases.
- Trends over time in Africa reflect increases in infectious diseases – largely attributable to HIV/AIDS and malaria – while other low- and middle-income countries show increases in noncommunicable diseases.
- A large proportion of risk factors are preventable.

In contrast to mortality estimates, burden of disease estimates highlight the importance of non-communicable diseases in LMIC other than African countries. Disease burden captures not only premature death but also morbidity. As such, the weight of conditions before death can be quantified, such as was described in Chart 3.7. While some of this disease burden can be averted through known interventions, the application and scaling-up of implementation in low- and middle-income countries is not straightforward. Research can help identify tools and programmatic pathways to implement knowledge into action.

Despite a continuing improvement in average health status in many low- and middle-income countries, there are widening health inequities within and among countries and even health reversals in some regions. 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, hard-won declines in mortality have reversed. Overall, one third 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 in the world is characterized by three major trends:

- slowing down of gains and widening health gaps;
- increasing complexity of the burden of disease; and
- the globalization of adult health risks.

¹ World Health Organization: *Investing in health research and development. Report of the Ad Hoc Committee on Health Research Relating to Future Intervention Options*. Geneva: WHO; 1996.

² World Bank: *World Development Report 1993. Investing in health*. New York: Oxford University Press for the World Bank; 1993. Murray CJL, Lopez AD. The Global Burden of Disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. 1, 211. 1996. Cambridge, Harvard University Press. Global Burden of Disease and Injury Series.

³ World Health Organization: *Investing in health research and development. Report of the Ad Hoc Committee on Health Research Relating to Future Intervention Options*. Geneva: WHO; 1996

⁴ Mathers CD, Bernard C, Iburg KM, Inoue M, Ma Fat D, Shibuya K *et al.*. Global Burden of Disease in 2002: data sources, methods and results. GPE Discussion Paper No. 54. 2003. Geneva, World Health Organization.

⁵ World Health Organization: *World Health Report 2004: Changing History*. Geneva: WHO; 2004.

⁶ World Health Organization: *World Health Report 2002. Reducing Risks, Promoting Healthy Life*. Geneva: WHO; 2002. Ezzati M, Lopez A, Vander Hoorn S, Murray CJL. Global and Regional Burden of Disease Attributable to Selected Major Risk Factors. *Lancet*. 2002.

Chapter 4

Focusing Research to Improve Global Health

4.1 A changing world

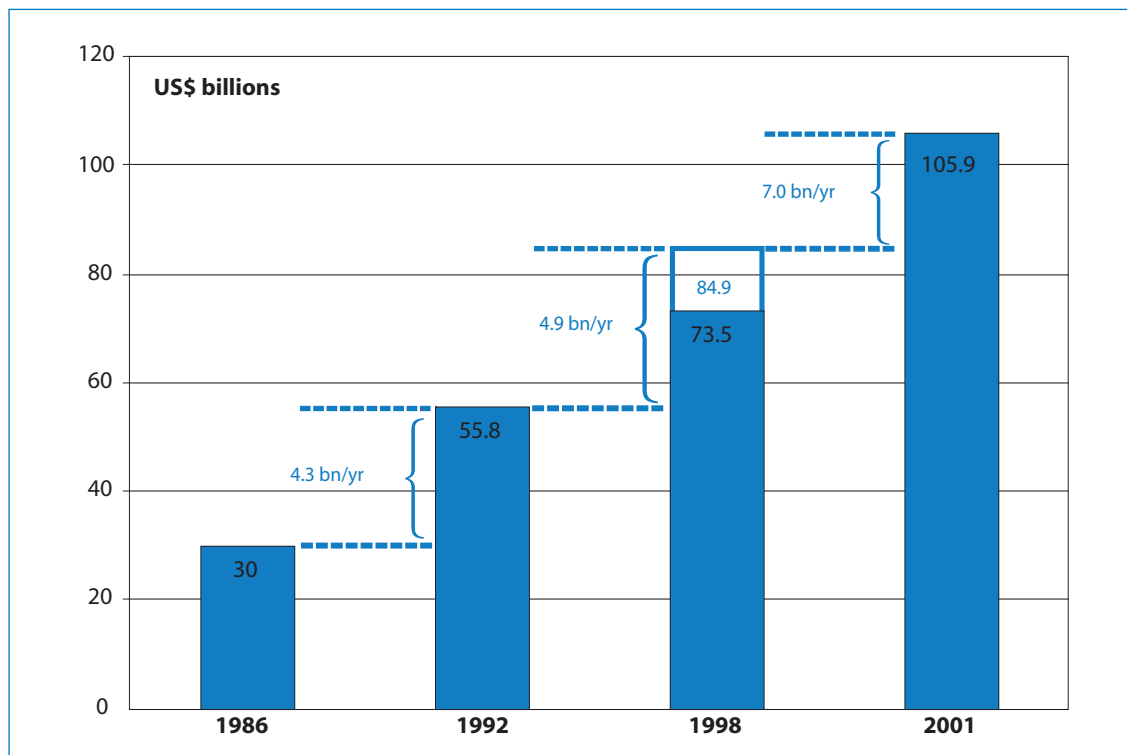
The picture regarding what the world spends on health research, where the resources originate, how they are used, and what problems and priorities they address, is a rapidly changing one. This chapter assesses what we have learned and what it may mean for the future.

4.1.1 Sources of funding

The three previous estimates of health R&D spending – US\$30.0 billion in 1986, US\$55.8 billion in 1992, and US\$73.5 billion in 1998 – suggested an average annual rate of increase of around US\$4.0 billion per year over that 12-year period. The results presented in

Chapter 2 show that the new estimate of global spending on health R&D for 2001 was US\$105.9 billion. An adjustment was also applied to the previous estimate for 1998, based on newly ‘found’ money as the methodologies were improved, lifting the total for that year from US\$73.5 billion to US\$84.9 billion. This adjustment means that the average annual rates of increase during the period grew modestly from about US\$4.3 billion per year for the six-year period 1986-1992 to US\$4.9 billion for the six-year period 1992-1998 and subsequently increased markedly to US\$7.0 billion per year in the three-year period 1998-2001 (see Chart 4.1).

Chart 4.1 Global health research expenditures, 1986-2001



What are the origins of the significant annual increases in global health R&D expenditures that took place over the 1998-2001 period, only a fraction¹ of which can be accounted for by inflation?

Total health R&D expenditures fluctuated as a proportion of total estimated national health expenditures world-wide, standing at 3.4 per cent in 1992, 2.8 per cent in 1998 (based on the corrected estimate of US\$84.9 billion research expenditure) and 3.5 per cent in 2001. The dip may well reflect the global economic downturn during the 1990s and subsequent recovery, illustrating the sensitivity of health research investments to the economic climate as alluded to in earlier chapters.

While total spending on global health R&D was rising by an average of US\$7.0 billion per year during the 1998-2001 period, the proportions derived from public, private and private for-profit sectors changed very little (see Chart 4.2). Thus, the contribution of the private for-profit sector to the global total of health R&D spending was 47.8 per cent in 1998 (based on adjusted data), and 48.3 per cent in 2001; the private not-for-profit sector contributed 6.9 per cent in 1998 (based on adjusted data), and 7.6 per cent in 2001; while public sector financing fell slightly from 45.3 per cent in 1998 (based on adjusted data), to 44.0 per cent in 2001.

Chart 4.2 Global health research expenditures by sector, 1998 and 2001

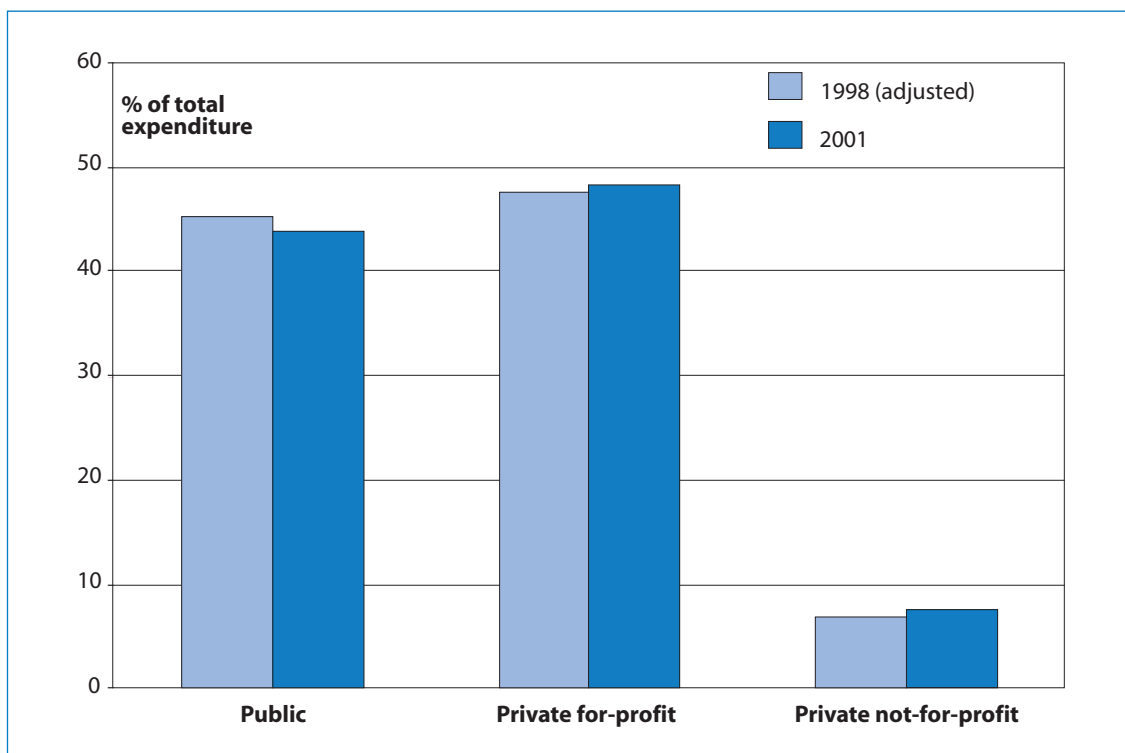


Table 4.1
FDA new molecular entity (NME) approvals

Year	1998	1999	2000	2001	2002	2003
Total NME	30	38	39	24	17	21
Total NME	0	0	1	3	0	0

Source: Data from annual reports of U.S. Food and Drug Administration (FDA)

The surprisingly constant proportion of sector contributions during a period of accelerated increase in global spending on health research has its origins in a combination of factors separately influencing each sector. Some important elements include:

- During a period of consolidation in the pharmaceutical industry and a falling rate of registrations of new drug entities in the United States (see Table 4.1), the rising level of private for-profit investments may reflect the overall rising costs of bringing each new drug to market. Analysis by the Tufts Center for the Study of Drug Development estimates the fully capitalized cost of a new drug to be at least US\$800 million (2000 dollars). This figure includes total average pre-clinical and clinical costs up to the time of receiving Food and Drug Administration (FDA) marketing approval. The figure rises to US\$897 million if studies conducted after receiving regulatory approval are added. How much these findings can be generalized has been questioned, as they were calculated using data for a few selected drugs. Nevertheless, when compared with the Tufts Center estimate in 1991 – an average development cost of US\$231 million (1987 dollars), equivalent to US\$318 million in 2000 dollars – there is no doubt that a major escalation has occurred. During the 1990s, clinical development time was a major source of the increase in drug development costs. Other factors included a greater emphasis on developing treatments for

conditions associated with chronic and degenerative diseases, increasing clinical trial sizes, rising subject recruitment costs, and more procedures performed per subject.^{2,3}

- In the public sector, the growth in health research funds in the United States has been the dominant factor in the rising total global expenditures on health including, in particular, the more than doubling in appropriations from Congress to the National Institutes of Health (NIH) from US\$11.9 billion in 1996 to US\$27.1 billion in 2003. Government expenditures on health R&D in other countries were mixed. In some, including many low- and middle-income countries, public investments in health R&D also increased, but to a lesser extent, or remained constant. Other countries that typically have invested in health R&D decreased their investments, notably New Zealand – where total public expenditures on health R&D was nearly halved – Denmark, Finland, Germany, Greece, Sweden and the United Kingdom.
- Important new sources and modalities of financing for health research applied to the needs of low- and middle-income countries have appeared. These include:
 - The Bill and Melinda Gates Foundation, created in 2000, expended US\$131.0 million on health research in 2001, including US\$101.0 million focused on international research relating to diseases of largest global burden.

- The number of public-private partnerships addressing product development, access to drugs for neglected diseases, and other health issues predominantly affecting low- and middle-income countries has mushroomed from a handful in the early 1990s to around a hundred. Some 20 of these partnerships alone attract funding of more than US\$200 million every year. Their efforts focus on development of drugs, vaccines, diagnostics and microbicides for HIV/AIDS.
- Since 1998, there have been significant increases in the proportions of national health budgets devoted to health research (see Chapter 2). Mexico, Cuba, India and Brazil, for example, have reached the two-per-cent mark suggested as a target by the 1990 Commission on Health Research for Development. The Eastern Mediterranean Regional Office of the World Health Organization (WHO) recently assigned 2 per cent of its budget to health research.
- New taxes on alcohol and tobacco consumption have been introduced in certain countries (e.g., Brazil, Colombia) to finance health research.

4.1.2 Burden of Disease

The 2002 Global Burden of Disease (GBD) Study conducted by WHO, summarized in Chapter 3, incorporates much new data and a greater understanding of the limitations of routinely available data sets, compared to the original 1990 GBD study. While the two data sets are, therefore, not strictly comparable, there are major trends evident over this period. These provide important evidence of the successes and failures of past efforts to improve global health and indicate where greater efforts are needed. Crucially – when combined with knowledge about the efficacy of existing interventions, the strengths and weaknesses of health systems, and the needs for new knowledge and technologies to fill the gaps –

data and trends on burden of disease can be used to develop vital guidance on priorities for future health research.

Key conclusions from the GBD studies and trends are that, overall, the state of adult health is characterized by three major trends: slowing down of gains and widening of health gaps; increasing complexity of the burden of disease; and the globalization of adult health risks.

While a significant degree of globalization is taking place in the nature of health problems, substantial differences remain both between high-income countries and low- and middle-income countries, and among low- and middle-income countries themselves, both within and between regions. In 2002, the world population of 6.22 billion people experienced 1.47 billion DALYs² (years of healthy living lost to illness and premature death); 78 per cent of the global population lives in low- and middle-income countries and experience 86 per cent of the global burden of disease. While high-income countries generally have a relatively low burden of disease, with noncommunicable diseases greatly predominating, many low- and middle-income countries endure a ‘triple burden’ comprised of noncommunicable diseases, infectious diseases, and injuries – a multi-front battle now greatly compounded by the wildfire impact of HIV/AIDS.

Malnutrition is one of the largest single causes of the high burden of disease in low- and middle-income countries. It plays an important underlying role in increasing both mortality and risk for many conditions, including infectious diseases, low birthweights and maternal mortality. Overall rates for communicable diseases, maternal and perinatal conditions are nine times higher in LMIC than HIC, while rates for injuries are nearly twice as high; rates for noncommunicable diseases are roughly the same (see Table 4.2).

Table 4.2

Rates of disease burden by disease group and country income in 2002, measured by DALYs per 100,000 population^a

Group	Developing countries ^b	Developed countries ^b	Relative burden ^c
Communicable diseases, maternal, perinatal and nutritional conditions	12,190	1,322	9.2 : 1
Noncommunicable diseases	10,897	12,318	0.9 : 1
Injuries	3,187	1,983	1.6 : 1

a Adapted from World Health Report, 2004⁴

b 'Developing countries' and 'developed countries' as defined in World Health Report, 2004

c Approximate rate ratio in developing countries as compared to developed countries

Without improvements in the social and economic environments in these countries, the situation will not be improved, given the reverberating links among poverty, inequities and malnutrition.

As detailed in Chapter 3, qualitative and quantitative elements of this mixed picture include:

- Low and middle-income countries tend to have much higher rates of mortality and many more people dying at younger ages.

- The persistence of infectious disease in tropical and LMIC, especially in tropical and sub-tropical regions, and the advent of new epidemics such as HIV/AIDS.
- Large increases in the burden of noncommunicable diseases in LMIC, particularly in China.
- Massive increases in road traffic injuries in LMIC, with rates now about twice the level of those in high-income countries.

4.2 Implications for the future

These trends have numerous implications both for the nature of the discourse around the “10/90 gap” and for the future directions and priorities in health research.

4.2.1 Measuring the “10/90 gap”

The origins of the term “10/90 gap” lay in estimates by the 1990 Commission on Health Research for Development and the 1996 WHO Ad Hoc Committee, based on 1986 and 1992 data respectively, that only about five per cent of global resources for health research was being devoted to 90 per cent of the world’s health problems. The expression became shorthand – and a rallying cry – for the continuing under-investment in health research for the needs of low- and middle-income countries. Indeed, there is evidence of better awareness and increased initiatives on the issue. As Chapter 2 describes, there have been a variety of positive developments in the last several years – including the appearance of new resources from public and private sources, special networks and initiatives for neglected diseases, public-private partnerships for product development, the creation of global challenge funds, and rising levels of investment in health research by low- and middle-income countries themselves.

Given this evidence of elevated levels of interest in closing the health research gap as a means of addressing global health inequities, is it desirable and possible to measure this gap with precision on a global scale? On consideration, it would appear not. The gap is still so large as to make more refined measuring rather indiscernible; as well the technical difficulties of going beyond rough estimates are considerable, especially as the complexities of health and health care continue to emerge. For example, the base studies mentioned above focused on conditions “specific to developing countries” – infectious diseases and issues such

as malnutrition, rather than noncommunicable diseases. With the substantial growth in the prevalence of noncommunicable diseases in low- and middle-income countries, it is difficult to justify this omission and yet impossible to quantitatively estimate the overall fraction of expenditure on research into noncommunicable diseases that could fairly be apportioned as benefiting low- and middle-income countries. Likewise, realistic and accurate assessments would require some apportionment of benefits to high-income countries from research on infectious diseases, such as HIV/AIDS and SARS, that are becoming more globalized in character – another very tough methodology issue.

Yet another fundamental methodological problem is how to assess the relative value to both country groups of basic research that may provide the keys to better understanding of biological processes and ultimately lead to the development of new health products. In the estimates made in the 1990s, investments in basic research were simply set aside to avoid dealing with this problem. It is now known that these investments are as high as 30 per cent of total investments in health research in high-income countries – and so could not be ignored.⁵

Even if a precise calculation could be carried out to arrive at a ratio of allocations benefiting high-income versus low- and middle-income countries, this figure would obscure or distract attention not only from the real health needs of many populations (given the diversity of health problems in different populations and sub-groups in countries and regions) but from the more complex determinants of health such as poverty, inequities, gender, violence and abuse, access to education, and opportunities to participate and be part of decision-making processes.

Nevertheless it remains apparent, as discussed below, that there is still gross underfunding of health research in many specific areas related to the needs of the vast majority of the world's people and the expression "10/90 gap" remains as appropriate as it was a decade ago to capture the sense of this unmet need.

What is needed is the initiative to take forward and refine the case that has been established by the "10/90" concept. This requires much more detailed analysis at different levels of disaggregation – in particular, focusing on specific neglected areas of health research (see next section); the particular needs of different countries and regions; and on specific areas, such as sexual and reproductive health, and distinct populations, such as adolescents, women and seniors. There is also a need to develop frameworks and tools for studying inequities in health and health research arising out of social hierarchies based on characteristics such as gender, ability, race, social class and geographic region.

Analysis of the resource flows to address these needs – and hence the identification of specific gaps – will require the development of more refined methodologies for tracking the applications as well as the origins of resources. It will be important to pay attention to the resources available at country level in low- and middle-income countries as well as high-income countries, since much of the applied research needs to be funded and conducted in the endemic countries – though not necessarily only by those countries given the relative affluence of high-income countries and their responsibilities for and international commitments to global health.

The following sections present a survey of some information currently available on these topics and a discussion of some of the gaps and issues requiring detailed studies in the future.

4.2.2 Attention to neglected areas of health research

In general, only scattered and partial information is available on funding for specific diseases. Much more detailed studies of financial flows for both diseases and determinants and across the entire spectrum from biomedical to health services and systems, social sciences, behavioural and operational research will be required in future.

INFECTIOUS DISEASES

HIV/AIDS

Investments in HIV/AIDS control programmes are being tracked by UNAIDS Global Consortium on Resource Tracking established in 2002. Its most recent estimate⁶ indicates that global expenditure on HIV/AIDS was US\$4.7 billion in 2003, including US\$2.1 billion from in-country sources. UNAIDS projects that annual AIDS spending from all sources will increase to US\$10 billion in 2007, while the projected annual need for funding will already be US\$12 billion by 2005 and US\$20 billion by 2007.

However, UNAIDS Global Consortium has noted that evidence remains incomplete on the level of financing for the research and development of critical new AIDS technologies. Little information is available on spending on anti-retroviral drug research and development in the pharmaceutical industry. In the R&D quest for an AIDS vaccine, the International AIDS Vaccine Initiative (IAVI) has established a robust methodology for data collection and has made an estimate⁷ for 2002 that the global investment was US\$646.0 million, with the public sector accounting for 67 per cent, the philanthropic sector 17 per cent and industry 15 per cent. If the US\$100-million multi-year grant from the Bill and Melinda Gates Foundation is excluded, the total for 2002 was US\$546 million, with the public sector accounting for almost 80 per cent (see Chart 4.3). Funds actually spent in 2002 amounted

Chart 4.3 Global investment in HIV/AIDS vaccine R&D, 2002, by source of funding

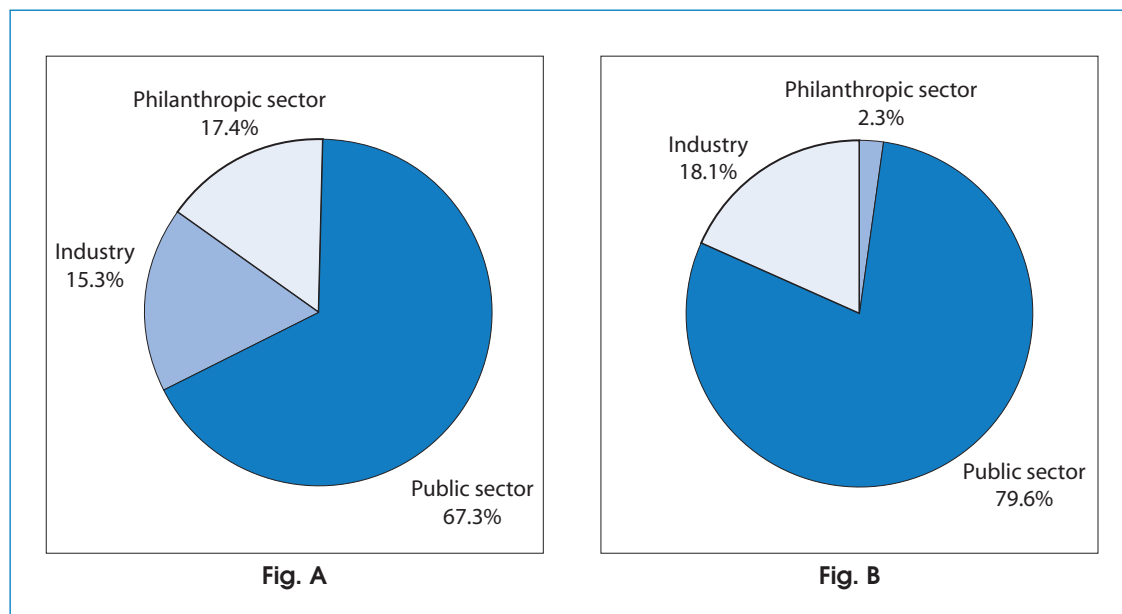


Figure A includes and Figure B excludes a US\$100-million multi-year grant from the Bill and Melinda Gates Foundation

Source: “Global Investment and Expenditures on Preventive HIV Vaccines: Methods and Results for 2002”, IAVI 2004

to US\$549 million, of which 43 per cent was invested in pre-clinical research, 28 per cent in clinical trial support, 21 per cent in basic research, and 8 per cent on cohort development, clinical trial infrastructure, vaccine education, advocacy and policy development activities.

Funding for microbicide R&D has increased considerably in recent years, as detailed in the 2004 report of the UNAIDS Global Consortium. In the period 1997-2003, public sector and philanthropic pledges totalled US\$532.2 million, including US\$334.4 million from the United States government, mainly through its National Institutes of Health (NIH) with 77 per cent. NIH support for microbicide R&D doubled from US\$ 24.7 million to US\$ 60.9 million during this period.

As for the public sector in other countries, no significant investments were made until 2002/03, when the Department for International Development (DFID) in the United Kingdom provided approximately US\$23.0 million to its Medical Research Council (MRC), primarily for the advancement of its lead microbicide candidate, and the Government of France provided support for microbicide research at its National Agency for AIDS Research. Establishment of the International Partnership for Microbicides (IPM) catalyzed support for a product development programme from the governments of Denmark, Ireland, the Netherlands, Norway, and the United Kingdom, as well as modest contributions from the United Nations Population Fund (UNFPA) and the World Bank. Philanthropic agencies have increased

their level of resources for microbicide R&D. The Gates Foundation provided a US\$26-million grant in 2000 and a US\$12-million grant in 2002 to the Global Microbicide Project (GMP), a US\$20-million grant to the Population Council in 2001 and a five-year commitment of US\$60 million to IPM in 2003. In 2002, the Rockefeller Foundation raised its commitment with a US\$15-million phased grant to IPM. Estimates for fiscal year 2004 suggest that investment in microbicide R&D will be US\$143 million.

Malaria and other tropical diseases

Calculations extracted from the WHO Ad-Hoc Committee report indicate that R&D funding for malaria amounted to US\$60.0 million in 1992 – equivalent to US\$1.89 per 1990 DALY, or 0.1 per cent of total investments in health research. Similarly, R&D investments for acute lower respiratory-tract infections came to US\$0.51 per DALY or 0.1 per cent of the total; for diarrhoeal disease US\$0.32 per DALY or 0.06 per cent of the total; for road-traffic injuries US\$0.83 per DALY or 0.05 per cent of the total; and tuberculosis US\$0.68 per DALY or 0.05 per cent of the total.

Data from the mid-1990s indicate that total expenditures for research on selected tropical diseases (leishmaniasis, malaria, trypanosomiasis and tuberculosis) that together account for five per cent of global disease burden (or 75 million DALYs) amounted to US\$383.0 million or 0.5 per cent of total world investments in health research. The Wellcome Trust estimated the annual investment on malaria research to be US\$100 million (or US\$2.20 per DALY). The Global Forum for Health Research estimates that the average investment per DALY for all health research is US\$73.00.

In 2002, total annual investments for malaria research in the field of medicines, diagnostics and vaccines, were estimated to be in the order

of US\$125.9 million.⁸ There has been no update on funding for other tropical diseases research.

Welcome signs have recently appeared on malaria research funding. In 2003, the Gates Foundation announced a US\$168-million, five-year malaria drug and vaccine grant package. Further, four pharmaceutical companies (GlaxoSmithKline, Sanofi, Pfizer and Novartis) each recently launched malaria-related research projects. In 2004, the U.S. Congress increased USAID anti-malarial funding by more than 50 per cent, from US\$65.0 million to US\$101.5 million, and directed 10 per cent of the total to research for new anti-malarial drugs and vaccines.⁹

The Drugs for Neglected Diseases Initiative (DNDi), a public-private initiative to focus research on malaria and other tropical diseases, received US\$30.0 million support for five years. Donations received by the Medicines for Malaria Venture (MMV), whose mission is to discover, develop and deliver new anti-malarial treatments through effective public-private partnerships, increased from US\$8.0 million in 2000 to US\$20.0 million in 2003.¹⁰ Project-related expenditure amounts to more than 88 per cent of the budget. MMV has received US\$95 million to date from the Gates Foundation, its major donor in 2003 at US\$15.0 million.

Tuberculosis

According to data presented at a workshop of the Initiative for Public Private Partnerships for Health (IPPPH) in April 2004, funding for product-development partnerships was reported as US\$45.0 million for TB drugs in 2002.¹¹

Summary of R&D spending on HIV/AIDS, Malaria and TB

Precise estimates of the total R&D spending on HIV/AIDS, TB and malaria are difficult to

make, but the order of magnitude appears to be around US\$1.4 billion for 2002 (US\$549 million for HIV vaccine R&D; plus a similar amount assumed to be spent for R&D on HIV anti-retroviral drugs; US\$142 million for microbicides, US\$45 million for TB; US\$126 million for malaria). Thus, for these three diseases, which collectively accounted for 12% of the global burden of disease in 2002, the average R&D spending was about US\$8.4 per DALY. This amounts to only about one tenth of the average of about US\$73 per DALY spent globally on all health research in 2002. There is very little investment in R&D for new antimicrobial agents for drug-resistant bacterial infections.

DIAGNOSTICS

New initiatives have emerged in response to the critical need for new tools to detect infectious diseases: for example, the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR). In 2003, the Gates Foundation announced an initiative focused on developing new diagnostic tests for the world's most deadly diseases. The Foundation for Innovative New Diagnostics (FIND), a collaboration between TDR and industry, received US\$30.0 million for five years. Further, the Grand Challenges in Global Health initiative, supported by the Gates Foundation, has provided US\$200.0 million for a major new public-private partnership effort with NIH. Priority areas have now been identified.¹²

4.2.3 Attention to specific health research needs of Africa

Special attention to the research needs of sub-Saharan Africa is warranted by its unique epidemiological characteristics:

- the high share (70 per cent of disease burden) of Group I conditions (communicable diseases, including HIV/AIDS; maternal, neonatal, nutritional conditions);

- continuing very high under-five mortality and morbidity (due to malaria, pneumonia, diarrhoeal diseases, malnutrition); and
- high maternal mortality rates.

Many countries in the region lack adequate research infrastructures. This involves a combination of poorly resourced institutions, lack of skilled human resources (exacerbated by an ongoing brain drain), and a weak research culture among policy makers and service providers that perpetuates disconnection among evidence, policy and practice.

An analysis of global research effort for diseases that are neglected to different extents was reported by the Commission on Macroeconomics and Health in 2001 (see Table 4.3).¹³ It is striking that most of the 'very neglected' diseases – with the exception of Chagas disease, a parasitic condition found only in Latin America – are most prevalent in Africa.

4.2.4 Special areas requiring attention

Young people

Half the world's population is under 25 years old and in 68 countries more than four in 10 persons are under 15 years old – 180 million of whom, aged 10-24, are disabled¹⁴. These young people carry a high burden of mortality and morbidity in many countries. Thus, under-five mortality is still very high and the burden of disease in this age group is 36 per cent of the global burden of disease, compared with 18 per cent for HIV/AIDS, malaria and TB, and about three per cent for maternal conditions (see Chart 4.4) – all targets of the UN Millennium Development Goals (MDGs).

Of the total global burden of disease for the 0-4 age group, 98.9 per cent – or virtually all – resides in low- and middle-income countries. 99.7 per cent of the burden of HIV/AIDS, malaria and TB is also in these countries; and

Table 4.3Global research effort for three types of diseases^a

Disease category type	Global research effort	Epidemiology	Examples	Notes
Not neglected diseases (Type I)	High	Occuring both in HIC and LMIC. Large vulnerable populations worldwide.	Hepatitis B. <i>Haemophilus influenzae</i> Type B diabetes. Cardiovascular diseases.	High incentives for R&D. Not widely applicable, nor accessible or sustainable for developing countries.
Neglected diseases (Type II)	Low	Occuring both in HIC and LMIC. Substantial proportions of burden in poor countries.	HIV/AIDS. Tuberculosis. Malaria. ^b	Substantial research in HIC. R&D spending is not commensurate with global disease burden. Low accessibility for LMIC.
Very neglected diseases (Type III)	Very low	Overwhelming or exclusive incidence in LMIC.	Chagas disease. Schistosomiasis. Leishmaniasis. Trypanosomiasis. Onchocerciasis. Lymphatic filariasis.	Very little R&D funding. No commercially based R&D in HIC.

^a Adapted from: World Health Organization, *Macroeconomics and Health: Investing in Health for Economic Development*, Report of the Commission on Macroeconomics and Health, December 2001. Geneva.

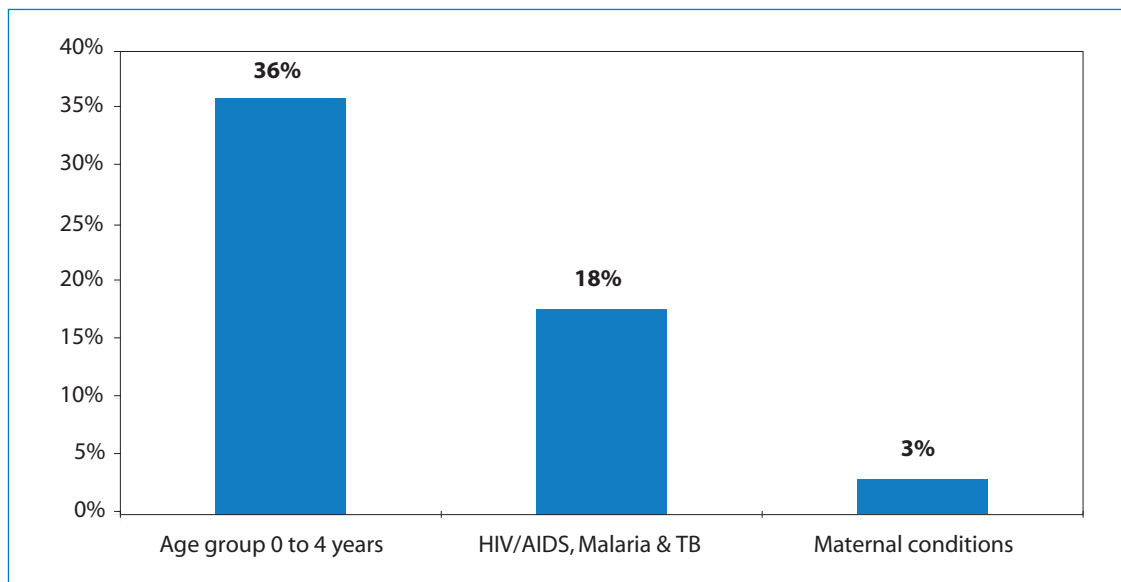
^b Malaria is mentioned by the Commission on Macroeconomics and Health as a possible neglected disease (Type II) or a very neglected disease (Type III).

88.6 per cent of the burden of disease related to maternal conditions. The burden of disease for under-fives is particularly high in Africa (42 per cent of the global total) and South Asia (India alone accounting for 21 per cent). This burden is largely due to lower respiratory-tract infections, diarrhoeal diseases, perinatal conditions and, in Africa, malaria. Of these, only malaria has begun to attract significant investments in research, as noted above.

Sexual and reproductive health

Increased attention to sexual and reproductive health, including adolescent sexual and reproductive health, must be a major priority if overall health is to be improved and if the MDGs for reducing HIV/AIDS and maternal mortality are to be met. Research is needed into safe, appropriate methods of contraception and into methods of avoiding reproductive tract infections and HIV/AIDS transmission, with

Chart 4.4 Global burden of disease estimates relating to Millenium Development Goals 4, 5 and 6 (WHO, 2000 data)



Source: WHO Burden of Disease estimates, 2000

the object of proving a range of options enabling both male and female to take responsibility for their health.

The global scale of unmet needs for contraceptives and/or barrier methods of preventing the transmission of sexually transmitted infections (STIs) is evidenced by the large numbers of unwanted pregnancies in every country (even in the United States, about half of all pregnancies are unplanned), many of which lead to unsafe abortions; the high rates of HIV/AIDS infections in Africa and rapidly expanding numbers of new infections in several regions including Asia and the former Soviet Union; and growing rates of other STIs such as chlamydia and syphilis. It is estimated that well over 100 million couples have unmet needs for contraception.

Research to provide family planning products that are safe, reliable and affordable, and to study the wide range of health policy and

systems issues as well as psychosocial and behavioural aspects of sexual and reproductive health, remains severely under-funded – with the exception of work on microbicides to interrupt HIV transmission. Two indicators serve to illustrate this point:

- Only a tiny number of new molecular entities for family planning use were registered by the U.S. Food and Drug Administration (FDA) in recent years (see Table 4.1).
- Funding for the Special Programme of Research, Development and Research Training in Human Reproduction (HRP), co-sponsored by UNDP, UNFPA, the World Bank and WHO, adjusted for inflation, decreased by 44 per cent from 1990-1991 to 2000-2001 (see Chart 4.5). This was in spite of HRP's expanded focus from fertility regulation to a broader reproductive health agenda during that period, including safe motherhood, adolescent reproductive

health, STIs, and reproductive rights. Current activities include clinical, socio-behavioural and epidemiological research; development, identification and elaboration of norms and standards; and advocacy and dissemination of information materials.¹⁵

Ageing

With the exception of Africa and some transition countries of the former Soviet bloc, life expectancy has been increasing in all regions of the world so larger numbers of people are living into old age. There are many unmet needs for products and services that will enable older people to remain healthy and active and for research that addresses the social determinants of health, in particular attitudes and behaviours towards senior citizens.

Gender

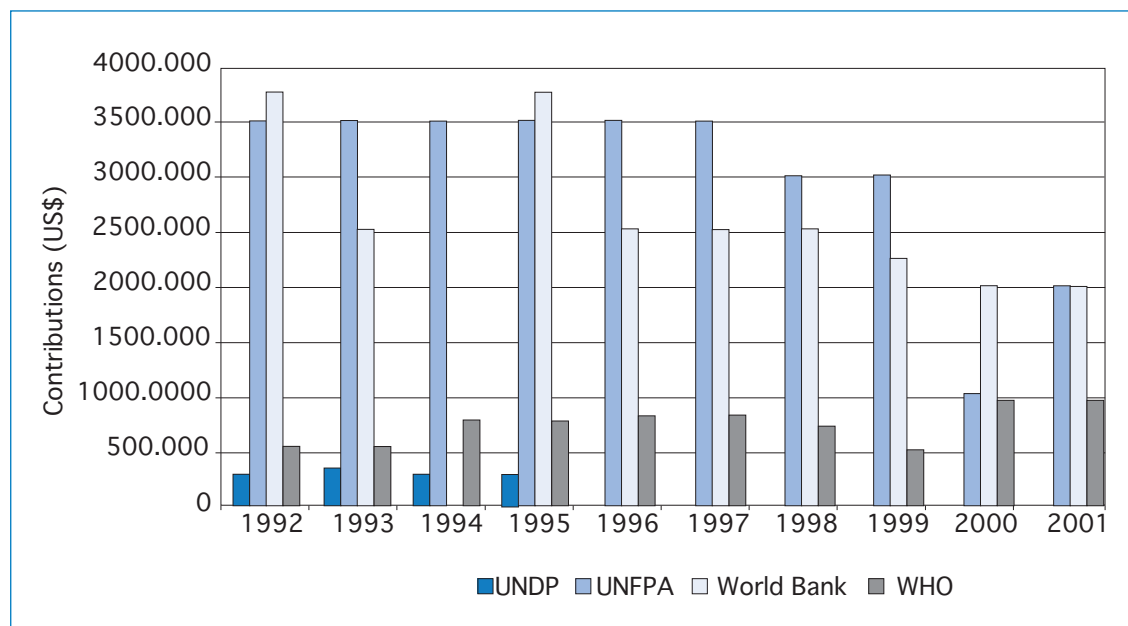
Research into gender-based differences and disparities in health and into inequities in

access to societal resources necessary for health, including health research, are severely under-resourced, despite the attention that has been drawn to the field by the 1994 Cairo International Conference on Population and Development and the 1995 Beijing World Conference on Women.

Disability

About 10 per cent of the world's population has a significant degree of physical or mental impairment. Discrimination against disabled people persists in such critical areas as social status, employment, housing, education, income, public accommodation, transportation, communication, recreation, health services, voting, access to public services and decision-making. Very little research is conducted globally into their health problems and needs, and into the effects of biases in society, in medicine and in health research on the health of disabled people.

Chart 4.5 Contributions of co-sponsors to HRP, 1992-2001



Basic research

Basic research is an important component of health research, and one that can be considered as a global public good that can be applied to any disease. The proportion of basic research to total research varies by country. Information available indicates that between 1989 and 1999, the USA, Canada, the United Kingdom and United States spent an average of 28 per cent of total research as basic research.¹⁶ The study reported that, during that period, Canada spent 22 per cent, the United Kingdom 32 per cent and the United States 30 per cent on basic research. Other types of research were “applied (clinical) research”, and “others (post-marketing, regulatory, patents and post-distributional research)”.

In addition to the magnitude of funding, there are important issues to be addressed in basic research concerning how priorities are set, what fields of research are favoured, and who determines these fields and priorities.

Determinants and cross-cutting issues

Financial flows studies to date have focused largely on diseases rather than on social and other determinants of health. Selected cross-cutting issues deserve attention in the analysis of health research financing. These include poverty, inequity, gender, class/caste, ability, health systems, and research capacity strengthening. While disparities in the level of investment in research for different diseases have been highlighted in a number of reports, data that tracks financial flows for health research on determinants are, in general, not readily available. Unless biases based on gender, ability, race, social class and other social hierarchies are addressed, health inequities – and the “10/90 gap” – will persist.

Transferability of results

Health research is a global public good – at least as it relates to diseases, determinants and contexts that are shared widely around the

world. In principle, therefore, low- and middle-income countries should benefit from health research undertaken in high-income countries that invest far larger funds in health research. If there are diseases and determinants that do not experience this trickle-down or cascade effect, then responses – both national and international – need to be developed.

Demographic and epidemiological transitions are being experienced in many low- and middle-income countries and they are experiencing increases in the patterns of morbidity and mortality related to noncommunicable diseases similar to those in high-income countries. Theoretically, therefore, LMIC should increasingly benefit from the findings of research undertaken in HIC. However, for this to happen in practice, there are several prerequisites. First, there needs to be access to the information or products produced by the research. In the case of information, access is often limited due to the lack of funds for journals and online subscriptions, or of funds and infrastructure for the necessary information technology. In the case of products, such as new drugs, vaccines, diagnostics and equipment, countries may lack the funding, human resources, training and infrastructures to support their delivery and appropriate use, e.g. a reliable cold chain for vaccines. There may also be variations in the strains of infective agents, drug resistance factors, or genetically related disease susceptibilities. All of these factors can militate against the true global usefulness of research that has been conducted in better resourced places and with objectives and design criteria that have not considered the challenges of applicability in resource-poor settings.

Examples that illustrate these challenges and concerns include:

- Drug R&D for diseases prevalent in low- and middle-income countries should ideally provide products that are inexpensive to produce, stable to tropical conditions

without requiring special storage, easy to administer in oral formulations, requiring few doses in short courses and a minimum of sophisticated laboratory back-up or clinical monitoring. Such criteria traditionally have not been built into the design of anti-infective agents but have, for example, been adopted in MMV R&D work.

- Vaccines developed for industrialized country markets may not be effective against the different types of viruses and bacteria prevalent in developing countries. This is a particular concern in the current efforts to develop a vaccine to prevent HIV transmission, given the different geographical distribution of evolutionary strains of the virus.
- Interventions for noncommunicable diseases available in high-income countries may not be directly adaptable, appropriate, or cost-effective in LMIC due to costs and infrastructure requirements.
- Determinants of ill health, and appropriate prevention and treatment measures, can vary greatly among regions, even where the same diseases or conditions arise. To take two very different examples:
 - While a large proportion of road traffic injuries in high-income countries are due to passenger vehicle collisions – spawning productive research into injury prevention (e.g., seat belts, speed limits, alcohol consumption limits, air bags) and high-impact injury treatment – most road traffic injuries in low- and middle-income countries involve collisions between vehicles and cyclists or pedestrians, requiring different research into prevention and treatment.
 - Research in high-income countries has shown that, for persons who have developed cardiovascular disease, there are proven survival benefits from regularly taking drugs such as aspirin, beta blockers, ACE inhibitors, statins and diuretics. The relevance of these findings for low- and middle-income countries has yet to be examined, both in terms of the economics of treatment and the medical suitability for different populations, e.g., haemorrhagic stroke is much more common in Asia and the risks of chronic use of aspirin may, therefore, be greater.
- The levels of development and performance of health systems and services vary greatly between countries and, consequently, so can the applicability of research results.
- Access to treatment, medicines and other research results are very different among and within countries.

4.3 The way forward

This study of financial flows for health research conducted by the Global Forum responds to widespread interest on the part of those who fund research, manage and set priorities in different institutions, and use our results to try to improve the health of populations around the world.

While presenting a more detailed picture of health research resources than has been achieved hitherto, the study has also exposed major gaps in the availability of good quality data from all sectors, disease-specific information and the measure of complex determinants such as poverty, inequity, and gender.

The importance of understanding the connections among sources of funding for health research, applications of resources and the priorities to which they are directed has been underlined in this report. It is clear that there is a need for a more regular reporting and analysis of resource trends and a more detailed and disaggregated examination of how well resources are being matched to priority areas. This tracking and analysis needs to be done not just at the global level but also focusing on individual diseases and determinants and at the regional and country levels and for different populations, including marginalized populations. It needs to recognize conditions that are increasingly global and have a major impact on health, such as cardiovascular disease, tobacco-related diseases and injuries, and it must encompass the whole spectrum of research from biomedical to social and

operational. Above all, the generation and analysis of reliable, comprehensive, comparative data must point to concrete ways to shrink the “10/90 gap” – soon.

In keeping with its mandate, the Global Forum for Health Research will therefore continue to track global resource flows for health research, and for the future plans to issue regular updates on the global picture, for which data are available every two years. In addition, the Global Forum will conduct annual studies that focus on several individual areas selected from such categories as neglected health problems; regional/country needs; and special areas based on geography, demography and cross-cutting issues like poverty and equity, and biases in health research, policies and practices that result in disadvantage to groups of people on the basis of gender, ability, race, social class, age, geographic region, among others. For each topic selected, we will attempt to identify what are the needs (e.g., in relation to burden of disease, poverty, equity gaps), what are the current research efforts, where are the gaps, and how much effort would be needed (what kind, from whom) to solve the problems.

We believe that by focusing more attention at the level of specific problem areas, examining in detail what needs to be done and by whom, we can further increase the effectiveness with which we call attention to the vital importance of harnessing health research to improve global health, and thereby accelerate the pace at which the “10/90 gap” is closed.

-
- ¹ Inflation rates were typically 3-4 % or less in the major economies during this period and, in particular, were 2.5 – 3.0 % in the USA where by far the largest increases in health research funding occurred.
 - ² DiMasi JA Hansen RW Grabowski HG. The price of innovation: new estimates of drug development costs. *Journal of Health Economics* 2003 Mar;22(2):151-85.
 - ³ Tufts Center for the Study of Drug Development. See: <http://csdd.tufts.edu/NewsEvents/>
 - ⁴ World Health Organization, 2004. *The World Health Report, 2004: changing history*. World Health Organization, Geneva.
 - ⁵ Canada Patented Medicine Prices Review Board -PMPRB Study Series S-0217- Dec 2002. A comparison of Pharmaceutical Research and Development Spending: Share of R&D Spending to Basic Research in Selected Countries in Various Years (page 20).
 - ⁶ UNAIDS, 2004. *Financing the Expanded Response for AIDS 2004*. UNAIDS, Geneva. UNAIDS/04.39E.
 - ⁷ International AIDS Vaccine Initiative, 2004. *Global Investment and Expenditures on Preventive HIV Vaccines: Methods and Results for 2002*. IAVI, New York. Available at: <http://www.iavi.org/pdf/Global%20Investment%20Expenditure%20HIV%20Vaccines%202002.pdf>
 - ⁸ Michaud C., personal communication, July 2004.
 - ⁹ Editorial, Washington Post, July 2004.
 - ¹⁰ Medicines for Malaria Venture, 2003 Annual Report.
 - ¹¹ Widdus R, IPPPH, personal communication, 2004.
 - ¹² Varmus H. et al, 2003. *Grand Challenges in Global Health*. Science 17 Oct 2003:398-99.
 - ¹³ World Health Organization, *Macroeconomics and Health: Investing in Health for Economic Development*, Report of the Commission on Macroeconomics and Health, December 2001. Geneva.
 - ¹⁴ Adolescents and Youth with Disability: Issues and Challenges by Nora Ellen Groce, September 2003; <http://web.worldbank.org/WBSITE/EXTERNAL/TOPICS/EXTSOCIALPROTECTION/EXTDISABILITY/0,,contentMDK:20192328~menuPK:510279~pagePK:148956~piPK:216618~theSitePK:282699,00.html>
 - ¹⁵ UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction, 2003. External evaluation: 1990–2002. World Health Organization, Geneva. WHO/RHR/HRP/03.14.
 - ¹⁶ Canada Patented Medicine Prices Review Board -PMPRB Study Series S-0217- Dec 2002. A comparison of Pharmaceutical Research and Development Spending: Share of R&D Spending to Basic Research in Selected Countries in Various Years (page 20).

Appendices

Appendix 1: Concepts and Definitions

Bioavailability

Bioavailability is how well a drug will reach an effective therapeutic level in the body, and may be influenced by various factors. A drug may be safe and effective, but never reach an effective level in the body if bioavailability is poor.

Burden of disease

A widely used concept based on a statistical measurement (Disability-Adjusted Life Years – see DALYs below) of the gap between current health status and an ideal situation where everyone lives into old age free of disease and disability. WHO undertook a new study of Global Burden of Disease in 2002 using DALYs to measure and compare the main causes of burden of disease in low- and middle- income countries and to study trends since 1990. This concept and the way it is measured are being called into question as they define "disability" in a way that is strikingly at odds with current thinking about what constitutes a disability and what individuals with a disability have to contribute to society, in that they: a) assume a "reduced value" of lives lived with a disability; b) use the term disability interchangeably with ill-health, c) assume that living with a disability represents a net drain on society; and d) assume that individuals with a disability lie somewhere between life and premature death.

Classification of funders and performers

A. Funders

- Public sector (government departments, national aid agencies).
- Private sector (for-profit: pharmaceutical, biotechnology, genomic, nanotechnology, medical instruments firms; not-for-profit: foundations, NGOs, private universities).
- International (multilateral, bilateral agencies).

B. Performers

- Public sector (government departments, academic/research institutes, hospitals, others).
- Private sector (for-profit: pharmaceutical, biotechnology, genomic, nanotechnology, medical instruments firms; private not-for-profit: academic/research institutes, hospitals/laboratories, NGOs).
- International (foreign institutions, government departments, others).

Disability

Within a narrow medical model, disability is defined as a defect, a problem inherent in the person, directly caused by disease, trauma or other health conditions, and a deviation from certain norms. Management of the disability of the disabled person is aimed at cure,

prevention, or adaptation of the person (e.g. assistive devices). Medical care and rehabilitation are viewed as the primary issues, and at the political level, the principal response is that of modifying or reforming health care policy.

The social model of disability on the other hand, defines disability as a socially created problem and principally as a barrier to the full inclusion of individuals into society. Disability is not an attribute of an individual, but rather a complex collection of conditions, many of which are created by the environment, particularly the social environment and socially mediated aspects of the physical environment. Hence, the management of the problem requires social action, and it is the collective responsibility of society at large to make the environmental modifications necessary for the full participation of disabled people in all areas of social life. The issue is, therefore, an attitudinal or ideological one requiring social change, which at the political level becomes a question of human rights to be seen in the same way as the issue of gender and sexual orientation.

The social model of disability does not negate that a disabled person has a certain biological reality (e.g. having paralysis of the legs) which makes her/him different in her/his abilities from the norm. But it views the “need to fit a norm” as the disability and questions whether many deviations from the norm need a medical solution (adherence to the norm) or a social solution (change/elimination of norm).

Disability-adjusted life years (DALYs)

The Disability Adjusted Life Year or DALY is a health gap measure that extends the concept of potential years of life lost due to premature death (PYLL) to include equivalent years of ‘healthy’ life lost by virtue of being in states of poor health or disability. The DALY combines in one measure the time lived with disability and the time lost due to premature mortality. One DALY can be thought of as one lost year of ‘healthy’ life and the burden of disease as a measurement of the gap between current health status and an ideal situation where everyone lives into old age free of disease and disability.

DALYs for a disease or health condition are calculated as the sum of the years of life lost due to premature mortality (YLL) in the population and the years lost due to disability (YLD) for incident cases of the health condition. YLL are calculated from the number of deaths at each age multiplied by a global standard life expectancy for the age at which death occurs. To estimate YLD for a particular cause in a particular time period, the number of incident cases in that period is multiplied by the average duration of the disease and a weight factor that reflects the severity of the disease on a scale from 0 (perfect health) to 1 (dead).

Additionally, time discounting and non-uniform age weights that give less weight to years lived at young and older ages are used in calculating standard DALYs as reported in recent World Health Reports. With age weights and discounting, a death in infancy corresponds to 33 DALYs, and deaths at ages 5 to 20 to around 36 DALYs. Thus a disease burden of 3,300 DALYs in a population would be the equivalent of 100 infant deaths or to approximately 5,500 persons aged 50 years living one year with blindness (disability weight 0.6).

Foundation

The foundation and charity sector is a subset of the private non-profit sector also known as the “third sector”. What is defined as a foundation in one country may not qualify as such in another country. In 2001 Anheier proposed a useful definition that a foundation shall:

- be an asset-based entity, financial or otherwise
- be a private entity, institutionally and structurally separate from government
- be self-governing
- serve a public purpose.

Foundation types include:

- endowed organizations that engage in grant making for specific purpose, e.g. Wellcome trust in the UK;
- organizations that operate their own programs and projects, e.g. Institute Pasteur in France;
- a mix of the above.

Genomics

The term “genomics” was coined by mouse geneticist Tom Roderick to describe an approach to the study of DNA at the level of chromosomes, entire genomes, or large clusters of genes. The purpose of the term was to distinguish it from more traditional genetic approaches that focused on one gene or a family of functionally or structurally related genes or sequences. In addition, the concept of genomics was also associated with a large scale and high tech approach. Implicitly, genomics implied creating and using large databases, extensive use of laboratory automation, and generally a more “capital intensive biology,” than was the norm in the mid-1980s.¹

Gross domestic expenditure on R&D (GERD) includes R&D performed within a country and funded from abroad but excludes payments made abroad for R&D. According to the Frascati Manual, the national R&D expenditure breaks down into four performance sectors:

1. The business enterprise sector (private for-profit)

This sector includes: all firms, organizations and institutions (other than higher education) whose primary activity is the market production of goods and services for sale to the general public at an economically significant price, and those private non-profit institutes mainly serving these firms, organizations and institutions.

2. The government sector

This sector includes all organizations whose funds are administered by the central (federal), state, or local government authorities.

¹ Source: World Survey of Funding for Genomics Research Final Report to the Global Forum for Health Research and the World Health Organization September 2000, Robert Cook-Deegan, Carmie Chan, and Amber Johnson
Stanford-in-Washington Program, 2661 Connecticut Avenue, NW
Washington, DC 20418 www.stanford.edu/class/siw198q/websites/genomics/
bobcd@stanford.edu (01) 202-332-6235 phone; (01) 202-332-1416 fax)

3. The higher education sector

This sector includes: all universities, colleges of technology, other institutes of post-secondary education, and all research institutes, experimental stations and clinics operating under the direct control of or administered by or associated with higher educational establishments.

Generally, Higher Education is funded from Direct Government, General University Funds (public or private) and private sources. The distinction between these categories remains fuzzy. Research in the Higher Education sector may also be funded by private sources such as public-private partnerships or the private not-for-profit sector.

General University Funds (GUF) generally refer to funds that have been paid by education ministries in forms of grants to higher education for research. GUF may be divided in two sub-categories whether it is composed of public or private sources. Private GUF administered by universities are also classified as private not-for-profit.

4. The private not-for-profit sector (PNP)

This not-for-profit sector encompasses: non-market, private not-for-profit institutions serving the general public, as well as private individuals and households. In addition to funding from foundations, general university funds not from public sources but still administered by universities are also classified as private not-for-profit. Research in the private not-for-profit sector in LMICs usually refers to research performed in universities funded by the PNP sector.

Health Research/Research and Development (R&D)

"Research and experimental development comprise creative work undertaken on a systematic base in order to increase the stock of knowledge, including knowledge about man, culture and society, and the use of this knowledge to devise new applications" – Frascati Manual.

The type and nature of health research differ across sectors of the economy. Health research includes applied research; experimental development; research capacity strengthening; health policy research; research on health determinants; and other types of health related research.

Research-related decisions in the for-profit sector are largely – and by definition – driven by potential. The not-for-profit sector focuses on issues such as the impact of remedies on health and providing high-quality information to decision-makers.

Health policy research assesses the impact of policies on public health in a broad manner. Such policies generally relate to funding decisions, programmes, models and regulations that have a direct impact on health.

Health R&D to total national R&D expenditure

Most countries distinguish between civilian and non-civilian R&D within total national R&D expenditures. Cross-country comparability of the ratio of health R&D to total R&D ratio can be severely affected depending on whether non-civilian R&D is included in the national total.

- **Fields of science**

Unesco proposed a classification of S&T and R&D by fields of science, described in the Frascati Manual. Health-related R&D usually includes Medical Sciences, portions of research reported under Natural and Exact Sciences and the General Knowledge field. The Environment field is excluded from health R&D, although environmental issues have an impact on health.

Medical sciences field includes R&D on food hygiene and nutrition; radiation used for medical purposes, biochemical engineering; medical information; rationalization of treatment and pharmacology (including the testing of medicines and the breeding of laboratory animals for scientific purposes): as well as research relating to epidemiology, prevention of industrial diseases and drug addiction. Not all countries have a published field for medical sciences.

- **Non-oriented and fundamental research**

Non-oriented research such as environment and life-sciences overlaps with health research globally. The extent to which environment and life-sciences research contributes to the health field is not well known. The Eurostat series for recent years do permit one to break-out non-oriented research in advancement of research and in GUF but full responses are available for only half a dozen countries.

- **Medical instruments and equipments**

The OECD collects industrial R&D data broken down according to the International Standard Industrial Classification (ISIC) Rev 3. These results are pretty consistent with the European NACE rev 1 classification. However, the OECD survey does not show a field for medical instruments and equipment, but for "instruments watches and clocks". The exact title should be "Medical, precision and optical instruments, watches and clocks" according to ISIC and NACE class 33.

The United States and Canada use another classification: the North American Industrial Classification System (NAICS). The different nomenclature and classification systems make it difficult to compare medical instruments and equipment R&D across countries.

The Medical instruments and equipment field includes: medical and surgical equipment and appliance, measuring and testing equipment as well as diagnosis equipments, electro-medical instruments.

- **Research funded by the ODA sector**

Most ODA health research includes operational research, capacity strengthening, health policy and other types of health-related research.

Health research as described by DFID (United Kingdom) includes: health policy, developing new products and technologies that meet the needs of poor people, testing the practical application of new knowledge and technologies, communicating new knowledge and transferring new technologies to users, refining and validating methods for data collection, capacity strengthening research.

Health Research Resource Flows Classification:

The Global Forum for Health Research proposes the following classification scheme (it is a modified version of what was included in Monitoring Financial Flows 2001).

- A.1 Non-oriented, fundamental research**
 - No further disaggregation
- A.2 Health conditions, diseases and injuries**
 - A.2.1 Group I (communicable, maternal, perinatal and nutritional conditions)
 - A.2.2 Group II (non-communicable diseases)
 - A.2.3 Group III (injuries)
- A.3 Exposures, risk factors and determinants**
 - A3.1 Within the health system
 - A3.2 Outside the health system
- A.4 Health systems research**
 - A.4.1 Policy and planning research
 - A.4.2 Health services delivery research
- A.5 Research capacity building**
 - A.5.1 Recurrent expenses
 - A.5.2 Capital expenditures

High-Income Countries (HIC)

Countries classified as high-income based on national income levels. For countries identified as HIC in this report, see Appendix 3

Inequities

Partiality that is not fair or equitable; injustice by virtue of not being equitable.

Low- and Middle-Income Countries (LMIC)

Countries classified as low- or middle-income countries based on national income levels. For countries identified as LMIC in this report, see Appendix 3

MicroNano Technology

Product miniaturization and development of sound manufacturing processes are major goals of microtechnology research. The scope of micro- and nano- research may be described as following:

- Fundamental research: micro- and nano-structures for research in physics. Micro-electrodes for chemistry and biology. Microstructures for the characterization of new materials
- Manufacturing processes: new manufacturing processes in silicon and other materials. Integration and encapsulation techniques for microsystems. New processes for microelectronics. Silicon post-processing.
- Components and microsystems: multidisciplinary research on new microsystems.

Nanotechnology

Nanotechnology or nanosciences enables a new paradigm of science and technology that sees different technologies converging at the nanoscale namely (a) nanoscience and nanotechnology; (b) biotechnology and biomedicine, including genetic engineering; (c) information technology, including advanced computing and communications; (d) cognitive science (neuro engineering) ("NBIC" – nano-bio-info-cogno).

NBIC technologies

The convergence of nanotechnology, biotechnology, information science and cognitive science in research and research applications.

Pharmaceutical R&D

Pharmaceutical R&D includes preclinical trials and Phase I-IV studies.

Preclinical studies

Such studies include animal studies to test whether a drug is carcinogenic, mutagenic, or teratogenic (causing fetal malformations), and to understand how the drug is absorbed and eliminated.

Phase I studies

Phase I studies are primarily concerned with the safety of a drug. They are performed on a small number of volunteers who are usually healthy. The purpose is to determine how the drug is absorbed, metabolized, and eliminated. They also look at what side effects occur as dosage levels increase, as well as to obtain early evidence on drug effectiveness.

Phase II studies

Phase II studies are performed with patients who have the disease or condition that the experimental drug is expected to improve or cure. In addition to ensuring that the experimental drug is safe, Phase II studies are designed to evaluate the effectiveness of the drug. The typical approach is to give one group of patients the experimental drug, and a second "control" group a standard treatment or placebo. Phase II studies are often designed to determine optimal dosage most effective with the least number of side effects.

Phase III studies

During Phase III studies, the drug is tested in several hundred to several thousand patients with the disease to provide a more thorough understanding of the drug's effectiveness, benefits, risks, and possible adverse side effects.

Phase IV studies

Phase IV studies include post-marketing and surveillance studies. One of the purposes is to continue gathering specific information about an approved product. A Phase IV clinical trial is a post-marketing study in the sense that one of the purposes is to delineate the drug's benefits and side-effects, optimal use and potential, in large groups of patients world wide.

Purchasing Power Parity

According to the World Bank definition, PPP is a method of measuring the relative purchasing power of different countries' currencies for the same types of goods and services. Since goods and services may cost more in one country than in another, PPP allow more accurate comparisons of standards of living across countries. PPP estimates use price comparisons of comparable items but since not all items can be matched exactly across countries and time, the estimates are not always "robust." The underlying assumption is that the goods and services consumed do not differ across countries and economies.

Poverty

According to one World Bank definition, poverty can be measured by the proportion of population living on less than US\$1.08 per day. This poverty line includes consumption from own production and income in kind.

Absolute poverty is generally considered to be a level of poverty at which certain minimum standards – for example for nutrition, health and shelter go unmet.

The **poverty line** is the level of income below which one cannot afford to purchase all the resources one requires to live. People who have an income below the poverty line have no discretionary disposable income, by definition. (<http://www.fact-index.com/>).

Research capacity strengthening

Research Capacity Strengthening (RCS) may be viewed as a way to foster self-reliance in biomedical science research in LMICs by building a critical mass of human resources, institutional capacity, and an environment conducive to public research needs.

RCS includes the development of an adequate in-country resource base of:

- healthcare infrastructures, devices, products and services for the diagnosis, treatment, prevention and control of diseases and injuries in both urban and rural areas;
- research centers for the improvement of knowledge and for the training of staffs, professionals and specialists;
- laboratories with proper equipments, storage and maintenance;
- systems for the storage and delivery of such products and services.

Unsustainable

Any practise that cannot be continued indefinitely because it uses up the resources on which it depends is unsustainable.

Appendix 2: Methodology

Conceptual Model

The dataset covered in this report includes data for health R&D efforts of high-income countries, low- and middle-income countries, and an area of convergence of health R&D funded by HIC and carried out in and for the primary benefit of LMIC. The latter includes research funds transferred from high-income countries to low- and middle-income countries, health research carried out in LMIC by HIC entities, R&D carried out in high-income countries that is relevant to the needs of low- and middle-income countries and health research carried out in high-income countries by researchers from low- and middle-income countries.

Sources of data

OECD database

The OECD database is designed to provide analysts with comprehensive and internationally comparable time series on R&D (including health-related R&D) by sectors of performance and sources of funds when such data are available. The OECD database has been created for 19 of the largest R&D performing countries, and also provides a zone total for the European Union. LMIC that publish R&D expenditures are usually the ones with major contributions to global health R&D. The subset of LMIC documented may not be representative of other low-income countries.

ANBERD database

The ANBERD database (Analytical Business Enterprise R&D) was developed with the objective of creating a consistent data set that overcomes the problem of international comparability and provides for time series consistency. In conformity to the Frascati definitions and methodologies, ANBERD incorporates annual R&D expenditure carried out in the business enterprise sector, regardless of the origin of funds, for a variety of industrial sectors. Several factors may have a substantial effect on the consistency of ANBERD, such as the completeness of the set of enterprises for which R&D data are collected and classification scheme for firms associated with more than one sector. It is difficult to maintain consistency over time due to these factors, hence time series may have large discontinuities.

RICYT database

The RICYT (Red Iberoamericana de Indicadores de Ciencia y Tecnologia) database provides both a percentage distribution of S&T and/or R&D expenditure by socio-economic objectives as well as total national R&D time series for several countries in South and Latin America, Spain, Portugal and the USA.

Data for public sector expenditures for international health research

Data on health R&D funded by Official Development Assistance (ODA), bilateral and multilateral agencies, development banks and national health research institutes were also

compiled by consultants under contract to the Global Forum. Data sources include material obtained from various official organizational publications and web sites, and through personal communications to Global Forum consultants from organizational officials.

Private not-for-profit sector data

Funding data for health research by foundations and other not-for-profit organizations were compiled by consultants under contract to the Global Forum. Data sources include The Foundation Center for U.S. Foundations and the European Foundation Center (EFC), material obtained from various official organizational publications and web sites, and through personal communications to Global Forum consultants from organizational officials.

Private sector data

Data for the private sector were obtained from the performer base of the OECD and RICYT databases and from data from official publications and web sites of PhRMA and other pharmaceutical associations, and other publications detailing private sector expenditures.

Other data sources

Various other data sources were used to fill in, supplement and contextualize data from the above sources. These include publications from UNDP and WHO for data on public health expenditures; WHO for data on injuries and communicable diseases; the World Bank Group for GDP data; the World Bank for data on purchasing power parity and absolute poverty; and data from web sites, publications and communications from organizations such as the Kaiser Foundation and various international initiatives, such as the International Aids Vaccine Initiative (IAVI) and the National Institute of Allergy and Infectious Diseases (NIAID), for disease-specific research.

Specific references to these and other data sources are cited throughout the text, charts and tables in the report as appropriate.

Estimations and Methodologies

Performer reported R&D

The reference manual for methodology regarding the monitoring of R&D expenditures used by the OECD is the Frascati Manual, and the Bogotá manual for RICYT data. The maximum of R&D by health objectives and fields of science was used for health research with the OECD data. Note that R&D by health objectives and fields of science are generally consistent with each other. For the RICYT data, a portion of advancement of knowledge (research in higher education) was included as health research.

Pharmaceutical R&D

Pharmaceutical data in this report include data covering preclinical trials, Phase I to IV of clinical trials, drug approval and marketing.

Health R&D updates

For several countries such as India, South Africa, Australia and others, health R&D data were collected directly from national surveys, pharmaceutical associations and other publications. In such instances, the OECD, ANBERD and RICYT figures were updated accordingly.

Methods of estimation for missing data

Various factors resulted in incomplete or missing data for health R&D expenditures for a given country and year:

- Missing health R&D expenditure for the government or business enterprise sector.
- Unknown distribution of health R&D expenditure of a sector by sources of funds.
- Unpublished health R&D expenditures for the private not-for-profit sector.
- Missing data-point on a time series. Most countries report/publish health R&D data at regular time intervals, such as odd or even years, although some do so at irregular time intervals.

In such instances, methods of estimation have been used when appropriate to estimate the missing health R&D expenditures. Whenever possible, the health R&D expenditure for a missing year was extrapolated from the trend in GERD. The interpolation method was used by default, provided the outer data points were at reasonable time proximity from the missing point. This method is practical and easy to apply, and the error is limited to the extent that the two external points are accurate. Extrapolation methods not based on a secondary trend indicator such as GERD were avoided as the error resulting from such estimates is generally unbounded. The health R&D expenditure for a given sector was redistributed by sources of funds, such as distributing according to a preceding year's figures, distributed according to total the GERD, based on rules.

Reconciliation between 2001 health research and 1998 reported figures

A retroactive adjustment of the previously reported 1998 figures was used for consistency purpose. The 2001 figure for the global health R&D expenditure is US\$105.9 billion versus US\$73.5 billion published in 1998. This increase resulted from the growth in health R&D sources of data.

The adjustment due to changes in the estimation methodology was computed from the actual growth in total health R&D expenditure from 1998 to 2001, using time series of R&D expenditures from OECD. Due to the limited set of historical data available in LMIC, the corresponding growths may not be representative of all LMIC. Variation in local currency exchange rate relative to US dollars may have a substantial effect on the growth, as health research expenditures were converted to current US dollars for each country.

Global Burden of Diseases (GBD)

WHO has undertaken a new assessment of GBD for 2002 and this is used to provide an overview of the main causes of burden of disease in low- and middle-income countries and of major trends since 1990. The data sources and methods used in the GBD2000 study are documented on the World Wide Web (www.who.int/evidence/bod).

Principal risk factors of inaccuracies in estimations

The actual flows of funding for health research are difficult to trace due to various factors such as incompleteness, misclassification, risk of double counting, incorrect recognition of expenditures, and inconsistency between sources of data. Each of these may have varying and potentially substantial effects on the estimates.

Completeness/incompleteness

Health research expenditure data were not available for all countries. Indeed, performer reported data were available for most HIC but not for all LMIC. OECD provided performer reported data for LMIC that likely account for the greatest proportion of health research expenditures among these countries.

Risk of misclassification

Classification may have a substantial effect on the estimates of health R&D expenditures and their consistency over time. Changes in methods of classification vary, resulting in variations from one reporting period to the next, or from one country to another. For example, firms may be associated with more than one sector making it difficult to maintain a consistent classification scheme.

Risk of double counting

There are two sources of risk leading to double counting of health research flows.

(1) Flows through multiple agencies

Whenever funding flows through several agencies or other entities, a risk of double counting arises. The first entity may fund a project through a second entity and the amount is reported twice. Hence, the whole flow of funding needs to be tracked from source to final point of expenditure.

(2) Intramural and extramural expenditures

Due to the nature of the health research sector, the trend in the business enterprise sector is to outsource some research to other laboratories, research institutes or hospitals; for instance, to conduct clinical studies. This may arise, among other considerations, from the decision to focus on the value-added activities of the firm and the capacity to invest in expensive equipments, consumables and the maintenance of a laboratory. Although most large pharmaceutical companies own some research facilities, access to such services is critical to the development of smaller pharmaceutical companies.

To avoid double counting, extramural expenditure has been subtracted from the pharmaceutical R&D whenever possible. Unfortunately, the extramural pharmaceutical R&D expenditure often is not identified.

(3) Health research ODA and public funding in LMIC

Some of the ODA health research expenditures in LMIC may be included in the government sector. Hence, there is a risk of double counting between health research ODA and public expenditures on health in countries receiving ODA.

Recognition of expenditures

Health research expenditure estimates are based either on performers' surveys or from funders directly. Some variability may arise because such surveys may not include all funders or performers, although typically they do account for all the major players. Performer-based expenditures, either budgeted or actual, are recognized in the year expenses are incurred. In contrast, transferred funds from the funder may not be expended by the recipient during that same year, but rather over several years.

Consistency across different sources of data

Financial data on health research have been gathered from a variety of sources such as the OECD, RICYT and ODA data, The Foundation Center, pharmaceutical associations, national surveys and publications among others. The different classifications used for health R&D make it difficult to assure consistency across different sources of data. Estimates were produced using consistent assumptions and methodologies to assure the best possible data.

Appendix 3: WHO Member States by geographical region and income level

Country groupings according to WHO classification of countries, separated by level of income. (Source: Appendix 2 of WHO "Injury" 2000.)

AFRICAN REGION <hr/> 46 Member States Low- and middle-income Algeria Angola Benin Botswana Burkina Faso Burundi Cameroon Cape Verde Central African Rep. Chad Comoros Congo Côte d'Ivoire Democratic Rep. of the Congo Equatorial Guinea Eritrea Ethiopia Gabon Gambia Ghana Guinea Guinea-Bissau Kenya Lesotho Liberia Madagascar Malawi Mali Mauritania Mauritius Mozambique Namibia Niger Nigeria Rwanda Sao Tome and Principe Senegal Seychelles Sierra Leone	South Africa Swaziland Togo Uganda United Republic of Tanzania Zambia Zimbabwe <hr/> REGION OF THE AMERICAS <hr/> 35 Member States High-income Bahamas Canada United States of America Low- and middle-income Antigua and Barbuda Argentina Barbados Belize Bolivia Brazil Chile Colombia Costa Rica Cuba Dominica Dominican Republic Ecuador El Salvador Grenada Guatemala Guyana Haiti Honduras Jamaica Mexico Nicaragua	Panama Paraguay Peru Saint Kitts and Nevis Saint Lucia Saint Vincent and the Grenadines Suriname Trinidad and Tobago Uruguay Venezuela <hr/> SOUTH-EAST ASIA REGION <hr/> 10 Member States India Low- and middle-income Bangladesh Bhutan Democratic People's Republic of Korea Indonesia Maldives Myanmar Nepal Sri Lanka Thailand <hr/> EUROPEAN REGION <hr/> 51 Member States High-income Andorra Austria Belgium Denmark Finland	France Germany Greece Iceland Ireland Israel Italy Luxembourg Monaco Netherlands Norway Portugal San Marino Spain Sweden Switzerland United Kingdom Low- and middle-income Albania Armenia Azerbaijan Belarus Bosnia and Herzegovina Bulgaria Croatia Czech Republic Estonia Georgia Hungary Katakhtan Kyrgyzstan Latvia Lithuania Malta Poland Rep. of Moldova Romania Russian Federation Slovakia Slovenia Tajikistan The Former Yugoslav Rep. of Macedonia	Turkey Turkmenistan Ukraine Uzbekistan Yugoslavia <hr/> EASTERN MEDITERRANEAN REGION <hr/> 22 Member States High-income Cyprus Kuwait Qatar United Arab Emirates Low- and middle-income Afghanistan Bahrain Djibouti Egypt Islamic Rep. of Iran Jordan Lebanon Libyan Arab Jamahiriya Morocco Oman Pakistan Saudi Arabia Somalia Sudan Syrian Arab Republic Tunisia Yemen <hr/>	WEST. PACIFIC REGION <hr/> 27 Member States China High-income Australia Brunei Darussalam Japan New Zealand Republic of Korea Singapore Low- and middle-income Cambodia Cook Islands Federated States of Micronesia Fiji Kiribati Lao People's Democratic Republic Malaysia Marshall Islands Mongolia Nauru Niue Palau Papua New Guinea Philippines Samoa Solomon Islands Tonga Tuvalu Vanuatu Viet Nam <hr/>
--	--	--	---	--	---

