

Investing in Health Research and Development

Report of the Ad Hoc Committee on
Health Research Relating to Future
Intervention Options

*convened under the auspices of the
World Health Organization*



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Preface

Many factors shape the health of individuals and the great variability of health within and across populations. Genetic endowments, of course, play a role. Economic status strongly affects outcomes by working through a range of more proximal determinants—including consumption of food that is adequate in quantity and quality, access to clean water and satisfactory sanitation, adequate shelter and access to health services. Poverty, thus, is a major cause of poor health—and it also perpetuates it: investments in health have become essential to economic growth policies that seek to improve the lot of the poor. Education, like economic status, works through multiple channels to influence health. Educated individuals quickly learn and adopt sanitary behaviours, more efficiently use food, more effectively utilize health services for themselves and their families and are more likely to avoid health risks such as tobacco use. Measured effects of education on health prove consistently large.

Half of all the gains in human life expectancy of the past several thousand years have occurred in this century. Some of these gains have resulted directly from the improvements in economic and educational standards that have recently transformed the material lives of most—but far from all—of the world's population. Improvements in income and education account, however, for only part of this century's remarkable improvements in health. At the turn of the century the people of a country with an income level of US\$ 5 000 per capita (in purchasing power adjusted for inflation) would typically have had a life expectancy under 50 years; today the number is close to 75. Why this enormous difference *after* controlling for income? Important as income and education undoubtedly are, another factor—advance in scientific knowledge and its application both in creating powerful interventions and in guiding behaviour—has, perhaps, become even more important.

What are the implications for policy? One is that if knowledge gains prove even partially as important for future health improvements as they have in the past century—and this Report points to a number of reasons for expecting this to be so—then investments in health R&D will continue to have high payoffs in health status and economic productivity. Assuring an adequate level of R&D investment then holds strong claim on health budgets—a claim for more than the approximately 3% now committed. Equally important—or more important—is that the investments be *efficient* in generating useful new knowledge and products.

This Report deals with policy for health R&D investments of particular relevance to the poor in low-income and middle-income countries. We estimate these investments to have been about US\$ 2 billion annually in the early 1990s (out of a total of something over US\$ 50 billion spent globally on health R&D). The Report addresses the central question of how best to focus R&D investments when resources are tightly constrained. It also

addresses the institutional question of how to create an incentive and information environment that leads to efficient utilization of R&D investments, including the related issues of competitive resource allocation and of appropriate incentives for engaging the private sector more fully. Since most of the products of health R&D can be shared by many or all countries—in that sense they are international “public goods”—the Report deals with an additional set of issues involving the generation and coordination of international collective action. Collective action has been neglected, and the Report suggests directions that might be taken to correct this.

This Report results from the deliberations of the Ad Hoc Committee on Health Research Relating to Future Intervention Options and of staff work undertaken to inform those deliberations. Two lines of thought led to the formation, under the auspices of the World Health Organization, of the Ad Hoc Committee. The first, summarized in the preceding paragraphs, pointed to the central role that advances in knowledge have played (at least in the past century) in driving the enormous improvement in human health. In particular, the World Bank's *World development report 1993: investing in health* (World Bank 1993) had reached this conclusion and pointed to the importance of improving the use of international assistance for health by paying more careful attention to the role of knowledge generation and dissemination. At about the same time several private foundations that had actively supported tropical disease research noted not only that their own efforts were likely to decline but, also, that replacement funding sources remained to be identified. These foundations and a range of other investors in health R&D then joined with WHO in establishing the Ad Hoc Committee to address priorities for health R&D, prospects for funding, and institutional changes (at both the national and international level) that might enhance the productivity of ongoing R&D expenditures.

The Ad Hoc Committee's mandate was broad: in addition to research, it was to address *development* of the products and procedures that translate research findings into practical tools (and, therefore, it was to pay careful attention to the role of the private sector); it was to include considerations of nutrition and family planning; it was to address issues of behavioural science and health systems research as well as biomedical and clinical R&D; and it was to operate under the assumption that, at best, only very limited additional resources from outside the health sector would be available for financing health R&D in the future.

The composition of the Ad Hoc Committee reflected this broad mandate. Its core membership included the chairs or representatives of the scientific advisory panels for WHO programmes with major research components; but membership was extended to be broadly representative of the disciplines contributing to health R&D. (The Committee Chair, for example, is an econo-

mist; the Co-Chair an immunologist.) Senior representatives of research-oriented pharmaceuticals houses served on the Committee, as did a number of individuals with experience in the highest levels of public service. The Report results from their deliberations (mostly in small groups) over a period of several years. While all members of the Committee agree with the broad thrust of the Report, it is fair to say that each member of the Committee—including the Chair—will differ with a number of specific points in the Report. The Committee sought to inform debate with its Report; no effort was made to reach consensus on every point.

Too often priorities for public sector health R&D investments are determined with little concern for the magnitude of the problem to be addressed, for the extent to which scientific judgement supports the possibility that new products and initiatives will be more cost-effective than available alternatives, or for ongoing efforts elsewhere. These considerations figure prominently in private sector product development decisions. The Committee endeavoured to generate information relevant to an analytical approach that combines use of available quantified data with informed judgement. This approach facilitated identification of specific high priority product development opportunities and led the Committee to the conclusion that available R&D resources would be more productive if concentrated on these “best buys” rather than remaining dispersed.

Because of limited time and resources, this approach could not be applied across the whole field of health R&D. The Committee nonetheless generated a wealth of information that was useful in its work and that, we hope, will prove valuable to others in assessing policy for health R&D and resource allocation. In particular, the Committee’s commitment to careful consideration of the problem of the *magnitude* of disease burden has led to a major reassessment of global patterns of cause of death and disease burden, to assessment of burden resulting from major risk factors (to guide resource allocation concerning prevention), and to projecting burden forward to the year 2020. This work on disease burden substantially revised and extended work undertaken earlier for the World Bank and the World Health Organization. Annexes 1 and 2 summarize findings from this effort; detailed results appear in a series of companion volumes to this Report, the Global Burden of Disease and Injury Series, edited by C. J. L. Murray and A. D. Lopez and published by Harvard University Press for the World Health Organization and the World Bank.

What, then, are the conclusions reached and directions suggested? The Committee concluded that four challenges to health systems will remain important for a decade or more to come and that specific R&D initiatives would contribute significantly to meeting these challenges.

- Despite progress there remains a huge and unnecessary burden of infectious disease among the poor that can be addressed with available cost-effective interventions. Addressing this *unfinished agenda* is most-

ly a matter of political will and (modest) commitment of resources. But R&D can help through operational and behavioural research to facilitate implementation (often by developing and evaluating linked packages of care, such as the proposed Mother-Baby package) and by selective development of new tools, including improvements in vaccines.

- A more global class of challenges results from the *continually changing nature of microbial threats*. New pathogens—such as HIV—and evolution of drug-resistant variants of familiar ones (e.g. ones causing tuberculosis and malaria) create needs for biomedical understanding, for understanding of systemic determinants of the spread of drug resistance, and for new drugs and vaccines.
- Low-income and middle-income countries increasingly face major (and hitherto neglected) epidemics of noncommunicable diseases and injury. Selected psychiatric conditions, heart disease, stroke and road-traffic accidents dominate the disease profile we project for these countries for the year 2020. R&D is required to ascertain ways of preventing and managing these conditions under budgetary constraints far more stringent than in the high-income countries, which have dealt with the problems far longer.
- Finally, *health systems themselves vary greatly in how efficiently and equitably they provide services*. Research can assist decision-makers to solve specific problems, to learn from the experience of others, and to place the performance and characteristics of their systems into international and historical context. Such research should pay careful attention to measurement of performance and should include investigation into health systems and their finance, the determinants of the behaviour of health care providers and the behaviour of individuals and households.

In some cases additional resources (probably from lower priority areas within national health budgets or health aid budgets) will be required to meet these R&D needs adequately. In many cases institutional change will be necessary to create the information and incentives required for efficient resource allocation. At the international level resource allocation has often lacked focus (resulting in failure to bring results to the point of application) and has neglected important conditions and issues while providing (relatively) generously for less important ones. Reform is needed. Successful models of competitively driven international funding (and experience-sharing) networks should be applied to currently neglected clusters of conditions. For development of new drugs and other tools, the Report proposes establishing a Health Product Development Facility to address problems that the private sector now neglects; this would be accomplished in part by improving incentives for engaging private sector talent.

In addition, and importantly, a mechanism is needed for exchanging ideas about progress and priorities in R&D, for tracking flows of funding and identifying im-

portant gaps, and for creating an environment where investors and research institutions can agree on approaches to close those gaps. To meet this need, the Committee proposes creation of a Forum for Investors in International Health R&D. The Report elaborates these proposals.

Global challenges demand, in some sense, a global response. All nations share the fruits of R&D. Even though each country may invest a relatively modest sum towards collective goals, the aggregate effort potentially benefits all substantially. Collective action is the economically rational approach to "public goods" such as R&D; here, responsibility for catalysing collective action lies principally in the hands of the global community. Far from overshadowing action at the national level, global efforts help both to make national R&D efforts more productive and to lead to a global result that exceeds the sum of national ones.

Thus, among the many competing demands on the funds allocated to international assistance for health, those contributing to generation of the new knowledge, products and interventions that can be shared by all have special merit.

Yet the commitment to R&D has been declining. If the international system collectively fails to invest in productive R&D—or to generate incentives for individual countries or the private sector to do so—then, in all likelihood, great opportunities to improve human welfare and productivity will be missed entirely. The chal-

lenge to donors in times of budgetary stringency is to recognize that their own comparative advantage lies in supporting the generation and dissemination of knowledge—knowledge that, with its multiplier potential for empowering individuals and health systems, can yield a health impact that far exceeds what donors can achieve with their limited capacity to finance or deliver services.

We complete this preface at the final meeting associated with the Ad Hoc Committee's work. That meeting—convened by the Swiss Agency for Development and Cooperation, and hosted by the World Health Organization in Geneva, 27–29 June 1996—brought together researchers, government officials, NGOs and investors in research to review the final draft of this Report. Participants in the meeting raised a range of critical points and suggested changes in emphasis or priority; but, on the whole, the meeting conveyed a broad sense of agreement on the direction the Report suggests. In particular, participants endorsed the Report's recommendation for a Forum on International Health R&D that brings together investors in R&D with other stakeholders for discussions on priorities—discussions to be informed by ongoing analytic efforts. We have every hope that the forum will prove to be a mechanism for mobilizing the efforts that will lead to a growing knowledge base for improving the health, well-being and productivity of the poor.

29 June 1996

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Addresses, phone numbers and brief biographical sketches of the study participants may be found in Appendix A.

Acknowledgements

Three individuals made critical contributions to the Committee's work. Dr Thomas Nchinda of WHO both managed and informed the Committee's work throughout the past two years; his good cheer and substantive contributions were of great value. Mr Leslie Evans of the Center for Pacific Rim Studies, University of California, Los Angeles, served as Production Editor for the Committee's Report; in this role he contributed to and managed the editing process, oversaw typesetting and layout and made all arrangements for publication. His skill, long hours and good humour contributed enormously. Ms Phyllida Brown, a free-lance science writer, wrote the Report. Working closely with the Committee and WHO staff, she translated ideas, background materials, fragmented draft materials and the Committee's conclusions and recommendations into clear English. She played an invaluable and central role in the Committee's work.

The Report's genesis lay both in recognition of the central role that generation of new knowledge has played—and, in all likelihood, will continue to play—in improving health and in the concern of several agencies that fragile funding prospects threatened future health

R&D relevant to the needs of low-income and middle-income countries. In particular, the Edna McConnell Clark Foundation, the John D. and Catherine T. MacArthur Foundation and the Rockefeller Foundation convened a meeting in Bellagio, Italy, in 1993 to address the problem of providing a solid financial basis for health R&D. The proposal for this Committee's work emerged from that meeting. Other agencies then joined the original three in providing WHO with the financial resources to undertake this effort; these included the Wellcome Trust, the Canadian International Development Research Centre, the International Health Policy Programme, the World Bank and the bilateral development assistance agencies of the governments of Australia, Norway, Sweden, Switzerland and the United Kingdom. The financial contribution of these agencies, their ongoing support and their critical reactions to early drafts facilitated the work of the Committee throughout.

We close on a sad note. Professor B.O. Osuntokun, a member of the Ad Hoc Committee and a distinguished neurologist, died during the period of the Committee's work. All of us who worked with him on this effort remember him with respect and fondness.

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Accompanying volumes

An important input to and product of the Committee's work was a major revision of available data on mortality by cause and the burden of disease, extension of that work to assess burden from selected risk factors and projections of mortality and burden to the year 2020. Results appear in a 10-volume series—the Global Burden of Disease and Injury Series, edited by Christopher J. L. Murray and Alan D. Lopez. The series is being published by Harvard University Press on behalf of the World Health Organization and the World Bank.

Two volumes in the series appear simultaneously with this Report; the remaining volumes will appear over the coming year. Available now are:

1. *The global burden of disease: methods, results and projections*—edited by Christopher J. L. Murray and Alan D. Lopez. Cambridge, MA, Harvard University Press, 1996.
2. *Global health statistics: incidence, prevalence and mortality estimates for over 200 conditions*—by Christopher J. L. Murray and Alan D. Lopez. Cambridge, MA, Harvard University Press, 1996.

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Abbreviations and acronyms

ACHR—Advisory Committee on Health Research	IDRC—International Development Research Centre (Canada)
ACTION TB—programme of Glaxo Wellcome	IFPRI—International Food Policy Research Institute
APOC—African Programme for Onchocerciasis Control	IHPP—International Health Policy Programme
ARI—acute respiratory infections (also used to refer to the WHO ARI control programme)	IHRCs—international health research centres
BCG— <i>bacille Calmette-Guérin</i>	IMSC—Integrated Management of the Sick Child (also referred to as IMCI, Integrated Management of Childhood Illness, now the official name)
CDD—Diarrhoeal Disease Control programme (WHO)	INCAP—Instituto de Nutrición de Centroamérica y Panamá
CDR—Division of Diarrhoeal and Acute Respiratory Disease Control (WHO)	INCLEN—International Clinical Epidemiology Network
CG—Consultative Group	IRRI—International Rice Research Institute
CGIAR—Consultative Group on International Agricultural Research	ISNAR—International Service for National Agricultural Research
CHRD—Commission on Health Research for Development	LAC—Latin America and the Caribbean*
CIMMYT—Centro Internacional de Mejoramiento de Maíz y Trigo	MDR—multidrug-resistant
CIOMS—Council for International Health Organizations of Medical Sciences	MDT—multidrug therapy
CMR—Centre for Medicines Research	MEC—Middle Eastern crescent*
COHRED—Council on Health Research for Development	MRC—Medical Research Council (UK)
DALY—disability-adjusted life year	NCD—noncommunicable disease
DEC—diethylcarbamazine	NGO—nongovernmental organization
DOTS—directly observed treatment, short course, for tuberculosis	NIAID—National Institute of Allergy and Infectious Disease (USA)
EHIP—Essential Health Interventions Project (Tanzania)	NIH—National Institutes of Health (USA)
EMEs—established market economies*	NSF—National Science Foundation (USA)
ENHR—Essential National Health Research	OAI—other Asia and islands*
EPI—Expanded Programme on Immunization	OCP—Onchocerciasis Control Programme
EPI-plus—Expanded Programme on Immunization plus micronutrient supplements and locally relevant antigens	ODA—official development assistance
FAO—Food and Agriculture Organization	OECD—Organization for Economic Cooperation and Development
FDA—Food and Drug Administration	ORS—Oral Rehydration Solution
FSE—formerly socialist economies of Europe*	ORSTOM—L'Institut Français de Recherche Scientifique pour le Développement et Coopération (<i>Note: acronym continues to be used, although it represents the old, no-longer-used name Organisation de Recherche Scientifique des Territoires d'Outre Mer</i>)
GDP—Gross Domestic Product	ORT—oral rehydration therapy
GPA—Global Programme on AIDS (WHO)	OTA—Office of Technology Assessment (USA)
GPV—Global Programme for Vaccines and Immunization	PCR—polymerase chain reaction
GUF—general university funds	PEM—protein-energy malnutrition
HHMI—Howard Hughes Medical Institute (USA)	PMA—Pharmaceutical Manufacturers Association
HRP—Special Programme of Research, Development and Research Training in Human Reproduction (WHO)	RCS—research capability strengthening
IARC—International Agency for Research on Cancer	REMO—rapid epidemiological mapping of onchocerciasis
ICDDR,B—International Centre for Diarrhoeal Disease Research, Bangladesh	SAMRC—South Africa Medical Research Council (South Africa)
	SAREC (Sweden)—Swedish Agency for Research Cooperation with Developing Countries
	SIC—Standard Industrial Classification
	STAC—Scientific and Technical Advisory Committee (of TDR)
	STD—Science and Technology Development Programme (of the European Union)
	STDs—sexually transmitted diseases

*These are regional groupings of countries as used in this Report. Appendix C lists all eight regions and the countries included in them.

TAC—Technical Advisory Committee
TDR—UNDP/World Bank/WHO Special Programme
for Research and Training in Tropical Diseases
UNDP—United Nations Development Programme

UNFPA—United Nations Population Fund
USAID—United States Agency for International De-
velopment