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Item Type	Book
Authors	Matlin, Stephen
Publisher	Pro-brook Publishing Limited
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Global Forum
for Health Research
HELPING CORRECT THE 10|90 GAP

Global Forum Update on Research for Health Volume 2

Poverty, Equity and Health Research



Global Forum Update on Research for Health Volume 2

Poverty, Equity and Health Research

Edited by **Stephen Matlin**



Pro-Brook London

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Pro-Brook Publishing
Alpha House
100 Borough High Street
London SE1 1LB
United Kingdom

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ISBN 2-940286-36-1

First published 2005

The Global Forum Update on Research for Health Volume 2: poverty, equity and health research



Article by Pramilla Senanayake

Health disparities exist within and between populations in all parts of the world, but the largest gaps are seen between high-income countries (HICs) and low- and middle-income countries (LMICs) – for example, when comparing indicators such as life expectancy and maternal and infant mortality. There have been concerted efforts made and initiatives undertaken to close the gaps, including the Health for All movement, the growing focus on health as a vital component of development and the setting of specific health targets within the Millennium Development Goals.

Nevertheless, some of the gaps have grown wider in recent years. This is partly due to biological factors, e.g. the development of resistance to drugs available for treatment of tuberculosis and malaria, and the emergence of new infectious diseases such as HIV/AIDS. Another factor has been the global spread of noncommunicable diseases, which were for a long time regarded as 'diseases of affluence' but are now overtaking communicable diseases as the main burden of disease in many LMICs. The multiple disease burden experienced by many developing countries is compounded by the higher rates of injuries they experience, compared with HICs and has challenged countries to improve the structure and functioning of their health systems.

While much of the mortality and ill-health resulting from these factors can be prevented by improving the availability and quality of health products and services, this is not enough. During recent years, an increasingly clear and detailed picture has emerged of the ways that poverty, exclusion from education and social disadvantages – including discrimination based on biases related to gender, ability, social class/caste and ethnicity – all lead to inequities in health.

Research has a vital role to play in reducing these inequities, through examination of the underlying causes and effects of social and economic disadvantages on health, through experimental investigations of approaches to prevent or overcome them and through studies of the efficiency and effectiveness of programmes designed to address them.

The articles in this volume of the *Global Forum Update on Research for Health* focus on the theme of poverty, equity and health research, which is also the theme of Forum 9 held in Mumbai on 12–16 September 2005. We are very grateful to all of the contributors for generously giving their time to set down their experiences and perspectives, and we look forward to a vigorous debate about the way forward, both in and after Forum 9. ❑

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

Introduction: poverty, equity and health research



Article by Stephen Matlin

The dramatic overall gains in health experienced by the world's population in the last century have been very unevenly distributed and increasing divergences have especially been noted within the last couple of decades. This is highlighted by data[1] for the young, the poor and those living in Africa. Thus, of the 57 million deaths in 2002, one in five involved children under the age of 5 years and of these 10.5 million deaths, 97% were in low- and middle-income countries (LMICs). Life expectancy at age 15 years increased by 2–3 years for most regions in the last 20 years, but decreased by nearly 7 years from 1980–2001 in Africa, and decreased by 4.2 years for males and 1.6 years for females in the transition countries of Eastern Europe. Across the world, the poor die younger (Figure 1).

Along with a number of other factors, improving public health and providing treatment for diseases have contributed to the gains that have been made in health. Both these areas have been underpinned by the acquisition and application of new knowledge and technologies for health that have resulted from investments in research and development. But despite the gains, why have health inequities persisted? Three complementary factors seem to be at play:

- Lack of investment in health systems in lower income countries
- Lack of attention to determinants of health that originate outside the health sector, especially economic and social determinants
- Lack of investment in appropriate health research.

The impetus to address these inequities in health has come from several sources. In particular, in recent years there has been growing recognition of health as:

- A human right
- A major aspiration of all people everywhere
- Both an outcome of and a key contributor to development. Health spending is increasingly viewed not as expenditure but as an investment with very high rates of return, and improving health as vital to supporting poverty alleviation and reducing inequities.[2]

The case for health as a necessary component of development was made explicit by the Commission on Macroeconomics and Health[3] (CMH) and recognized in the setting of the Millennium Development Goals (MDGs). The contribution of the CMH will be complemented by the newly created Commission on Social Determinants of Health, which was established in March 2005 and will pursue a 3 year programme of work.[4] With the evidence gathered by the 'Reaching the Poor' project[5] conducted by the World Bank, this combination of efforts is providing the world with a clear and detailed picture of the ways that poverty and social disadvantages, including discrimination based on biases related to gender, ability, social class/caste and ethnicity, all lead to inequities in health. Research must continue to play a central role, both in uncovering these inequities and in leading the way to explore effective remedies.

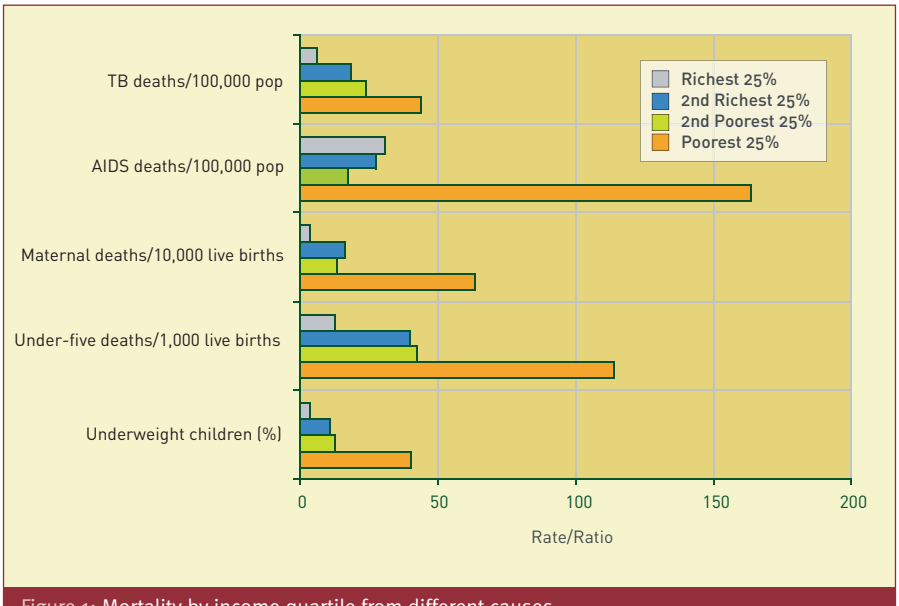


Figure 1: Mortality by income quartile from different causes

Imbalances in financing health research

The inequalities observed in the health of populations are mirrored not only in an uneven distribution of investments in health systems, but also in imbalances found in health research. Most of this research has been conducted in and for the needs

of higher income countries, so that both the technologies and the knowledge about how to apply them in local settings have been less relevant to the needs of lower income countries.

As a contribution to the debate about prioritization in the way that resources are used for health research, the Global Forum for Health Research has undertaken the tracking[6,7] of expenditures on health research and development (R&D). Figure 2 illustrates the more than three-fold growth in these expenditures in the period 1986–2001. The first calculation, made by the Commission on Health Research for Development,[8] put the global expenditure on health R&D at US$30 billion for 1986, and they estimated that at that time only some US$1.6 billion (or 5%) of this was devoted directly to addressing the health problems of developing countries where 90% of the world's population lived. This imbalance has subsequently become known as the '10/90 gap' – an expression that still serves qualitatively as a symbol of inequity in the distribution of research resources and a rallying call for efforts to focus attention on neglected areas of health research.

Subsequent estimates of global health research expenditures made by the WHO Ad Hoc Committee on Health Research Relating to Future Intervention Options[9] for 1992 and by the Global Forum for Health Research[6,7] for 1998 and 2001 show that global spending on health research rose by US$4-5 billion/year during the period up to 1998, but then accelerated during the period to 2001 with an average annual rate of increase of US$7 billion/year, so that global spending passed the US$100 billion/year mark around the year 2000.

Of the US$105.9 billion expended in 2001, 44.0% came from the public sector, 48.3% from the private-for-profit sector and 7.6% from the private not-for-profit sector. The largest contributors in all three of these sectors are United States based: the biggest single public-sector funder of health research is the National Institutes of Health, whose allocations from Congress increased massively from US$11.6 billion in 1996 to over US$27 billion in 2004; 43% of the private sector expenditure on R&D occurred in the United States in 2001; and the Gates Foundation, created in 2000, has rapidly become the largest not-for-profit private sector contributor to research on neglected diseases.[7]

Despite these large increases in spending, research on many of the health problems of LMICs continues to receive inadequate resources. For example, the Global Forum has estimated[7] that combined spending on R&D for HIV/AIDS, tuberculosis (TB) and malaria (which are targeted for major reductions in impact by 2015 in the MDGs, and which collectively accounted for 11.4% of the global burden of disease in 2002) was of approximately US$8.4 per disability adjusted life year (DALY) in 2001 – that is, approximately an order of magnitude below the average global spending on R&D for all health research of around US$72 per DALY in 2001.

The changing profile of ill-health in LMICs

The global studies of burden of disease (BoD) conducted periodically by the WHO since 1990 have revealed profound changes in the world's profiles of mortality and morbidity. Figure 3 shows the BoD data[1] for the world in 2002, with causes of mortality being aggregated into three groups:

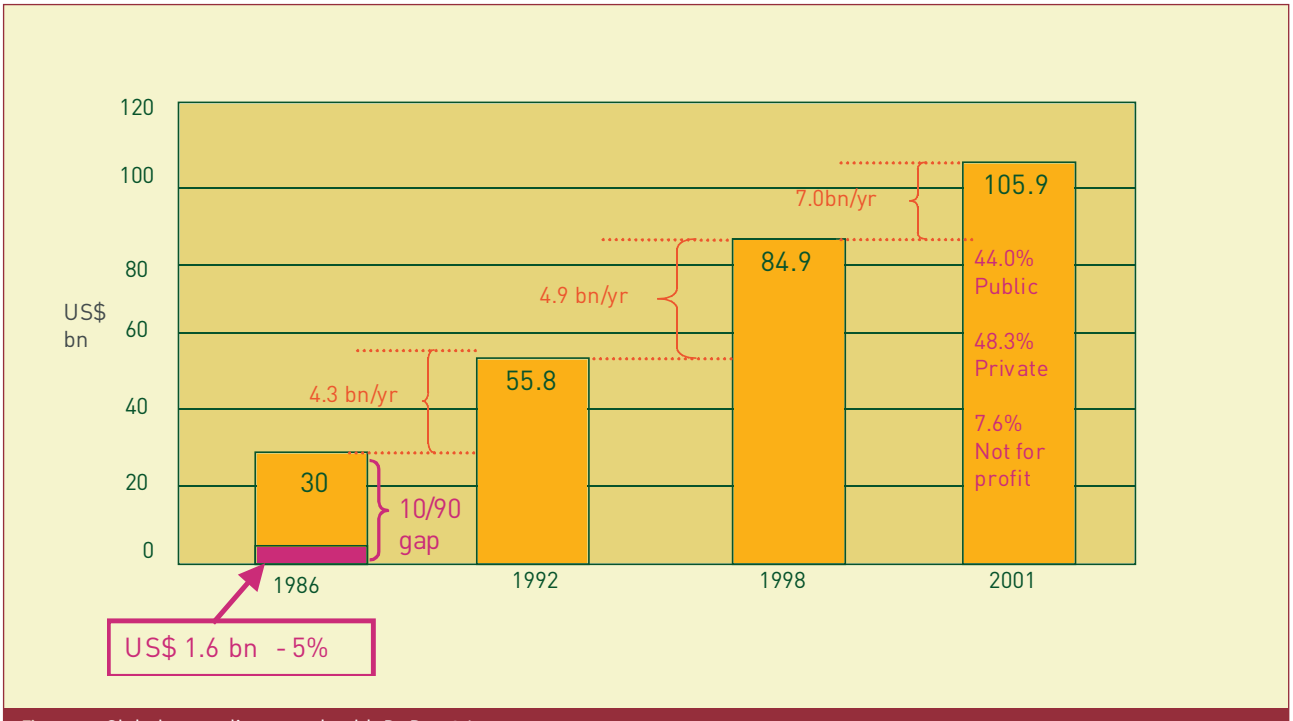


Figure 2: Global expenditures on health R&D 1986–2001

- **Group 1:** communicable diseases, maternal and perinatal conditions and nutritional deficiencies
- **Group 2:** noncommunicable conditions (NCDs), including cardiovascular disease, diabetes, cancer and mental and neurological conditions
- **Group 3:** injuries, both intentional and unintentional

It will be noted that, for high-income countries (HICs), the BoD in 2002 was dominated by noncommunicable conditions, whereas for LMICs the situation was more complex. A long-standing stereotype has held that noncommunicable conditions are 'diseases of affluence' characteristic of developed countries, while developing countries mainly suffer from communicable diseases. It is clear that this no longer applies and that a major epidemiological transition has taken place: there is an almost equal level of BoD due to Group 1 and Group 2 for LMICs and a significantly higher rate of DALYs in LMICs due to injuries.

The aggregated data for all LMICs portrayed in Figure 3 masks large variations in patterns both between and within different regions. When the BoD data is disaggregated by both cause and by country groups (Figure 4), it is notable that, among LMICs, China now has a pattern of disease that is heavily dominated by NCDs; for India, there is a roughly equal level of Group 1 and Group 2 causes of BoD; while for Africa, the massive impact of HIV/AIDS, together with TB, malaria and other infectious diseases, results in heavy domination of the profile by Group 1 conditions.

The future agenda for health research must now take account of these changing and varying patterns of disease burden. In this context, health research – broadly defined as the creation of new knowledge and technologies – encompasses not only biomedical research (leading to the development of new drugs, vaccines, diagnostics and medical appliances), but also health policy and systems research, social sciences and behavioural research, and operational research. All of these forms of research taken together form the underpinning for both medicine (treating ill health in individuals) and public health (promoting health in populations).

Imbalances in capacity for health research

The research agenda is not only for the richer countries to address. It is vital that LMICs establish their own capacity for essential health research at the national level, as advocated in 1990 by the Commission on Health Research for Development[8] and subsequently facilitated by the Council on Health Research for Development (COHRED). To finance essential research, the Commission recommended that developing countries should spend the equivalent of 2% of the government's health budget on health research, and that this should be completed by the allocation of 5% of donors' health assistance for health research and research capacity spending. According to data collected by the Global Forum[7] in 1998, no developing country had reached the 2% level of

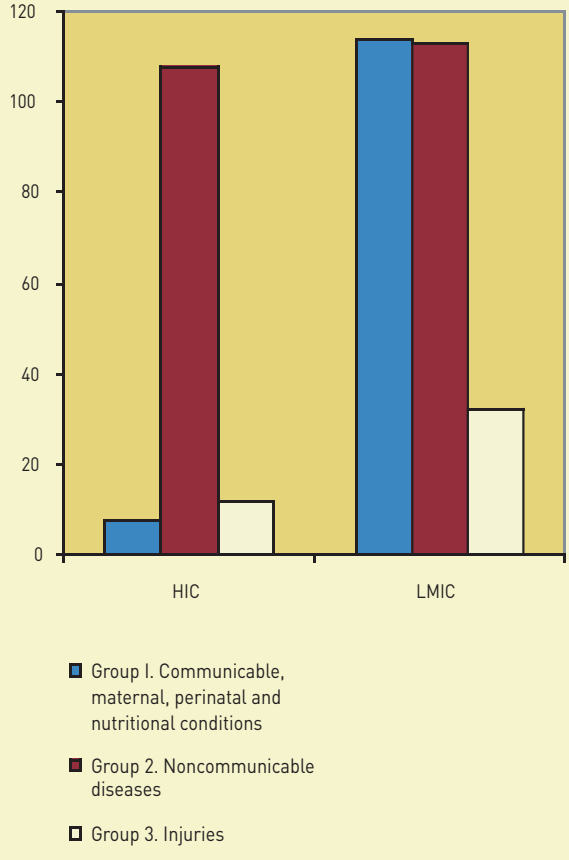


Figure 3: Burden of disease patterns for 2002

spending on health research, whereas by 2001 at least four countries – Mexico, Cuba, Brazil and India – had done so. While this represents some progress, these figures should be viewed in the context of the very different levels of government spending on the health sector as a whole, as a proportion of gross domestic product (GDP), which can vary from less than 1% to more than 6%.

It is encouraging that the Ministerial Summit on Health Research,[10] convened in Mexico City in November 2004 and partially joined with the 8th Forum of the Global Forum for Health Research,[11] added its voice to the recommendation for LMICs to reach the 2% level of spending on health research and this was subsequently endorsed by the WHO Executive Board at its meeting of May 2005.

In 1996, the WHO Ad Hoc Committee[9] identified three research capacities that are essential to development: capacities for the generation of new knowledge, and research capacities in terms of human resources and institutions. We would add a fourth: in many cases, the limiting factor in the health research capabilities of countries is the lack of capacity utilization, which limits the extent to which a country is able to sustain and take advantage of investments made in research capacity strengthening.

Consideration of the problem of research capacity utilization directs attention to some important questions:

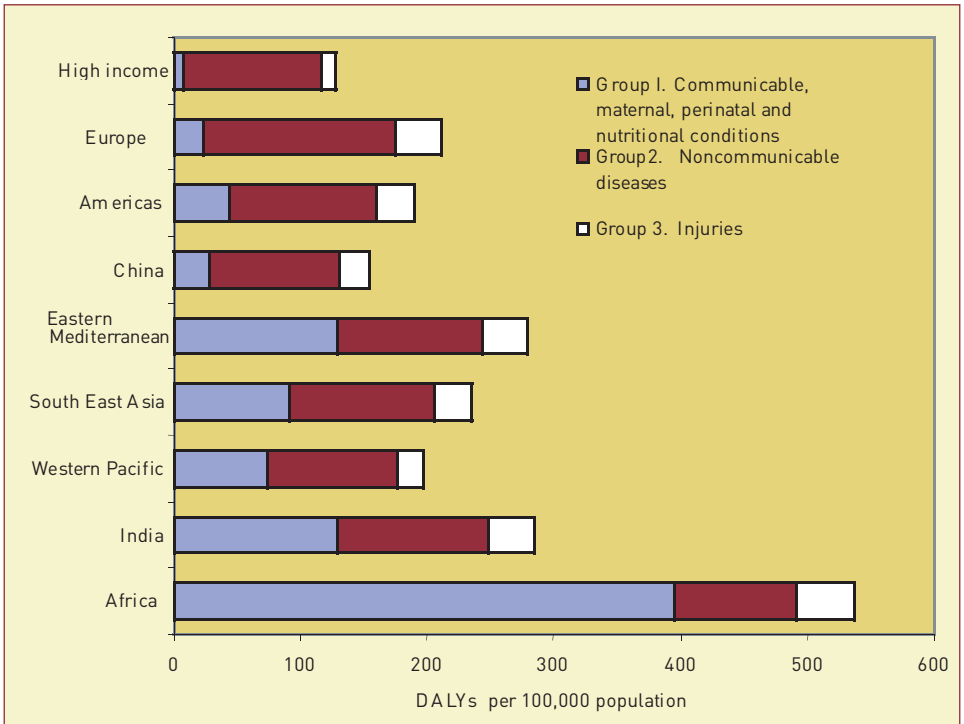


Figure 4: Burden of disease by major cause groups and country groups, 2002

Who sets the research goals? What are the drivers of research? Who uses the results? Overall, these questions can be seen as components of a larger issue: is there a health research system? Such a system must connect three essential components: the need for research, the performance of research, and the use of research (Figure 5). Without such a system in operation, there is likely to be wastage of resources and capacities for research on one hand, and on the other a failure of the health system to be evidence-based and priority-driven.[12] This is intimately connected with the problem of brain drain and with issues of the priority given to developing and resourcing the local infrastructure necessary to support research.

The growing capacities of some developing countries to conduct their own R&D has led to the identification[13] of a number of innovating developing countries (IDCs) that are characterized by:

- Growing capacity to undertake 'health innovation', which includes: development of new drugs, vaccines and diagnostics; new techniques in process engineering/ manufacturing; and new approaches/policies in health systems and services
- Spanning the spectrum from innovative research to product delivery.

Innovating developing countries have demonstrated their capacities for high quality research through their production of leading scientific papers that are highly cited in the world's literature and by the growing presence of scientists from LMICs among the authors of United States patents in drugs, vaccines and pharmaceuticals.[14]

Delivering the promise of health research

The trends in disease burden and in health research resources and needs summarized in this article point to a series of important opportunities that must be grasped and priorities that must be applied if the promise of health research is to be delivered:

- New technologies, including genetics and biotechnology offer great opportunities, but they need to be developed and applied to the problems of all populations, including those that are poor and disadvantaged
- Health systems have emerged as central to delivering better health, but need to be strongly supported by health policy and systems research and operational research
- The epidemiological transition to noncommunicable diseases requires a much greater attention in lower income countries to health promotion and disease prevention. This requires cross-sectoral action in many fields, supported by research
- There is a new conceptualization of 'global health' emerging, which is bringing important recognition of the connectivity between global and local health problems
- There is an evolving recognition of the role of health research systems, which can provide the framework of organizational principles and practices to ensure that health research is needs-driven and that the results are used to inform policy and practice. This requires a systemic approach, involving: investments in financial, institutional and human resources; application of rational and systematic processes to set health research priorities and to allocate resources accordingly; development of a 'culture of research' in which both the producers and users of research are engaged with one another and share common ground in the generation and application of new knowledge and tools; and monitoring and evaluating the results, not only in terms of the creation of new knowledge and tools but also their translation into practice and their health impact.

The Global Forum Update on Research for Health, Volume 2

This year we have again assembled a diverse range of articles that have been commissioned from leading international experts from HICs and LMICs, including Ministers of Health and other policy-makers, officials in agencies concerned with health and development, representatives of the private sector and public-private partnerships, and academics and leading figures in research institutions. They have been asked to give their perspectives on the health research issues and challenges relating to poverty and equity.

The Global Forum for Health Research expresses its gratitude to all these contributors, who have provided clear, concise and authoritative overviews and perspectives on these critical topics. We also acknowledge the many contributions from colleagues and collaborators behind-the-scenes who provided ideas and guidance – including Richard Feachem (Executive Director, the Global Fund to Fight AIDS, TB and Malaria) who kindly agreed to Chair the Editorial Board again, and Claudia Garcia-Moreno (WHO) and Chen Reis (Sexual Violence Research Initiative) who assisted with gender perspectives. We thank Tim Probart and Trevor Brooker of Pro-Brook Publishing for continuing to partner with the Global Forum for Health Research in the development of this vehicle for delivering important messages about the vital role that health research must play in achieving better health for all people. ❑

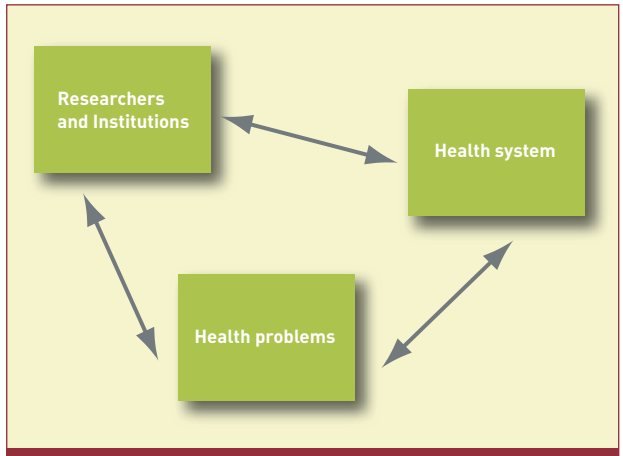


Figure 5: Linkages in the Health Research System

Professor Stephen Matlin *is Executive Director of the Global Forum for Health Research and a Senior Research Fellow in Oxford University. His former positions include Chief Education Adviser in the UK Department for International Development, Director of the Health and Education Departments in the Commonwealth Secretariat, London and Professor of Biological Chemistry, Warwick University, UK.*

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Global Forum for Health Research

The Global Forum for Health Research is an independent international foundation established since 1998 in Geneva, Switzerland. It works to promote more health research to combat the neglected diseases and conditions that are major sources of ill-health in developing countries.

Health research encompasses a wide spectrum of activities that generate new knowledge and technologies – ranging from biomedical research that creates new drugs, vaccines and diagnostics, to health systems and policy research which ensures that health systems are better informed and managed, to social science and operational research to improve access and uptake and to help us better understand what affects the health and the choices of people in the community.

The Global Forum works to encourage all these aspects of health research to focus more on the health needs of poor, marginalized and disadvantaged people everywhere. It does this through advocacy, brokerage and catalytic roles and by serving as a generator and incubator of ideas and initiatives. This can be achieved by creating a platform for debate and by acting as a convenor of individuals and groups representing all types of interest in health research and its benefits.

The annual Forum meeting has become a key gathering on the agenda of those who direct, prioritize, fund and carry out research. The meetings have proved successful in stimulating and facilitating dialogue and exchange between a very wide range of actors from all parts of the world, providing the opportunity for groups to come together to explore how best to increase research into a particular problem area.

Many of the themes that feature in the annual Forum are also pursued as elements of the annual work programme of the Global Forum and through its collaborations with partners. Key areas of work include priority setting, equity, gender, poverty, research capacity strengthening and studying resource flows for health research and the relationship between resource flows and burden of disease.

Partnerships and collaboration are integral to the Global Forum's strategies for amplifying its messages, leveraging action and increasing its impact. In addition to the partnerships formed with the Networks and Initiatives that the Global Forum has helped create and nurture (see Box 3), we work closely with the World Health Organization and we are developing an especially close relationship with the Council on Health Research for Development (COHRED). Early in 2005, the Global Forum and COHRED signed a Memorandum of Agreement, formalizing their intensive collaboration that complements and supports each other's activities at country, regional and international level for the benefit of health research for development.

Other Geneva-based agencies such as the Special Programme for Research and Training in Tropical Diseases (TDR), Medicines for Malaria Venture (MMV), and Drugs for Neglected Diseases Initiative (DNDi) are part of our close network. The Global Forum is also committed to partnership with research councils, national institutes of health, researchers, NGOs and community-based organizations, fostering systematic collaborations to improve global health.

The flagship, biennial 10/90 Report on Health Research has become a widely known and cited text and regular publications on resource flows are eagerly awaited. The first volume of a new series targeted at policy-makers, Policies for Health Research, will be published before the end of 2005 and subsequent volumes will continue through 2006, focusing on areas such as research capacity strengthening, priority setting, burden of disease, child health, gender, maternal health, public-private partnerships and resource flows. All our publications can be consulted, printed and ordered from our website. Paper copies are available free of charge. New titles are in preparation for early 2006. ❑

Box 1 | Annual meetings

- 2002: **Forum 6**, Arusha, Tanzania
- 2003: **Forum 7**, Geneva, Switzerland
- 2004: **Forum 8**, Mexico City: Health research for the Millennium Development Goals, held jointly with the WHO Ministerial Summit on Health Research
- 2005: **Forum 9**, Mumbai, India, 12-16 September: Poverty, equity and health research
- 2006: **Forum 10**, Cairo, Egypt, 29 October to 2 November: Combating disease and promoting health

Box 2 | Initiatives and networks

- Alliance for Health Policy and Systems Research
  www.alliance-hpsr.org
- Global Network for Research in Mental and Neurological Health
  www.mental-neurological-health.net
- Initiative for Cardiovascular Health Research in the Developing Countries
  www.ichealth.org
- Initiative on Child Health and Nutrition Research
  www.chnri.org
- Road Traffic Injuries Research Network
  www.who.int/violence_injury_prevention/road_traffic/en
- Sexual Violence Research Initiative
  www.who.int/svri/en

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Global Forum for Health Research
Publications

Current

10/90 REPORTS

In 2001, the world spent approximately US$ 106 billion on health research, of which 44% by the public sector, 48% by the private for profit sector and 8% by the private not-for-profit sector. Despite these positive increases, there is still a massive under-investment in health research relevant to the needs of low- and middle-income countries – the imbalance of the "10/90 gap". The 10/90 Reports describe the progress made towards correcting the "10/90 gap" by focusing on research activities and initiatives that address problems of middle and lower income countries and generating funds to support these initiatives.

The 10/90 Report on Health Research 2003-2004

also available as a CD-ROM

May 2004

The report focuses on health and health research as sound economic investments; priority setting in health research; progress in measuring the "10/90 gap"; research capacity strengthening; information networks in health research; gender, the MDGs and health research; and networks in the priority research areas.

RESOURCE FLOWS

Monitoring Financial Flows for Health Research - 2004

October 2004



This report 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. The study presents a new estimate of global spending on health R&D for 2001 but also exposes 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.

PRIORITY SETTING

The Combined Approach Matrix: a priority-setting tool for health research

June 2004

The Combined Approach Matrix (CAM) publication describes a tool used for the purpose of priority selection in health research: the matrix enables the collection, organization and analysis of the mass of information needed to help set priorities. It incorporates criteria and principles from earlier methods and links them into a matrix with the actors and factors that play a key role in the health status of a population. The method aims at helping institutions at national, regional and global levels to set their priorities in health research.

Health Research for the Millennium Development Goals (Forum 8 Report)

May 2005



The first report published by the Global Forum on an annual meeting summarizes the main themes of Forum 8 from plenary presentations and includes a CD-ROM with all the presentations, media and final documentation of the meeting. The report clearly demonstrates that a great deal is known about the kinds of research that are urgently required to accelerate and intensify the efforts necessary to achieve the Millennium Development Goals (MDGs). The report profiles health research challenges pertaining to poverty, maternal and child health, HIV/AIDS, malaria, and TB, cardiovascular diseases, diabetes, neglected diseases, road traffic injuries, public-private partnerships and research networks.



RealHealthNews

(Quarterly)

The newsletter RealHealthNews is targeted at policy-makers at all levels, including those in health and finance ministries – the men and women who hold the power and the purse strings. For them – in the briefest of forms, but with links to wider reading – we aim to create a "knowledge fair", a global sharing of potential solutions to their problems. The content is a combination of short items, articles and reflections, bringing important news, information and perspectives on global health and health research issues to the attention of its target audiences.

RealHealthNews is an independent e-magazine with a quarterly print version that is supported by the Global Forum for Health Research. Its editor Robert Walgate is a past news editor of New Scientist, Nature and The Bulletin of WHO. All stories, in some cases extended and with links to further information, can be found on the RealHealthNews page at: www.globalforumhealth.org

The Global Forum Update on Research for Health 2005

November 2004

This report is the first fruit of the collaboration between the Global Forum for Health Research and Pro-Brook Publishing. Published specifically for Forum 8 and the Ministerial Summit on Health Research and with a global circulation, the report takes as its theme the role of health research in achieving the Millennium Development Goals. It contains some 35 articles written by a selection of health ministers and other policy-makers, representatives of international and bilateral development agencies, the funders, controllers and users of research, and senior research leaders from around the world.

AVAILABLE ON CD-ROM

- Publications of the Global Forum for Health Research 1999-2004
- Forum 8 – Mexico City, 16-20 November 2004 – presentations, media, final documentation
- The 10/90 Report on Health Research 2003-2004
- The 10/90 Report on Health Research 2001-2002



Gender and Health Sector Reform: a literature review and report from a workshop at Forum 7
by Lesley Doyal
October 2004
This overview of the existing evidence base relating to gender and health reform examines the different components of these reform processes and why they might have different implications for women and for men. While available evidence on different aspects of health care are mentioned, the review pays particular attention to sexual and reproductive services. The text ends with conclusions, proposals for a research agenda, and a bibliography.

Child Health Research: a foundation for improving child health
May 2002 (reprinted May 2003)
Joint report of the World Health Organization and the Global Forum for Health Research, Child Health and Nutrition Research Initiative.

The goal of this report is to highlight the practical applications of research results aimed at improving child health around the world. It examines successful cases and stresses the need to invest further in research, building on the lessons learnt and the advances that have occurred to tackle the challenges of the future.

Interventions against antimicrobial resistance: a review of the literature and exploration of modelling cost-effectiveness - by Richard D. Smith et al
October 2001 (reprinted February 2003)
Antimicrobial resistance (AMR) is one of the biggest challenges currently facing global public health. A systematic literature review was undertaken to describe and appraise studies of various aspects of AMR, such as the cost and/or effectiveness of various strategies that may prevent the emergence of AMR and/or limit the transmission of resistant organisms, or resistance determinants.

Documents published by the Global Forum for Health Research on behalf of the Initiative on Public-Private Partnerships for Health and the Alliance for Health Policy and Systems Research

Combating Diseases Associated with Poverty: Financing Strategies for Product Development and the Potential Role of Public-Private Partnerships
by Roy Widdus and Katherine White
November 2004
Initiative on Public-Private Partnerships for Health (IPPPH)
(This title and all past IPPPH publications are available on the CD-ROM: Publications of the Global Forum for Health Research 1999-2004)

Strengthening Health Systems. The promise of health policy and systems research
by Anne Mills et al.
November 2004
Alliance for Health Policy and Systems Research

Forthcoming Publications 2005-2006

Policies for Health Research – A series of policy briefs jointly published by the Council on Health Research for Development (COHRED) and the Global Forum for Health Research (see page 018 for a glimpse of this series).

10/90 Report 2006 – Overcoming barriers to better health
This new streamlined 10/90 Report will provide a snapshot of recent changes in the global scene that relate to focusing health research to improve health throughout the world.

Financial Flows Report of a Three-Country Study – This report will be the fruit of a project that aims to build a comprehensive, sustainable data collection system for ongoing estimation and analysis of financial flows for health R&D in Brazil, India and South Africa, with the goal of reducing inequities in health and health research and improving the overall health of their populations.

Gender, Health and the Millennium Development Goals
This resource briefing examines the gender dimensions of the discussions at Forum 8 (Mexico City, November 2004). The author explores the links between gender and the health-related Millennium Development Goals, with the implications of these for research priorities.

No development without research: a challenge for capacity strengthening – Health research capacity strengthening (RCS) has been high on both national and international agendas, as is evidenced by a steady stream of peer-reviewed and grey literature, training tools, programmes and grants, workshops, task forces and conferences on various issues in the broad and complex area of RCS. This report aims to identify key issues, problems and challenges in RCS and to bring the pieces together into a conceptual framework or system.

Forum 9 Synthesis Report – Poverty, equity and health research, 12-16 September 2005, Mumbai, India

On CD: Forum 9 Report and full documentation; Publications of the Global Forum 1999-2005

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The full texts of our reports are available (as pdf files) on the website www.globalforumhealth.org where publications can also be ordered, free of charge. In addition, we encourage you to register on the website to receive regular information on all Global Forum activities.

Poverty, social determinants and health research

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How successful are pro-poor health programmes at reaching the poor?



Article by **Cesar G Victora**

This article addresses social inequalities in health within low- and middle-income countries. It reviews recent developments in the documentation and monitoring of inequalities, and the evaluation of health and related programmes from an equity standpoint.

Inequalities in health are everywhere

The term 'inequality' is used to refer to systematic differences between population groups, defined in terms of gender, race, wealth or other characteristics. 'Inequities' are inequalities judged to be unfair and unjust, and therefore theoretically preventable.[1]

The documentation of social inequalities in health has a long tradition. Nevertheless, wide inequalities persist and in many cases seem to be on the increase – for example, the gap in the mortality of children aged under 5 years between developing and developed countries increased from 10-fold in 1990 to 14-fold in 2000.[2] Within-country differences are also important – for most low- and middle-income countries, mortality among the poor is 2–3 times higher than for the better-off.[3]

Until recently, however, addressing health inequalities was nowhere near the top of the agenda for international agencies such as the World Health Organization, UNICEF or the World Bank. There seemed to be the tacit assumption that, by focusing on diseases of the poor, such as tuberculosis, malaria, diarrhoea and acute respiratory infections, international health programmes would automatically reach the poorest. However, existing data from recent Demographic and Health Surveys[3] carried out in 45 countries do not support such complacency. For example, child survival interventions that were largely disseminated in the 1980s – such as vaccines, antibiotics for pneumonia or malaria treatment – show higher coverage among the rich than among the poor in virtually all countries. Introduction of new technologies may even help increase poor-rich gaps by reaching first those that already have lower mortality levels.[4] Even within very poor societies such as rural Tanzania, there are important social inequalities in the coverage of key child survival interventions.[5] Thus, the overall national coverage of an intervention may be misleading because coverage among the poor is often much lower.

Social inequalities in health are mediated by several factors, most of which are outside the health sector. Poor nutrition, unhealthy environments and working conditions, inadequate water and sanitation and harmful behaviours play an important role in increasing exposure and susceptibility to disease among the poor. However, it is becoming increasingly clear that governmental spending in health can add to the unfavourable odds faced by the poor. A recent review of governmental health expenditure data from 21 countries showed that, on average, the top 20% of the population received 26% of the total financial subsidies, whereas the poorest 20% received less than 16%.[6] If private sector spending in health is added to that of government figures, the differentials will certainly be even greater.

What's new in international research on equity?

There is a current flurry of interest in research on inequalities in health, within low- and middle-income countries. This resulted from a combination of the widespread availability of population-based health surveys and of the dissemination of relatively simple approaches for estimating wealth.

Population-based data became widely available

Starting in the 1980s, maternal and child health surveys have been carried out in over 100 countries, with some countries having up to four surveys in different years.[7,8] Progress on measuring general adult health has been slower, but Living Standards Measurement Surveys provided information on morbidity and use of health services in two dozen countries,[9] and the World Health Survey initiative is about to produce substantial amounts of new data.[10]

Consistent methods for stratifying populations by wealth were developed

Measuring socioeconomic status in a consistent way throughout less developed countries is not an easy task. Data on income or expenditure, for example, may be difficult to collect and have limited validity, particularly in rural areas. Educational achievement alone is easier to measure, but variability may be low in many settings. An alternative to such traditional indicators is to make use of data on household assets, which are often collected in surveys. Such information may be combined with data on education, land tenure or occupation, in order to rank families in terms of their relative wealth. A variety of statistical procedures may

be used to derive a single item out of such indicators. Most often, principal components analysis has been used.[3,11] The appropriate items to be included in a wealth index will vary according to the local availability of household items. In rural Tanzania, for example, the wealth index included ownership of a tin roof, the household head having an income apart from farming, ownership of mosquito nets, renting a house, ownership of a bicycle or radio and the mother having an income apart from farming.[5] In urban Brazil, the number of bedrooms in the house, presence of a flush toilet, and ownership of a refrigerator, television set or motorcycle might be more relevant.

Indices derived through principal component analyses are continuous, and thus allow the sample to be stratified in several equal-sized strata. Typically, quintiles have been used, but fewer or more groups may be analysed. Because groupings depend on the distribution of the local sample, they may not be compared across countries in absolute terms. For example, the lower quintile in Tanzania will be poorer than that in Brazil. Nevertheless, they allow the study of within-sample inequalities in a consistent way.

Wealth indices are not devoid of problems. The choice of assets to be included in the analyses, and whether or not non-asset variables – such as education or employment – should also be included, are open to debate. However, systematic analyses of datasets from many countries show that such wealth quintiles are consistently able to detect important differentials in poverty-related health outcomes, such as child mortality and stunting prevalence.[3]

How to assess the equity performance of programmes?

Given that surveys provide data on health and wealth, the next issue is how to relate both sets of indicators. In the health field, a common approach is to compare the bottom and top quintiles in the study sample, by calculating ratios or differences.

The economic literature on distribution, on the other hand, often relies on more sophisticated approaches that make full use of data from the whole distribution instead of using only the extreme quintiles.[12] A common summary measure is a concentration index, that ranges from -1 (complete inequality, pro-rich), through 0 (complete equality), to +1 (complete inequality, pro-poor). Concentration indices seem to be becoming more popular in the health literature, but they are more difficult to interpret and to explain to the non-initiated than ratios or differences.

When evaluating the performance of a given programme, in health as well as in other sectors, economists are increasingly using 'benefit incidence' analysis.[13] These analyses show what proportions of the programme benefits reach different population strata. For example, a social marketing initiative in two rural Tanzanian districts included the distribution of low-cost, insecticide treated mosquito nets to reduce malaria transmission. The 'benefit' consists of the net. A population survey showed that 17% of the nets distributed through the programme ended up in the homes of the poorest quintile of the population in the districts. The 'incidence' of the benefit for the poorest, therefore, was 17%. (It is somewhat unfortunate that the economic literature uses the term incidence in a very different context to its epidemiological usage.)

A concept that is closely related to benefit incidence is that of 'focus', which has been proposed for evaluating nutrition programmes.[14] Focus is defined as the proportion, among participants receiving an intervention, who actually need the intervention.

From an epidemiological equity perspective, a key concern about any health programme is how well it reaches the poorest, for example, what coverage has been achieved in the bottom wealth quintile. We propose that the combination of coverage and benefit incidence, both for the poorest quintile, provides a simple and useful way of assessing the equity performance of a programme.

Figure 1 depicts a graph in which coverage among the poorest quintile in the population is shown in the y-axis, while benefit incidence or focus is on the x-axis. The oval shapes show some of the possible combinations of benefit incidence and coverage among the poorest. Ideally, an effective programme would reach high coverage among the poorest, being placed near the top of the chart. Regarding benefit incidence, a pro-poor programme would be located on the right hand side, indicating that a high share of its benefit is reaching the poor. If a programme is neutral in terms of benefit incidence, that is, neither pro-poor nor pro-rich, then 20% of the resources will be spent on the poorest quintile. The red vertical line in the graph shows this mark.

Programmes in the upper right hand side of the chart would have both high coverage among the poorest and also high benefit incidence, that is, pro-poor performance. Such

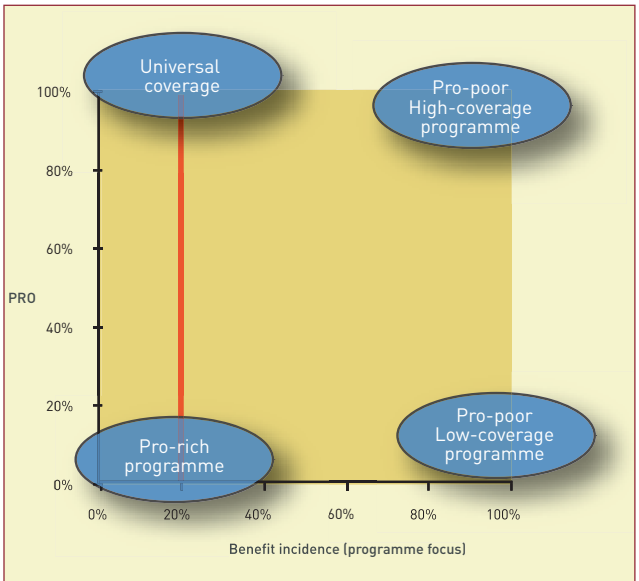


Figure 1: Possible combinations of coverage among the poorest and programme benefit incidence

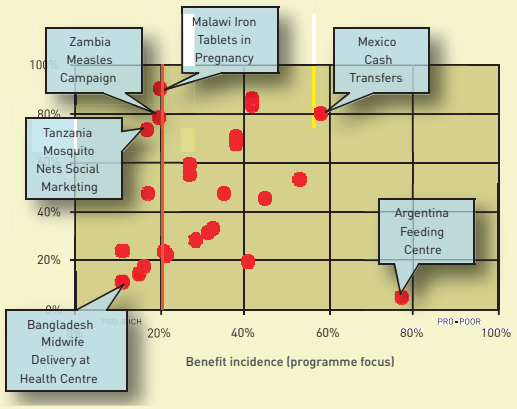


Figure 2: Plot of coverage among the poorest vs benefit incidence for selected programmes evaluated in the Reaching the Poor Conference

programmes would constitute excellent examples of well-targeted interventions.

In contrast, programmes aimed at reaching universal coverage in a population – for example, an eradication programme for a vaccine-preventable disease such as polio or measles – would also need to reach high coverage, but would not necessarily be pro-poor. If all vaccines were supplied by the public sector, an eradication programme would have a 20% benefit incidence for the poorest quintile, being located on top of the red line in Figure 1. Two other types of programmes are shown on the bottom part of Figure 2. On the left are pro-rich programmes, with benefit incidence below 20% and low coverage among the poorest. On the right are pro-poor programmes, with high benefit incidence, but nevertheless unable to achieve high coverage among the poorest.

Are pro-poor programmes reaching the poorest?

Given the framework presented in Figure 1, one may attempt to answer the question in the title of this paper. Ideally, this answer should be based on a systematic review of the published literature on health programmes in low- and middle-income countries. However, programme evaluations are often disseminated as limited-circulation reports commissioned by the programme sponsors, and results are seldom reported for different social groups. Also, benefit incidence results are seldom provided. For studying the performance of programmes in different settings, we took advantage of a recent initiative – the Reaching the Poor Programme[15] – that encouraged researchers from low- and middle-income countries to evaluate local programmes using benefit incidence analysis. Over 150 spontaneous applications were received from all over the world, and 18 projects were funded. These results, as well as approximately 30 other evaluations, were presented at a conference in early 2004.[16]

In Figure 2, all programmes or interventions presented in the conference that provided data on how well programmes were reaching different wealth quintiles, are summarized. Each programme is represented by a red dot. When data on benefit incidence were not presented directly, this was estimated from the coverage figures for each quintile. The estimates presented in Figure 2 allow us to highlight different types of pro-poor performance.

First, most programmes that were evaluated were somewhat pro-poor, with a median benefit incidence around 30%. Also, the median programme coverage among the poor was close to 50%. However, judging all programmes by the same standards may not be a good idea.

For example, programmes on the upper left corner included health sector interventions aimed at reaching universal coverage, such as immunization against measles in Zambia[17] and distribution of iron tablets during pregnancy in Malawi.[18] The Tanzanian KINET programme for social marketing of mosquito nets reached a remarkably high coverage in all social groups[19] and thus achieved high coverage among the poorest, despite low benefit incidence. None of these programmes were specifically targeted at the poorest.

On the bottom right hand corner of Figure 2, the Argentinean feeding centre programme is a clear outlier.[20] It had the highest benefit incidence of all programmes evaluated, but very low coverage among the poorest. This programme provides free meals for children at centres located in public schools in poor neighbourhoods. Both the physical location of these centres, and the possible social stigma associated with their utilization, may contribute to the combination of low coverage and high benefit incidence.

There are no programmes in the upper right corner of the chart, where perfectly targeted, high coverage interventions should be located. The Mexican PROGRESA programme – the provision of cash transfers to families conditional on their use of health and educational services – was the one closest to achieving this combination. Within programme areas, PROGRESA reached 80% coverage among the poorest and near 60% benefit incidence.[21] Such impressive performance was reached through a combination of geographical and family-level targeting.

Finally, programmes and interventions in the bottom left corner had mediocre performance on both coverage and benefit incidence. An example is delivery by trained midwives in Bangladeshi public-sector health centres, for which both coverage and benefit incidence were equal to 11%.[22]

The compelling message from Figure 2 is that most of these programmes and interventions still have a long way to go in terms of reaching the poorest. Also, the figure shows that interpretation of benefit incidence should take into account the programme objectives, whether it is universal coverage – for which low benefit incidence may be expected – or whether the programme is targeted to the poorest, in which case benefit incidence should be high.

Whether or not the programmes reviewed in this paper are typical of those being implemented in low- and middle-income countries cannot be ascertained for sure. As mentioned, many programme evaluations are sponsored by implementing

agencies, and may either end up in the grey literature or – if results are perceived as negative – may not be disseminated at all. Nevertheless, the studies featured here resulted from a broad, open request for research proposals on this topic, and most investigators had no links with the programmes they assessed, so the likelihood of dissemination bias is low.

Conclusions

There is a need to mainstream equity considerations. New programmes and interventions should be required to include an explicit statement of their expected impact on equity. Routinely collected statistics, for example in the health and education sectors, should be broken down by socioeconomic status. Programme evaluations should, in addition to overall impact, show how different social groups have benefited. Equity analyses should not be an afterthought, but an essential component of planning, monitoring and evaluating programmes. ❑

Acknowledgements

I would like to thank Dave Gwatkin, Abdo Yazbeck and Adam Wagstaff for their encouragement and insights.

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Figure 2 Reprinted from *Lancet*, Vol 365, Authors: Gwatkin DR, Bhuyia A, Victora CG, Title: Making health systems more equitable, Pages 1273-80, Copyright 2004, with permission from Elsevier.

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Making health research more pro-poor



Article by Abbas Bhuiya

Good health is not only an end in itself, but also a means of achieving individual and social development goals. 'Health is wealth' is part of the indigenous knowledge of any society, however, it is only recently that health and health research has been put at the centre of the development agenda.[1–4]

The average life expectancy at birth in the developing world has increased from a mere 40 years in 1950 to about 65 years at present.[5] Globally the progress is about 4 months each year.[6] This improvement has been due to both socioeconomic development and effective public health advances, but it seems that the latter has played a larger role.[7] Tragically, the overall improvement in health has also been accompanied by phenomenal and ever-growing inequities in health between the populations of various nations and subgroups of populations within nations.[8] The ones at the bottom of the scale are mostly the developing countries and socioeconomically disadvantaged groups within a country. These groups have poor access to modern health knowledge and health services – a situation quite similar to that of past famines in which lack of access rather than availability of food in the famine-stricken country was the main factor responsible in many cases.[9] This is an undesirable phenomenon with myriad consequences, which is likely to continue unless effective means are found and put in place to confront it.

Research in general played a vital role in finding solutions for major health threats faced by humankind and also in taking the solutions to the people. Nonetheless, reducing the lag between a discovery and the deriving of benefit from it by those in need irrespective of nationality and socioeconomic status is a daunting task. An examination of successful public health programmes clearly reveals that discovery of a solution is only a part of the final resolution. Taking the benefit to the masses is a step that is at least halfway if not more of the way toward the solution.[10] At present the available knowledge to improve health is not commensurate with the state of health in the poor nations in general and the state of health in the poor nations in general and the health of the poor in particular. This clearly indicates a need for realignment of the health research agenda – the focus, the way research is done, and the way success is monitored and evaluated. It is in this context that the present article is written with the hope of generating discussion to make health research more useful for the poor.

Poverty and poor health: strong nexus, weak actions

Poverty and poor health are almost synonymous and are related in a bi-directional way – the way malnutrition and infections are. Children of a mother from a poor family are most likely to be undernourished to begin with and vulnerable throughout their lives. The adverse effects of undernourishment continue. Poor health also increases vulnerability to financial loss, and poverty also limits access to modern services, be they health or developmental. Thus continues the never-ending cycle of poverty and poor health.

In the recent past health gain in countries like Bangladesh has been substantial and the gain has been quite large among the poor.[11] However, resistance has been encountered on many fronts including neonatal survival and maternal health, especially around pregnancy and childbirth. Currently, maternal health and the utilization of safe delivery services in poor nations are highly inequitable.[12] An examination of the situation leading to maternal death can provide useful guidance in identifying areas of knowledge generation for reducing inequities between nations and among various socioeconomic groups within a nation. The case narrative in Box 1 is one of the 17 maternal deaths that took place in a population of 150,000 in a rural area of Bangladesh during 2002–2004. Of the deaths, 14 were in households whose income earners were day-labourers or engaged in similar professions for livelihood. The proportion of such households in the community is only 46%, meaning that 82% of maternal deaths have been shared by 46% of the households – a highly inequitable situation.

The situation outlined also depicts an extreme scenario of the cycle of poverty and poor health, which can be typical of poor settings. As highlighted in the case narrative, the situation leading to the death of the woman illustrates the difficult conditions under which the woman and her family lived. She was from a poor family with no education, lack of financial resources, absence of social support and perhaps undernourished. She began reproduction at an earlier than ideal age with frequent pregnancies, had no control over her life, lacked a favourable environment during pregnancy, did not know what measures to take in what conditions, was

ignorant about where to go for services and was without the financial resources to procure the services. Her husband abandoned her and the other family members could only use whatever means at their disposal to ensure that she survived and had the baby, perhaps with the promise of escaping poverty someday. The outcome that they had hoped for was not realized.

A systematic review of the process may take us to quite early in her life perhaps when she was in her mother's womb. Nutritional deprivation likely made her a low-birthweight baby. Although she nearly made it to motherhood, her body most certainly had suffered through repeated infections during childhood. Her mother didn't know what and how often to feed her, and could not offer her the best during childhood in terms of nutrition and health care due to ignorance of science-based practices, lack of food, appropriate services and lack of financial means. Her parents also could not send her to school or could not keep her in school for long due to various socioeconomic and cultural impediments. The absolute deprivation she had been through was not due to a lack of availability of scientific knowledge in the world, but because of society's failure to avail her of the benefits of that science. The situation is not very different from a famine, which at times precedes a natural calamity, with the exception that she was a victim not of a natural calamity but of the sustained failures of the society and world she lived in.

The ability to apply oral rehydration therapy using mothers at home with common household ingredients in poor settings was empowering for the mothers and was instrumental in saving millions of lives. This is an example of a pro-poor solution to a health problem faced by the poor, in poor settings

Research: less in poor settings even less for poor

The health research agenda must be broad in scope. Solutions to health problems require innovation through bio-medical research, field-testing through epidemiological studies, and scaling up through social science and operations research. Effective public health interventions must have the advantage of research on all fronts in addition to financial support from a range of sponsors.[10]

Discovery of oral rehydration therapy (ORT) is an example of a solution for the health problems of the poor. Its invention was backed by sophisticated biomedical research and its distribution to millions of people was aided by social science and operations research for promotional activities to benefit the world's poor.[14] The ability to apply the solution using mothers at home with common household ingredients in poor settings was empowering for the mothers and was instrumental in saving millions of lives. This is an example of a pro-poor solution to a health problem faced by the poor, in poor settings. Wherever possible researchers should really look for solutions like ORT, which do not necessarily discapacitate individuals in managing their health problems.

There have been many success stories in the field of health, yet no dearth of challenges. Undernutrition could be a case in point. Factors responsible for undernutrition are also well understood, nonetheless, the tragic situation prevails. There is no disagreement about the importance of the problem or the technology to address it, however, there is a lack of agreement and effort as to how to tackle it.[15] Hastily done large-scale programmes with limited evidence-base seem to produce less than optimum results.[16]

It is clear, however, that ensuring access to the existing solutions to health problems at any particular point in time has been more challenging for the poor than the rich. Facing this challenge would require a lot of knowledge generation entailing inputs from various scientific disciplines from biomedical to social science, with emphasis on the programmatic issues at play in reaching the poor.[17] The investment in research on problems of the poor and the rich has been seriously imbalanced in favour of the rich.[18] Correcting this imbalance will not take place without decisive action in terms of allocation of resources and continuous monitoring of progress.

Pro-poor research topics: prevention vs cure

Prevention is always better than a cure, although this is truer for the poor than the rich. Once a person becomes sick, he or she loses work days and must resort to curative services. On both accounts it is more costly for the poor in a developing country situation because they are not covered by insurance and they do not have an employer to pay them during illness. Thus, illness can be more devastating for the poor than the rich. One could conclude that the poor can simply not afford to be sick. Immunization and health education are two preventive tools at hand, and the utilization of free immunization is found to be equitable at a high level of coverage.[19] Health education should also equip the poor to prevent sickness, however, equity in its acceptance and benefit has not been common in the literature. Thus, there is a need to test the efficacy of health education in improving the health and economic condition of the poor.

Reaching the poor: what do we need to know and do?

Bringing a solution to the poor is not an easy task. A

Health education should also equip the poor to prevent sickness, however, equity in its acceptance and benefit has not been common in the literature. Thus, there is a need to test the efficacy of health education in improving the health and economic condition of the poor

Box 1 | Poverty and maternal mortality

The following is a case narrative on one of the 17 maternal deaths that took place in the Chakaria field site of ICDDR,B during 2002–2004. (The name of the woman has been changed to maintain anonymity).

Begum (18 years old) was an inhabitant of a village in Chakaria in the south-eastern part of Bangladesh. Her husband (35 years old) was a rickshaw puller. He is originally from another district and came to Begum's village about 1.5 years ago and married Begum. Begum herself was not from a well-off family. Her father was a day labourer and could barely maintain his family of six with his income. He did not have any cultivable land of his own. Begum's father did not know much about her husband and his family before the marriage, but still agreed to the marriage because he did not have to pay any dowry for Begum. He knew that if he wanted to get his daughter married to a local person then he would have to pay a heavy dowry, which he was not capable of.

After 4 months of marriage Begum was pregnant. Unfortunately, 2 months following conception she had a miscarriage. She conceived again 2 months after this incident. In the first trimester she began vomiting and could not eat properly. Her husband brought medicines for her from a pharmacy in the nearby town. From the fifth month of pregnancy Begum developed oedema. This time her husband consulted a village doctor and brought medicines for her. A few days later, her husband left her without informing anyone or leaving a clue as to where he would be. Without her husband's support Begum suffered great hardship. She was struggling to get enough food for herself during the pregnancy. In time she developed severe oedema. Her parents went to a traditional healer and he treated her with amulets, spiritual water and oil. Her parents were forced to spend approximately Tk. 210 (US$4) for this treatment, and it did not improve her condition in any way. Her parents also brought some homeopathic medicine for her. Still her condition continued to deteriorate day by day. A month before her delivery she was having problems urinating. She was urinating only 1 or 2 times a day. Her mother consulted a village doctor for this problem. The medicines that the doctor prescribed did not improve her condition. During this time she also ate very little food, which exacerbated her weak condition. She went into labour on the morning 17 November 2003 and delivered a baby boy at 10pm with the help of a traditional birth attendant (TBA). Sadly, it was a stillbirth. After conducting the delivery the TBA inserted her hand into the uterus and pulled out the placenta. At this time Begum had a fever and was bleeding severely. The day after the delivery her body became more oedematous. Her mother called in the same village doctor who was contacted earlier. The doctor examined her and found that she had severe anaemia. He gave her medicines to control her anaemic condition. He also suggested that her parents take her to a private clinic to give her blood. From the evening of 19 November 2003 she became very restless. She began having difficulty breathing. The next morning her parents again called in the village doctor. Begum had a high fever by this time. The doctor examined her and gave her an injection. He then waited 15 minutes before giving her a second injection. Begum felt a little better after this and rested for a while. In the evening of the same day she became restless again and the troubled breathing worsened. Her mother gave her the medicine that she already had already been given by the village doctor. None of these medicines had any effect and eventually she died at approximately 9.30pm that night.

Reasons for Begum's untimely death as identified by her mother and neighbours: As Begum's parents were poor and could not afford to pay the dowry, she had to marry someone who they did not know. Her husband left her when she was ill. Begum did not get any proper health care due to their poor economic status and lack of awareness. All these factors led to the tragic end of her life.

common scenario has been that the benefit of health services is always disproportionately distributed between rich and poor with a bias towards the richer sector of society.[20] Lessons from successful programmes within and outside health sectors should be extracted and adopted in health and development programmes. Discovery of appropriate strategies to reach the poor is urgent and will not happen without adequate attention from researchers. Examples exist in the health sector where services have benefited the poor and rich both equitably and inequitably, for example, immunization services with a very high level of coverage have been egalitarian, and the safe delivery of services with low coverage have been very inequitable.[12] Education and socioeconomic development programmes sensitive to the life situation of the poor have been helpful in reducing inequities in education, income and health.[21,22] Policy-makers and programme designers should look for equity-achieving evidence and researchers should come forward to generate such findings.

The issue of targeting the poor vs targeting everybody in a society has often been argued on the grounds of efficiency. It was also observed that the benefit of a new service is first derived by the better off and later by the poor.[23,20] The question is whether for reasons of so-called efficiency and the hope of a trickle-down effect, one should wait or go forward and launch targeted programmes. Evidence has been accumulating showing that development and health programmes that are tailored to be sensitive to the life

situation of the poor can benefit the poor more than what could otherwise be achieved.[22] Systematic investigations in finding ways to reach the poor must be pursued. The question of efficiency is quite often raised when it comes to targeting the poor. Indeed, improving the condition of the poor may be expensive according to some criteria, however, the research community has failed to develop methods to do the calculation correctly by valuing the gain achieved by improving the health of the poor and reducing poverty. Economic efficiency in the context of the improvement of the condition of the poor has almost become a language of a different social class and certainly not of those who are excluded from the benefits. This notion of efficiency should be countered by objective information.

Monitoring progress: average vs disaggregation

The nations of the world have committed to achieving certain goals by 2015 as outlined in the Millennium Development Goals (MDG) documents. However, the targets can be achieved without making much of an impact on the lives of the world's poor.[24] This can be true for any health or development programme, which is often judged by average improvement. Countering such false complacency will require development of equity-sensitive monitoring and evaluation tools and ways of adopting them. The Millennium Project Task Force on Child Health and Maternal Health has thus recommended monitoring of the MDGs, not only on aggregate terms, but for each group in the population.[15]

Institutionalization of an equity-sensitive system is another challenge. The routine Management Information System (MIS) data especially in the developing world are quite often inadequate in terms of quality and scope. Some tailoring in the system has to be done to make MIS data useful to programme managers in identifying shortfalls in equity gain at the lowest levels of health service. It may also be of use to have complementary independent evaluation and monitoring systems in place. The EPI[30] cluster method of survey has been very effective for the EPI managers to monitor progress; however, its application at the lowest health work area level at frequent intervals makes it quite an endeavour. Therefore, there is a need to have more rapid and easy-to-use techniques for monitoring programme performance at the community level with equity focus. In the recent past, benefit incident analysis has been used at the facility level to monitor utilization by the poor.[25,26] Lot Quality Acceptance Sampling (LQAS) has also been used in many instances to classify work areas as adequate or inadequate by using much smaller sample sizes.[27] There is potential with LQAS to use it at the community and at facility level to monitor utilization of services by the poor. Researchers should really concentrate on finding simple and rapid techniques for monitoring programme performance with a focus on equity.

Improvement of health almost always requires modification in individual and/or group behaviour. Monitoring of programme performance by the community provides an opportunity for community members to participate. This exercise not only informs the beneficiaries of programme potential, but also initiates modifiable actions where necessary and establishes mutual accountability. This in effect provides a mechanism whereby the programme beneficiaries take responsibility for their own well-being and thus make programmes more effective than what could be achieved through monitoring by external agents only.[28] Despite the use of participatory methods on many occasions their institutionalization in the health system has not been very satisfactory. One of the reasons for low utilization of participatory methods in programme monitoring could be due to the lack of know-how for adopting these methods on a large scale. It will be useful to try out methods of institutionalization of Participatory Rural Appraisal (PRA) techniques in the health system.

Conclusion

Improving the health of the poor would need intelligent information generated through appropriate research. Thus, an understanding of the context in which poverty and poor health is perpetuated is a prerequisite for deciding on topics for investigation. It should not be forgotten that health problems may be biomedical in nature but their long-term solution may in fact lie outside the biomedical and/or health field. Challenges for health research therefore lie not only in finding solutions for the health problems of the poor but also finding ways to work together with other sectors for lasting improvement of the health of the poor and the eradication of poverty. The very conditions in which the poor live demand affirmative actions, therefore, targeting the poor with responsive programmes is imperative in order to be effective. Another challenge is to transform the poor from the state of passive recipient to active player for their improvement. This requires a massive shift in the attitudes toward the poor and the way the poor are treated. Finally, the progress of policies and programmes should always be monitored and evaluated in terms of the success achieved among the poor – remembering that things which are not measured are quite often not done. ❑

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Acknowledgements

This work is carried out at ICDDR,B: Centre for Health and Population Research under the auspices of the Poverty and Health Programme, which is supported by DFID. The author is grateful to Dr Mushtaque Chowdhury and Ms Rowen Aziz for their helpful comments on an earlier draft of the paper.

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To prevent diseases of poverty or to overcome poverty? When equity matters in research



Article by Roberto Briceño-León

A great part of the diseases that affect the majority of the world population are the product of conditions of poverty in which the families who suffer those illnesses live. Poverty produces some precarious environmental conditions and malnutrition in people, which facilitates the transmission of diseases or their development in weakened bodies, impeding them from working, developing their capacities and being productive for themselves and for society. They are diseases of poverty that produce more poverty.

Development prevents diseases

Historically we know that when an important level of social progress has been achieved in countries, regions or their social sectors, and people have had the opportunity to extricate themselves from poverty, above all extreme poverty, diseases have radically decreased. And this occurs because with development the material conditions of life of those people are modified and the transformation also provokes a change in their mentality, in the confidence that they have in themselves and in their capacity to prevent diseases that may be avoided as well as their awareness of the right to a healthy and free life.

This has occurred with many diseases. When sewers or septic tanks were built and human excrement ceased to be thrown in the rivers, schistosomiasis disappeared from endemic zones. The same occurred with the incidence of Chagas' disease when houses were improved and with malaria in zones where economic progress led to an increase of production and population of cattle, because the vectors began to bite the animals and not people.

The urbanization process also contributed to reducing the transmission of many diseases, because this meant an important change in the living conditions of people. Certainly, the rapid process of urbanization that occurred in Latin America or Africa did not mean the onset of development, as it was thought would occur in time, because in contrast with Europe it was not accompanied by industrialisation or improvement in the distribution of wealth. Nevertheless, cities helped to prevent many ailments of the countryside because they represented an important change in the conditions of rural life. But poverty persisted in the cities, acquired a new face, and the lack of basic services such as water and the need to store it for domestic use offered the conditions for other diseases such as dengue to prosper in the urban environment and become the threat that they are today in many places on the planet.

The effort to control diseases

In spite of this evidence, a great part of the effort that governments make is exclusively oriented to controlling diseases or curing patients, without altering the conditions of backwardness and poverty that produce them. Health ministries concentrate on disease control measures that allow eliminating by chemical means the presence of the vector insects of the disease and of host snails, but not the social and environmental conditions that make these vectors a threat to people.

In front of a contaminated river, we have dedicated ourselves to placing a warning sign with a skull in the banks of the river to stop people from bathing or washing their clothes, or spreading poison to kill the host snails of schistosomiasis, but not to modifying the reasons for which human faeces reach those rivers.[1] When the houses are full of triatomine bugs that transmit Chagas' disease, they have been fumigated or painted with pesticides, but the walls or roofs that allow insects to continue to live there have not been modified.[2] Health ministries have been efficient in placing larvicides in the precarious deposits of potable water of the slums of the cities, to avoid the reproduction of the *Aedes aegypti* mosquito which is the transmitter of dengue, but we have not been able to provide regular water to families to make it unnecessary to store it.[3]

Snail poisons, insecticides or larvicides prevent the disease. Those measures are efficient and ministries have applied them in good faith. But we know that they have temporary success because they temporarily reduce the risk of transmission of diseases, but do not modify the causes that permit their existence, and they do not alter the material and social conditions at the origin of the disease. They are measures dedicated to controlling the diseases of poverty, without altering the conditions of poverty.

The perspective of equity

Poverty and inequality have increased in many regions of the world. This has occurred either because with the growth of

the population an increase has been produced in the absolute number of poor people – although in some cases their relative percentage may have diminished – or because the improvement of some social sectors, like the urban populations of China and India, increases the distance that separates them from the rural populations that remain in their traditional poverty. In Latin America at the beginning of the 1980s there were 136 million urban poor and 73 million rural poor; 20 years later the poor had increased to 221 million in the cities and to 75 million in the rural areas,[4] and that is the population that suffers from malaria, schistosomiasis, Chagas' disease or dengue.

In the health sector we have carried out a great deal of research on parasites and vectors, but not on why the conditions of poverty-disease persist among that population, on what the cultural variables are that detain the effort for improvement and social advance or on what the objective and external factors are that foment the disease. We know that poverty produces these diseases, but we do not investigate why poverty persists, nor what we must do to be able to overcome it in a context of democracy and freedom. We simply take poverty as an immutable reality and we dedicate ourselves to curing the sick or killing the bugs that find their mode of living in poverty. We investigate the consequences, not the causes and therefore we are only trained to intervene with regard to the consequences and not the causes.

When equity is important in research

In research and control programmes it is not known what may be done differently. The people who work on these programmes learned a mode of investigation or of killing insects and continue to do the same. They do not know what other strategies can be used, they do not manage to locate themselves in a broader perspective than their specific programme goals. The door that can lead them to new paths of investigation on health and social transformation is tightly shut. The locks that keep the door shut stem from the fear of the unfamiliar (or new), to interdisciplinary work, to the loss of security of the known. Opening the door is difficult, because it requires implementing changes in our minds and in our institutions, and that leads to risks. It is easier to carry out the same rite of the past when one reaches a position to be able to place another lock, to close the door better, instead of wanting to open it and break the previous locks. It is for this reason that we have the impression so often of always hearing the same discourse at scientific meetings.

But that blame does not pertain to those who are at the front of the daily battle, responsible for carrying out programmes of control. It is the responsibility of those who have chosen as their profession inquiry and innovation, of those who have tools to imagine new paths. It is a task of investigation that must break down the walls and experiment with new avenues.

Much of the investigation that we do is dedicated to controlling the diseases of poverty and not to improving the quality of life of the population. How to overcome poverty and thus to be able to obtain a more permanent control of diseases, or better still, of the conditions of health of the population, is never considered. For several decades we have been repeating the same slogan of Alma Ata: health is something more than the absence of disease. But how does one translate that idea into research efforts? We are fascinated by scientific research, but we do not know if it is the answer to overcoming problems, it is simply what we know how to do. We continue to persist in financing and carrying out research in areas where we know that we cannot advance toward health. We seem like the individual who has lost the key of his house on a dark night and is looking for it eagerly under the only street lamp that exists in that area. The key was not lost there but on another part of the road, however, it is looked for under the street lamp, because the area around it is illuminated, instead of looking for it in the darkness.

Technological efficiency and social progress

If we have to be in the dark on the road that we do not know, the idea of equity and development must serve as our guide. Let us take the example of Chagas' disease, a terrible illness that affects close to 18 million people in South and Meso-America. A parasite (*Tripanasoma cruzi*) produces this disease which is introduced in people when it is deposited in the faeces of a vector insect that defecates, while it sucks the blood of the inhabitants of poor houses in rural Latin America.[5] The parasite can provoke an acute illness in a few days that can lead to death, or remain in a silent phase for up to 15, 20 or 30 years; it manifests itself in cardiac or digestive damage and may cause a sudden death that is very difficult to associate with the parasite and the vector. The insects live in the houses and feed on the blood of the families and can be counted in the dozens or thousands, depending on the place and the conditions of the house.[6] If houses did not have palm roofs, unplastered walls or earth floors, crops and hens inside, this type of transmission would be almost impossible.[7] The disease has no cure; there is a controversial treatment that is supplied in acute cases, but in regard to which there is no agreement for application in chronic cases, which make up the great majority.[8]

The parasite can provoke an acute illness in a few days that can lead to death, or remain in a silent phase for up to 15, 20 or 30 years; it may cause a sudden death that is difficult to associate with the parasite and the vector

On repeated occasions the need and aspiration to obtain a vaccine that impedes these people from being able to acquire the disease if they are bitten by an insect infected with the parasite has been proposed. To develop a vaccine requires important research efforts and financing to sustain it. Let us

suppose that that effort is successful and a vaccine is obtained that provides protection to the rural population. This would be an important advance that would fascinate our minds and would fill those who achieve this objective with glory, and science would be rewarded for its effort. But the problem does not end here. Let us moreover suppose that vaccines can be industrially produced in an abundant manner and at a modest price that the countries where this disease is endemic can afford to pay. Let us suppose further, that the vaccine can be applied simply, a single dose with lifetime protection and that the health services of the countries manage to efficiently apply it to the whole population at risk. Nothing that has been stated is simple or guaranteed, but let's be positive and give a vote of confidence to all of the previous processes. What would we have at the end? We would find a rural population that continues to live in the same unplastered houses and with palm or straw roofs, cohabiting with up to 7,000–11,000 insects who suck their blood,[9] but cannot give them the disease because they are protected with a high technology vaccine. Is this the health that we are seeking? Is this fair and equitable?

Equity obliges us to think in terms of health and of overcoming the conditions of poverty that provoke the disease, not only of controlling diseases and leaving the population living in the same poverty. The way forward through this new perspective is not simple, but it needs to be introduced with great effort and enthusiasm. The Spanish poet described the situation aptly when he said: 'walker, there are no paths; a path is made by walking through' (*caminante no hay caminos, se hace camino al andar*).[10] ❑

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Social determinants of health inequalities

Article by Sir Michael Marmot

The gross inequalities in health that we see within and between countries present a challenge to the world. That there should be a spread of life expectancy of 48 years among countries and 20 years or more within countries is not inevitable. A burgeoning volume of research identifies social factors at the root of much of these inequalities in health. Social determinants are relevant to communicable and noncommunicable-disease alike. Health status, therefore, should be of concern to policy-makers in every sector, not solely those involved in health policy. As a response to this global challenge, WHO is launching a Commission on Social Determinants of Health, which will review the evidence, raise societal debate and recommend policies with the goal of improving the health of the world's most vulnerable people. A major thrust of the Commission is turning public-health knowledge into political action.

There are gross inequalities in health between countries. Life expectancy at birth, to take one measure, ranges from 34 years in Sierra Leone to 81.9 years in Japan.[1] Within countries, too, there are large inequalities – a 20-year gap in life expectancy between the most and least advantaged populations in the United States, for example.[2] One welcome response to these health inequalities is to put more effort into the control of major diseases that kill and to improve health systems.[3,4]

A second belated response is to deal with poverty. This issue is the thrust of the Millennium Development Goals.[5,6] These goals challenge the world community to tackle poverty in the world's poorest countries. Included in these goals is reduction of child mortality, the health outcome most sensitive to the effects of absolute material deprivation.

To reduce inequalities in health across the world there is need for a third major thrust that is complementary to development of health systems and relief of poverty: to take action on the social determinants of health. Such action will include relief of poverty, but it will have the broader aim of improving the circumstances in which people live and work. It will, therefore, address not only the major infectious diseases linked with poverty of material conditions but also non-communicable diseases – both physical and mental – and violent deaths that form the major burden of disease and death in every region of the world outside Africa and add substantially to the burden of communicable disease in sub-Saharan Africa.

Box 1 | The Commission on Social Determinants of Health

The Commission will not only review existing knowledge, but also raise societal debate and promote uptake of policies that will reduce inequalities in health within and between countries.

The Commission's aim is, within 3 years, to set solid foundations for its vision: the societal relations and factors that influence health and health systems will be visible, understood and recognized as important. On this basis, the opportunities for policy and action and the costs of not acting on these social dimensions will be widely known and debated. Success will be achieved if institutions working in health at local, national, and global level will be using this knowledge to set and implement relevant public policy affecting health. The Commission will contribute to a long-term process of incorporating social determinants of health into planning, policy and technical work at WHO.

To understand the social determinants of health, how they operate, and how they can be changed to improve health and reduce health inequalities, WHO is setting up an independent Commission on Social Determinants of Health, with the mission to link knowledge with action (Box 1). Public policy – both national and global – should change to take into account the evidence on social determinants of health and interventions and policies that will address them.

This introduction to the Commission's task lays out the problems of inequalities in health that the Commission will address and the approach that it will take. This report will argue that health status should be of concern to all policy makers, not merely those within the health sector. If health of a population suffers it is an indicator that the set of social arrangements needs to change. Simply, the Commission will seek to have public policy based on a vision of the world where people matter and social justice is paramount.

Inequalities in health between and within countries: poverty and inequality

A catastrophe on the scale of the Indian Ocean tsunami rightly focuses attention on the susceptibility of poor and

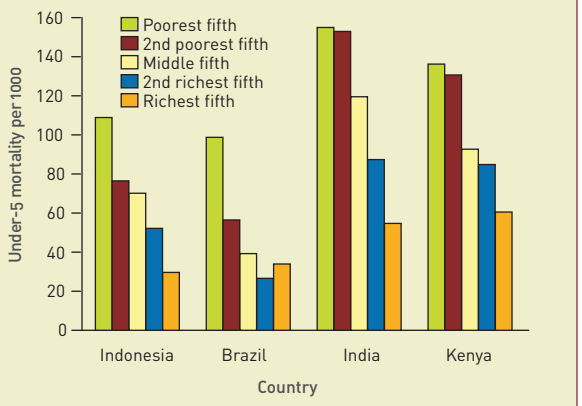


Figure 1: Under-5 mortality rates per 1,000 livebirths by socioeconomic quintile of household

vulnerable populations to natural disasters. It is no less important to keep on the agenda the more enduring problem of inequalities in health among countries.

Children

Under 5-mortality varies from 316 per 1,000 livebirths in Sierra Leone to 3 per 1,000 livebirths in Iceland, 4 per 1,000 livebirths in Finland and 5 per 1,000 livebirths in Japan.[1] In 16 countries (12 in Africa), child mortality rose in the 1990s,[7] by 43% in Zimbabwe, 52% in Botswana and 75% in Iraq.[8]

Figure 1 shows under-5 mortality rates for four countries with households classified according to socioeconomic quintile. Child mortality varies among countires.[9] Within countries, not only is child mortality highest among the poorest households, but also there is a social gradient: the higher the socioeconomic level of the household, the lower the mortality rate.

Adults

Differences in adult mortality among countries are large and growing. Figure 2 shows probability of death between age 15 and 60 years by region of the world between 1970 and 2002.[7] Mortality rose in Africa and in the countries of central and eastern Europe whereas it declined in the world as a whole. By 2002, for example, men in the high mortality countries of Europe had more than 40% probability of death between age 15 and 60 years compared to a 25% probability in southeast Asia. These data are for regions. Among countries, the differences are even more dramatic. The probability of a man dying between age 15 and 60 years is 8.3% in Sweden, 82.1% in Zimbabwe and 90·2% in Lesotho.[7]

A particularly telling example of health inequalities within countries is the 20-year gap in life expectancy between Australian Aboriginal and Torres Strait Islander peoples – life expectancy is 56.3 years for men and 62.8 years for women – and the Australian average.[10] The men in this population would look unhealthy in India (male life expectancy 60.1 years) whereas Australian life expectancy is among the highest in the world, marginally behind Iceland, Sweden and Japan. The poor health of Aboriginal and Torres Strait Islander peoples is not the result of a high rate of child deaths. Infant mortality is 12.7 per 1,000 livebirths. This figure is high by Australian standards, but on a scale from Iceland to Sierra Leone, it is much closer to Iceland than to Sierra Leone. The shortened life expectancy of Aboriginal and Torres Strait Islander peoples results from mortality in adults from non-communicable disease and injury. In this sense, the population is typical of the world health picture. Of the 45 million deaths among adults age 15 years and older in 2002, 32 million were due to noncommunicable disease and a further 4.5 million to violent causes.[7]

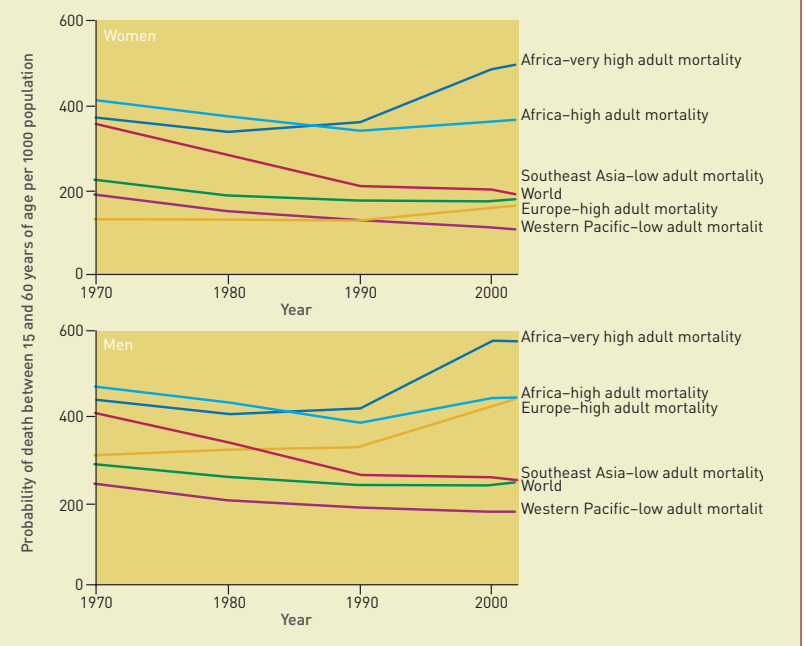


Figure 2: Trends in adult mortality by sex in regions of the world, 1970–2002. The graphs show the probability of death between 15–60 years of age per 1,000 population

Aboriginal and Torres Strait Islander peoples are a socially excluded minority within their country. But poor health is not confined to poor populations or those who are socially excluded. As with child mortality, there is a socioeconomic gradient in adult mortality rates within countries. Figure 3 shows that in Bangladesh, adult mortality rates vary inversely with level of education.[11] This gradient in mortality is quite remarkable. Within rich countries, with strikingly

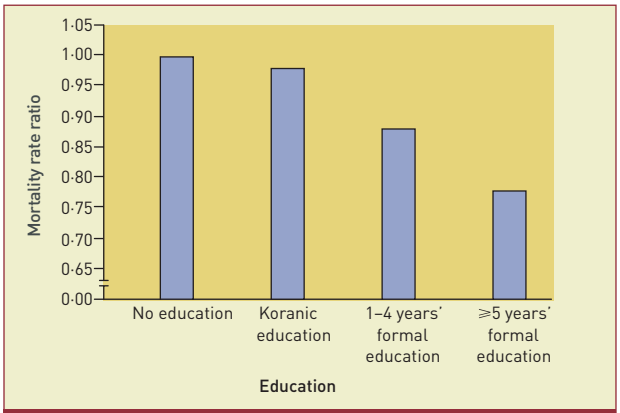


Figure 3: Mortality and education in men aged 45–90 years in Matlab, Bangladesh, 1982–98[11]

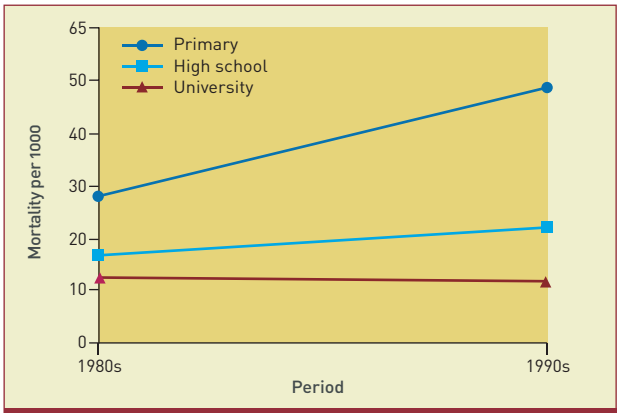


Figure 4: Increase in educational differentials in mortality between the 1980s and 1990s in St Petersburg men[16]

different material conditions from Bangladesh, there is a social gradient in mortality prompting consideration of the causal links between status and health.[12] Whether the social gradient in poor countries can be attributed to the same causal pathways is an urgent task for review. It is especially important because, in many countries, inequalities in health have been increasing.[13–15] In Russia for example, where life expectancy is low, social inequalities have grown (Figure 4).[16]

Mortality statistics are readily available. They should not, however, lead to ignorance of the burden of nonfatal disease.

Box 2 | The solid facts

Because the causes of the causes are not obvious, the WHO Regional Office for Europe asked a group at University College London to summarize the evidence on the social determinants of health, published as *The Solid Facts*.[22] It had 10 messages on the social determinants of health based on:

- the social gradient
- stress
- early life
- social exclusion
- work
- unemployment
- social support
- addiction
- food
- transport

As an indication that there was a ready audience for these messages, in the first 12 months after publication of the second edition it was downloaded from the internet 218,000 times.

The Solid Facts reviewed evidence from Europe, aimed mainly at reducing inequalities in health within countries. The task of the Commission will be to review evidence on the social determinants of health that are relevant to global health: inequalities among countries and within.

In particular, mental illness causes much suffering but its effect is not clear by inspection of mortality data. Worldwide, the second highest cause of disease burden among adults age 15–59 years is unipolar depressive disorder.[7]

The ageing of the world's population

It is convenient, but quite wrong, to think that the greying of the world's population is an issue only for rich countries. Figure 5 shows the projected increase between 2000– 2030 in the population older than 65 years in selected countries.[17] The fastest rates of increase are in countries at an intermediate level of human development, starting from a low base. The social determinants of the health of older people claim attention alongside those of health at younger ages.

Social determinants: poverty, inequality and the causes of the causes

In consulting widely in developing the plan for the Commission on Social Determinants of Health, a common question was: 'What's new? We know that poverty is bad for health. Does that need a Commission?'

It is not difficult to understand how poverty in the form of material deprivation – dirty water, poor nutrition – allied to lack of quality medical care can account for the tragically foreshortened lives of people in Sierra Leone. Such understanding is insufficient in two important ways. First, it fails properly to take into account that relief of such material deprivation is not simply a technical matter of providing clean water or better medical care. Who gets these resources is socially determined.[18] Second, and related, international policies have not been pursued as if they had people's basic needs in mind. The critics of the policies pursued by the International Monetary Fund in the global South have argued eloquently that the economic policies pursued under structural adjustment have not benefited disadvantaged people in poor countries.[19] Recognising the health effects of poverty is one thing. Taking action to relieve its effects entails a richer understanding of the health effects of social and economic policies.

Dirty water, lack of calories, and poor antenatal care cannot account for the 20-year deficit in life expectancy of Australian Aboriginal and Torres Strait Islander peoples. On a world scale, their infant mortality rate, at 12.7 per 1,000 livebirths, is low. Their high rate of adult mortality is from cardiovascular diseases, cancers, endocrine nutritional and metabolic diseases (including diabetes), external causes (violence), respiratory disorders and digestive diseases.[10] This fact is not to deny that poverty is important. But the form that poverty takes and its health consequences are quite different when considering chronic disease and violent deaths in adults, compared to deaths from infectious disease in children. It entails a richer understanding of the social determinants of health.

The health experience of Aboriginal and Torres Strait Islander peoples has relevance for the health of disadvantaged people worldwide. While in Africa the major contributor to premature mortality is communicable disease, in every other region of the world it is non-communicable disease.[1] Careful analysis of the global burden of disease has pointed to the importance of risk factors, such as being overweight, smoking, alcohol, and poor diet.[20] These are indeed potent causes. But would it be helpful to go into a deprived Australian Aboriginal population and point out that they should really take better care of themselves – that their smoking and obesity were killing them; and if they must drink, please do so in moderation? Unlikely. To borrow Geoffrey Rose's term, we need to examine the causes of the causes:[21] the social conditions that give rise to high risk of noncommunicable disease, whether acting through unhealthy behaviours or through the effects of impossibly stressful lives[12] (Box 2).

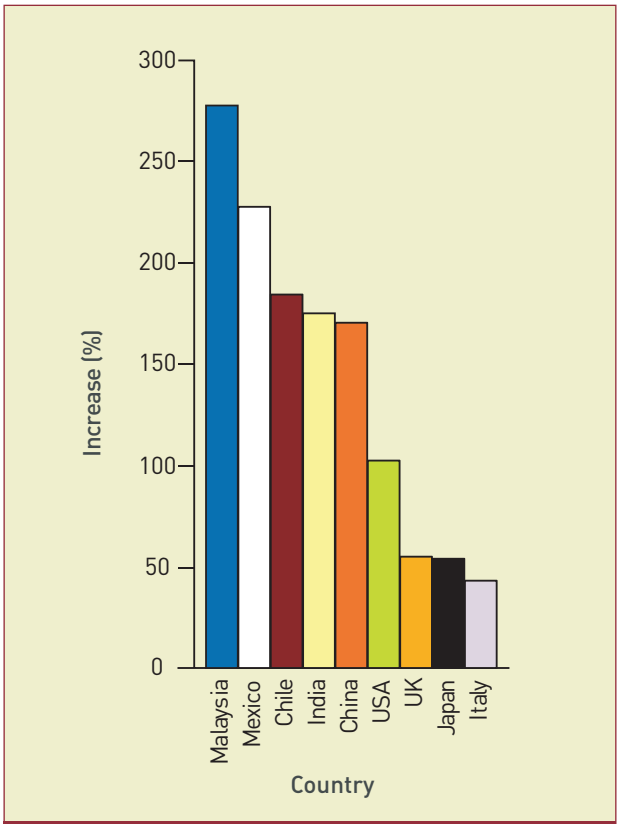


Figure 5: Projected percentage increase in the elderly population (older than 65 years) from 2000–2030 in selected countries

A further answer to the what's new question: although it might be obvious that poverty is at the root of much of the problem of infectious disease, and needs to be solved, it is less obvious how to break the link between poverty and disease. Income poverty provides, at best, an incomplete explanation of differences in mortality among countries or among subgroups within countries. It is well known that among rich countries, there is little correlation between gross national product (GNP) per person and life expectancy. Greece for example, with a GNP at purchasing power parities of just more than US$17,000, has a life expectancy of 78.1 years; the United States, with a GNP of more than $34,000, has a life expectancy of 76.9 years. Costa Rica and Cuba stand out as countries with GNPs less than $10,000 and yet life expectancies of 77.9 years and 76.5 years.[23]

We need to examine the causes of the causes: the social conditions that give rise to high risk of noncommunicable disease, whether acting through unhealthy behaviours or through the effects of impossibly stressful lives

There are many examples of relatively poor populations with similar incomes but strikingly different health records.[8] Kerala and China, famously, have good health, despite low incomes.[24] The social processes that lead to this beneficial state of health need not wait for the world order to be changed to relieve poverty in the worst-off countries. A social determinants perspective is crucial. It is also important to enquire whether the action that is taking place to relieve poverty is having the desired effect not only on average incomes, but also on income distribution and hence on the poorest people.

The social gradient in health is a particular challenge. Where material deprivation is severe, a social gradient in mortality could arise from degrees of absolute deprivation. In rich countries with low levels of material deprivation the gradient changes the focus from absolute to relative deprivation.[25] Relative deprivation relates to a broader approach to social functioning and meeting of human needs[12] – capabilities in the words of Amartya Sen,[26] spiritual resources to use Robert Fogel's term.[27] It is likely that both material or physical needs and capability, spiritual, or psychosocial needs are important to the gradient in health, which will, therefore, be an important focus.

A focus on material conditions and control of infectious disease must not be to the exclusion of social determinants. The circumstances in which people live and work are as important for communicable as they are for non-communicable disease. Social conditions powerfully

influence both the onset and response to treatment of the major infectious diseases that kill.[28,29]

The Commission on Social Determinants of Health will need to have in its sights poverty of the sub-Saharan African sort and the social determinants that account for Bolivia having 14 fewer years of life expectancy than Costa Rica or Aboriginal and Torres Strait Islander peoples having 20 years fewer than other Australians. As these examples illustrate, it will examine inequalities in health between countries and inequalities within.

Action is possible and necessary

A review of policies in European countries identified several that took action on the social determinants of health.[30] Although the reason for the policies was not necessarily to improve health they were nevertheless relevant to health: taxation and tax credits, old-age pensions, sickness or rehabilitation benefits, maternity or child benefits, unemployment benefits, housing policies, labour markets, communities and care facilities.

In Sweden, the new strategy for public health is 'to create social conditions that will ensure good health for the entire population'.[31] Of 11 policy domains, five relate to social determinants: participation in society, economic and social security, conditions in childhood and adolescence, healthier working life and environment and products. These are in addition to health promoting medical care and the usual health behaviours. The UK set reduction of health inequalities as a key aim of health policy. It assembled evidence and expert judgments on areas suitable for policy development.[32] These then formed the basis of a plan of action to reduce health inequalities.[33]

These are examples from rich countries. There are further encouraging examples. Familias en Accion in Colombia transfers cash to poor families. To qualify, families must ensure their children receive preventive health care, enrol in school and attend classes. The results are encouraging: favourable growth of children and fewer episodes of diarrhoea.[34] The Oportunidades programme in Mexico had somewhat similar aims with similarly encouraging results.[35]

Meeting human needs

Two linked themes provide the rationale for the Commission on Social Determinants of Health. First, there is no choice. If the major determinants of health are social, so must be the remedies. Treating existing disease is urgent and will always receive high priority, but should not be to the exclusion of taking action on the underlying social determinants of health. Disease control, properly planned and directed, has a good history, but so too does social and economic development in combating major disease and improving population health. Wider social policy will be crucial to reduction of inequalities in health.

There is a second theme that relates to the question of how one can tell if a population is thriving. One standard answer is to measure economic wellbeing with measures such as GNP, average income, or consumption patterns. A better answer is to measure health status.[36] There is no difficulty in convincing medical and health personnel that health is important – that is what we do. It is more challenging, but necessary, to convince policy-makers and others that the health of the population is important precisely because it is a measure of whether, in the end, a population is benefiting as a result of a set of social arrangements.

In other words, action on the social determinants of health is necessary not only to improve health, but also because such improvement will indicate that society has moved in a direction of meeting human needs.[37] There is a great deal of dogmatic dispute about the rights and wrongs of economic and social policies. People use labels – globalization, neoliberal economic policies – as badges of allegiance and terms of abuse. The Commission will have one basic dogma: policies that harm human health need to be identified and, where possible, changed. From this perspective, globalization and markets are good or bad in so far as the way they are operated affects health.

Inequalities in health between and within countries are avoidable.[38] There is no necessary biological reason why life expectancy should be 48 years longer in Japan than in Sierra Leone or 20 years shorter in Australian Aboriginal and Torres Strait Islander peoples than in other Australians. Reducing these social inequalities in health, and thus meeting human needs, is an issue of social justice. ❑

Acknowledgement

Grateful thanks to Ruth Bell, Hilary Brown, Tim Evans, Alec Irwin, Rene Loewenson, Nicole Valentine, Jeanette Vega, and members of the WHO Equity team who have worked to develop the Commission and the ideas in this report.

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Professor Marmot also chairs the BHF Primary Prevention Committee. He was a member of the Royal Commission on Environmental Pollution for six years. He was Knighted by Her Majesty The Queen in 2000 for services to epidemiology and understanding health inequalities. Internationally acclaimed, Professor Marmot is a Vice President of the Academia Europaea; a member of the RAND Health Advisory Board; a Foreign Associate Member of the Institute of Medicine, and he chairs the WHO Commission on Social Determinants of Health. He won the Balzan Prize for Epidemiology in 2004 and will give the Harveian Oration in 2006.

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Targeting or universal coverage with vitamin A? Costs, mortality and disparity reduction



Article by David Bishai (pictured) and Hugh Waters

Most health planners are aware that maximizing some measure of health is not the only goal of a health system. Individuals and societies are concerned about the distribution of the benefits of a health system.[1] But equity can never become the sole goal of a health system. Fundamentally, any inequity involves a situation where some people in the population are enjoying greater services or outcomes than others. If equity were to become the only goal then it could always be achieved through the perverse solution of systematically removing any advantages of more privileged groups.

It is frequently hoped that equalizing service availability will reduce disparities in health. Yet there is a concern that in the short-term, disparities could widen as middle income groups take disproportionate advantage of the new services, while the poorest of the poor lack the wherewithal to overcome even the newly lowered barriers to care.[2]

Although expanded primary health care provision remains a central issue in redressing health disparities, standard public health interventions such as micronutrient supplementation, vaccination, water and sanitation are even more important. Basic improvements in public health and nutrition are credited with much of the 20th century mortality improvements around the world, and played a more important role than access to clinical services.[3,4] Furthermore, traditional public health interventions such as measles vaccination or micronutrient supplementation have been shown to narrow socioeconomic and gender disparities in health when distributed through universal outreach programmes[5,6]

In many countries sub-populations can be identified that remain unreached by basic public health services. Given the potential for tremendous health gains and the reduction of health disparities when public health interventions are universally applied, ensuring that public health measures have been fully implemented remains a high priority. Yet preventive public health interventions suffer from perennial scarcity of resources. Policy-makers looking for ways to make tight public health budgets go further, naturally consider targeting interventions to those who are most in need.

In this vein it is reasonable to consider the case of a health planner who wants to allocate resources efficiently to both maximize the level of health achieved and to achieve an improvement in the equality of health outcomes among population groups.[7] Such a policy-maker would consider whether to target resources towards only the underprivileged or to universally distribute resources to an entire population. It is plausible that in some instances health resources applied to the underprivileged are more productive. For example, evidence suggests that measles vaccination in Bangladesh lowered mortality more for the poorest of the poor than for the less poor.[5] Thus a universal distribution approach would rely on the natural capacity of the more disadvantaged to derive greater benefit than their more advantaged counterparts, thereby narrowing the health disparities. But from an economic standpoint, targeting resources has the advantage of reserving their use for only the disadvantaged groups in the population and could save money.

We will build on our prior studies of vitamin A distribution in Nepal to consider the economics facing a planner in Nepal who wished to decide whether to target or universally apply vitamin A supplementation strategies in order to improve child health and to narrow health disparities.

Vitamin A delivery strategies

Deciding between 'mass treatment' vs 'screen then treat' is a classic problem in public health. Students are taught to think about the following criteria:

- The degree to which morbidity and mortality are concentrated in an identifiable subgroup.
- The sensitivity and specificity of the screening procedures.
- The cost of the screening procedure.
- The cost of the treatment.

Screening (to establish a diagnosis) before treating is the essence of clinical medical practice and has distinct advantages when treatments impose health risks and side effects. Public health planners often take a divergent path to achieve dramatic success using mass treatment methods to blanket a population with low cost, low risk, high benefit treatments like vaccines, vitamins and clean water. Yet there still remains ample scope for screening strategies in public

health, both to achieve efficiency when treatments are costly and also in order to target underserved groups who may have been victims of social inequities. When targeting disadvantaged groups the screening effort is devoted to determining the patient's economic or social status prior to offering treatment.

Targeting vitamin A supplements towards disadvantaged subgroups is often considered. Evidence that vitamin A supplements have stronger effects on the survival of girls vs boys and of low caste vs high caste children suggests that these subgroups might deserve special targeting.[6] Evidence of feeding practices that result in lower vitamin A intake by girls and low caste children helps to explain why vitamin A supplementation is more effective in these groups.[8,9]

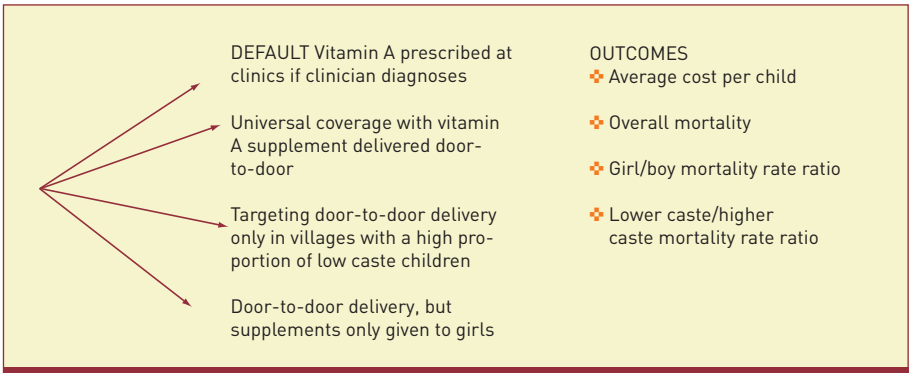


Figure 1: The four strategies modelled in this analysis

A potentially lower cost of reducing mortality is not the only reason to consider targeting high risk groups. Equity of opportunity and more equal health outcomes are other valid goals that could result from targeting. For instance, if there were villages or neighbourhoods with a high proportion of low caste children, health outreach workers might choose to focus their efforts in only those regions. This would reduce the expenditure on the supplement and eliminate costly trips to regions with high caste children who might benefit less. In a similar vein, one could also decide to offer vitamin A supplements to only girls, thereby cutting the expenditures on vitamin A by half.

A cost-effectiveness study in the Philippines evaluated the efficiency of targeting vitamin A strategies to just high risk children as determined by weight for age.[10] The Philippines study concluded that universal vitamin A supplementation prevented the most deaths for the least money because the burden of initially screening children for malnutrition essentially doubled the cost of a targeted strategy. The study did not evaluate any social equity goals that may have been achieved through targeting, nor did it consider potentially lower cost targeting criteria such as child gender or area of residence.

This paper will compute the relative cost-effectiveness of both a universal strategy and a socially-targeted strategy for vitamin A delivery in Nepal, with the primary goal of saving lives for less money and the secondary goal of equalizing death rates across society.

Methods

Figure 1 depicts the four strategies we will model in this analysis. They are as follows:

Horizontal strategy:

A default programme which makes vitamin A supplementation available at the primary health care facility. Whether or not a child receives vitamin A will depend on parental choices to attend the clinic and provider discretion that vitamin A supplementation is clinically indicated.

Vertical strategy – three different programmes:

- **(1)** A universal vitamin A distribution campaign where vitamin A is delivered door-to-door, just as it was in the experimental trials
- **(2)** A door-to-door programme targeted to children who are not in highest castes
- **(3)** A door-to-door programme targeted to girls only.

In each case we will calculate the average cost of implementing the strategy in a population of 10,000 children treated as well as the expected child mortality rate overall and for the relevant component groups. Finally, we will compute the incremental cost per death averted (relative to the default programme) for each of the three vertical programmes.

Estimating effects

Estimates of mortality for each strategy were obtained by observing the mortality outcomes in various subgroups from the Nepal Nutrition Intervention Program-Sarlahi (NNIPS).[11] This 1989 trial involved 30,000 children 6–60 months of age in 261 wards in 29 rural village development committees in Sarlahi, Nepal.[1] Children were randomly assigned by ward to receive either a placebo capsule with 300 mg retinol equivalent (1000 IU) or a capsule containing 60,000 mg retinol equivalents (200,000 IU) of vitamin A. In prior work we used these data to identify the ability of universal vitamin A distribution to lower death rates of children age 6–60 months from 26.9 to 17.9 per thousand for girls and from 19.1 to 16.5 for boys.[6]

Comparing experimental to control groups, high caste (Brahmin or Chettri) children had death rates of 11.5 and 11.2 without and with vitamin A, respectively, while lower caste and non-caste children had corresponding death rates of 25.2 and 18.6, respectively.[6] In other words, the survival benefits of vitamin A appeared to be larger for girls and lower caste children, so targeting these groups might be more efficient.

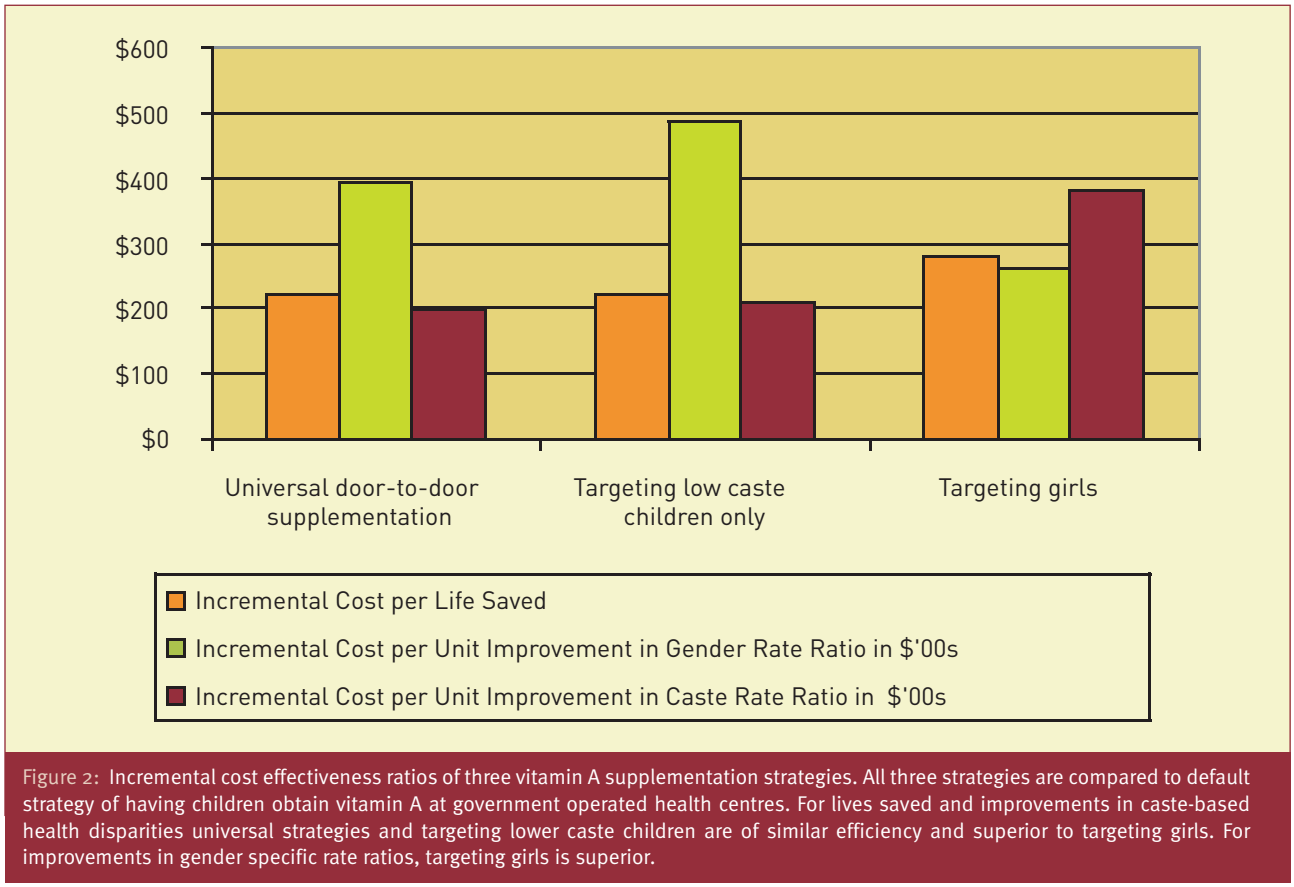


Figure 2: Incremental cost effectiveness ratios of three vitamin A supplementation strategies. All three strategies are compared to default strategy of having children obtain vitamin A at government operated health centres. For lives saved and improvements in caste-based health disparities universal strategies and targeting lower caste children are of similar efficiency and superior to targeting girls. For improvements in gender specific rate ratios, targeting girls is superior.

Estimating costs

Cost estimates are based on studies of the current Nepal National Vitamin A Program (NVAP). The programme consists primarily of distributing high-dose vitamin A capsules to all children aged 6–60 months old during twice-yearly campaigns. The campaign is complemented by ongoing treatment of clinical xerophthalmia and other acute infections in health facilities throughout the country. The capsule distribution is carried out by a network of female Community Health Volunteers. Estimates of coverage rates among targeted children range from 53–>90%. The cost of the programme ranged from $1.13–1.48 per child, with a best estimate of $1.27 per child.[12]

In order to estimate costs we made the following assumptions:

- Target population of 10,000 children living in 10 communities (panchayats) of 1,000 households
- To target just girls, health workers would have to visit each community and call upon each household, but would only provide supplementation to girls
- To target social groups (e.g. on the basis of caste), health workers would have to visit each community and call upon each household, but would only provide supplements in households of the targeted social groups.

If these targeting policies were actually implemented, there could be social resistance to these blatantly discriminatory policies. A subtle effect could be to cast a social stigma on households or children who receive the supplements. A strong effect might be a refusal of local officials to permit discrimination in their jurisdiction. Our model is not taking these effects into account because the nature of these events cannot be predicted.

We explored whether it would be possible to save costs by targeting at the level of the entire community. Although there are no communities that could be skipped for want of girls to treat, we checked whether perhaps there might be communities in the Terai of rural Nepal where there were so few children in the less elite castes that trips to these villages could be eliminated. Based on the data from the 1989 trial in Sarlahi, the lowest number of low/other caste children in any panchayat was 58%, indicating little scope for eliminating trips to any of the communities in our model.

As no trips could be eliminated, the primary cost savings occur from reducing the cost of vitamin A pills. There would be limited opportunity to lower personnel costs, because every household would still require canvassing. In the Nepal Vitamin A Program the cost of pills amounts to only 5.4% of the total cost.

Analysis

Estimates of the numbers of deaths and the total costs of each strategy were computed. Incremental cost effectiveness ratios were calculated for the universal strategy and for each targeted strategy with reference to the default of no vitamin

	Ordinary care	Universal door-to-door supplementation	Targeting low caste children only	Targeting girls	Source
Labour Costs		$12,014	$12,014	$12,014	Fiedler (2000)
Pill Costs		$686	$561	$343	Fiedler (2000)
Total Costs	0	$12,700	$12,575	$12,357	Fiedler (2000)
Boy Mortality (Deaths per Person Year)	1.91%	1.65%	1.70%	1.91%	(6)
Girls Mortality (Deaths per Person Year)	2.69%	1.79%	1.95%	1.79%	(6)
High Caste Mortality (Deaths per Person Year)	1.12%	1.15%	1.12%	1.14%	(6)
Low Caste Mortality (Deaths per Person Year)	2.53%	1.86%	1.86%	2.20%	(6)

Table 1: Parameters used for analysis (in US$)

A programme.

The incremental cost effectiveness ratio (ICER) is calculated as:

$$ICER=(C_{default}-C_i)/(Deaths_{default}-Deaths_i)$$

An analogous ICER for outcome equality can be calculated as:

$$ICER=(C_{default}-C_i)/(RateRatio_{default}-RateRatio_i)$$

Where C denotes cost, Deaths refers to estimates of deaths per 1000

RateRatio refers to either the ratio of the death rate in girls to the death rate in boys or the death rate in higher caste to the death rate in lower caste children.

Subscript 'i' can take the values 'default', 'universal', 'girls only' and 'low caste only' to refer to the treatment algorithm under consideration as depicted in Figure 1.

Results

Table 1 displays the parameters used in this analysis and their sources. The mortality rates for ordinary care are taken from the outcomes in the NNIPS trial population who received placebo.[11] The values for universal care are taken from the vitamin A recipients who received vitamin A supplements. In the targeted strategies, the individuals targeted derive the mortality of the vitamin A recipients in that group. Table 2 shows the expected number of deaths and the costs per death averted of the various strategies. It also shows the cost per unit change in the two health disparity indicators. These results are also displayed in Figure 2, which shows that universal coverage has similar efficiency to targeting only lower caste children with respect to dollars per life saved and dollars per unit change in caste-based mortality rate ratio. Targeting girls is a more cost-effective strategy for improving the gender-based mortality rate ratio, but this advantage may be outweighed by its poorer efficiency in saving lives.

Discussion

Since the data from the community-based trial showed that vitamin A had virtually no effect on improving survival in the highest caste children, a strategy which sought to exclude highest caste children could save pill costs and have virtually no reduction in overall mortality. As pill costs are negligible anyway, the overall cost effectiveness improvement of the

	Ordinary care	Universal door-to-door supplementation	Targeting low caste children only	Targeting girls
Total Deaths in Population of 10,000	229	172	172.56	185
Gender Death Rate Ratio	1.408	1.085	1.151	0.937
Caste-Specific Death Rate Ratio	2.259	1.617	1.661	1.934
Total Costs	Baseline	$12,700	$12,575	$12,357
Incremental Cost per Life Saved		$223	$223	$281
Incremental Cost per Unit Improvement in Gender Rate Ratio		$39,255	$48,854	$26,225
Incremental Cost per Unit Improvement in Caste Rate Ratio		$19,796	$21,022	$38,021

Table 2: Incremental cost effectiveness analysis (in US$)

targeted strategy is unremarkable. In contrast, trial data show that vitamin A offers benefits to both boys and girls, but it offered larger benefits to Nepali girls. Excluding boys from treatment saves pill costs, but lowers overall cost-effectiveness because the advantages of saving boys is lost. The dual effects of saving girls while not saving boys offers this strategy a greater degree of cost-effectiveness with respect to lowering gender disparities, but this strategy is the least efficient way to save lives. For most decision-makers the goal of saving lives is more important than the secondary goal of lowering health disparities.

Our analysis shows roughly equivalent cost-effectiveness for universal treatment and selective treatment of lower caste children with respect to two out of three policy goals. However, in practice universal coverage with vitamin A is less prone to political obstacles and would be preferred. ❑

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From promises to action: health research after the Mexico meetings



Article by Andres de Francisco

Mexico hosted two important meetings related to the common theme of health research needed towards achieving the Millennium Development Goals (MDGs) in September 2004. Held in conjunction, the meetings were the 'Ministerial Summit on Health Research' and the 'Eighth Annual Forum Meeting' – Forum 8 of the Global Forum for Health Research. The two meetings took place in venues close to each other, and shared opening, closing and some plenary sessions. Forum 8 brought together about 700 policy-makers, researchers and representatives of governments, development agencies and research institutions. The Ministerial Summit brought together 200 participants including health ministers and leaders from the health research and development communities.

Two complementary documents emerged from the meetings. The Ministerial Summit issued the *Mexico Statement on Health Research*, the text of which was finalized during the meeting[1] and the *Global Forum Statement* developed by the Secretariat of the Global Forum with the assistance of inputs from regional consultations and from participants at Forum 8.[2]

The *Ministerial Statement* emphasized the need for higher investment in health research to be funded by governments from developed and developing countries. It also called for better management of health research, for increased efforts to be made to secure public confidence in science and its products, and for more emphasis to be made to turn knowledge into action to improve health. Based on work undertaken by a task force on health systems research prior to the meeting, the *Ministerial Statement* called for an enhancement of research in health systems and for increased activity in identified priority health research areas. Furthermore, the *Ministerial Statement* indicated that health systems research was an essential component of health and proposed creation of an inventory of clinical trials in which all institutions, both from the private and public sectors, would report all clinical trials undertaken.

The *Global Forum Statement* urged that collective action be taken by partners to ensure higher political commitment and shared responsibility for health research. It recognized that improving health is essential to development and that, while government leadership is crucial in this process, delivering research results is the responsibility of all constituencies. Central to its message was the realization that, beyond the 'health specific' MDGs, all eight MDGs are important for health and therefore all sectors – not only health – have an important role to play. The *Global Forum Statement* emphasized that combating hunger, low education and gender inequalities (MDGs 1, 2 and 3) were as important as controlling other causes of morbidity and mortality (MDGs 4, 5 and 6), and that the process through which this would be achieved in a sustainable manner (MDG 7) included interactions between the public and private sectors (MDG 8). The *Global Forum Statement* highlighted the importance of inequities based on gender, ability, race and social class, and that health research needs to be sensitive to these if the MDGs are to be achieved in a way that encompasses people from disadvantaged population groups. The *Global Forum Statement* called on governments to fund health research, to set priorities in a systematic and transparent ways, and to interact with civil society and other constituencies to enhance the likelihood of improving health for the vast majority of the population of the world.

Progress since the Mexico meetings

The following is a brief review of progress made in the nine months since the Mexico meetings.

World Health Assembly

Since the publication of the *Ministerial Statement*, the World Health Organization pursued its endorsement at the Executive Board of the World Health Assembly (WHA) in January 2005. After much debate on the document, the Executive Board approved the statement for presentation at the World Health Assembly, which discussed the document in its session on 23 May 2005. The discussion during the WHA focused more on the process for undertaking and conducting a summit than on its content. The WHA praised its content and approved the document without major modifications. This is an important milestone in the political process of health research and a welcome outcome of this measure. The challenge now is for countries to take the recommendations forward, including the steady funding of health research.

A technical briefing was held during the WHA on the 17 May 2005 in which four Health Ministers (Manuel Dayrit, the Philippines; Julio Frenk, Mexico; Eyitayo Lambo, Nigera; and Manto Tshabalala-Msimang, South Africa), and

four additional representatives of key actors in the health field (Sally Davies, Director of Research and Development for the Department of Health and NHS, UK; Judith Witworth, Chair of the WHO Advisory Committee on Health Research; JW Lee-Wong, Director General of WHO; and Tim Evans, Assistant General of WHO) were present. The session was chaired by Richard Horton, Editor of the *Lancet*. Participants in the panel of this technical meeting endorsed the outcomes of the Mexico meetings and the content of the Ministerial Statement. Members of the panel indicated the relevance of health research for their work and reflected upon their future contributions towards the health research field. Minister Frenk framed his remarks starting with the 1990 Commission on Health Research for Development and the distinct progress made since their report was published.[3] He talked about the progress in the past 15 years, highlighting that the process of debate in health research was essential, and praised the role of WHO in embracing health research as a global public good. As the host Minister for the Mexico meetings, he reflected on the importance of having the Annual Forum meetings intercalated with Ministerial Meetings every four years to achieve the required high level policy debate.

The Minister of the Philippines proposed to have a programme in place to provide detailed insights on the way health systems research can help policy-making and provide a blueprint to facilitate the use of research findings in policy design. All recommendations given at that session were aimed at thinking beyond the Mexico Declaration and into the next meeting of Ministers on Health Research in Africa in 2008.

Health policies and systems research

It is now evident that the issue of health policies and systems research is on the table. The WHO presented in Mexico the *World Report on Knowledge for Better Health: Strengthening Health Systems*.[4] An important input to the design of this document was a special issue of the *Lancet* with a series of articles related to overcoming health-systems constraints and an international cooperative research agenda on health systems was distributed during the meeting.[5]

A champion in this area has been the Alliance for Health Policies and Systems Research, established in 2000 as an initiative of the Global Forum for Health Research and housed at WHO. Since its inception, the Alliance has established links with 350 research institutions in the developing countries working on this key and yet neglected area of health policies and systems research.[6] During its April 2005 meeting, the WHO Advisory Committee in Health Research discussed the results of an informal consultation held in London in February 2005 in which plans to establish a Special Programme on Health Systems Research for Public Health Improvement were debated. These discussions led to a proposal discussed by a number of partners from developed and developing countries to create a 'special' or 'partnership' programme at WHO to promote, coordinate and enhance work on health systems research. Such an institution would be key to raising the level of advocacy and scientific output in this area of work, and it is hoped that it would attract the resources required to undertake such an ambitious agenda. With the support of donors, such a programme could focus on developing countries, enhance their demand for healthy systems research results and further decentralize this function. The Committee responded positively to this option. There are now wider ongoing discussions about the future activities of research on health systems and this has been a very positive outcome of the Mexico meetings and their preparatory work.

There are now wider ongoing discussions about the future activities of research on health systems and this has been a very positive outcome of the Mexico meetings and their preparatory work

Clinical trials registry

During the discussion at the WHA technical briefing there was strong endorsement of an initiative to establish a clinical trial registry. There have been efforts in the past to establish such a registry, but none has been adopted widely and in a sustained manner. The discussion focused on the design and implementation of the clinical trials registry.

During the meeting, the International Federation of Pharmaceutical Manufacturers Association (IFPMA) indicated that they welcomed clinical trial registration. IFPMA reported that they had recently opened and made functional a portal on the internet where they were mapping research projects undertaken by the pharmaceutical industry worldwide, including in developing countries.[7] They briefly described the system and reported that the private sector will use that portal to report selected, non-confidential clinical trials.

This clearly poses a challenge to having one universal clinical trials registration system of the type advocated by WHO. A current paper by the coordinator of this initiative was published in the *Lancet* recently.[8] The team started the process with a meeting in April 2005 that all major stakeholders attended including governments, pharmaceutical companies, trade associations, journal editors, registry owners and independent researchers. The project aimed at setting norms and standards, enhancing access for researchers, advocating for compliance and building capacity where needed.

To date, agreement has been reached on the definitions of clinical trials and the minimum data set required at the time of trial registration. The discussion of the disclosure of trial results and exactly where to register them, has so far not been concluded. The paper indicates that an international, unambiguous trial-identification system is necessary and that WHO will continue working towards this end. It is necessary

that all constituencies and partners agree with the process and mode of registering clinical trials, otherwise the purpose of this initiative would not be fulfilled.

Tracking financial flows

Both statements in Mexico highlighted the importance of increasing financial flows for health research. The Global Forum presented in Mexico a comprehensive study with its most recent analysis of global resource flows for health research.[9] The document, highlighted by Mexico's Minister of Health as a landmark on resource flows measurements, included an analysis of the global health research funds invested in 2001 and reported a total investment of over US$100 billion spent on health research in that year from public and private sources.

It is necessary that all constituencies and partners agree with the process and mode of registering clinical trials, otherwise the purpose of this initiative would not be fulfilled

In endorsing the commitments made by governments on health research financing (2% of developing country health expenditures to be used for health research and capacity development, and 5% of developmental funds for health from developed countries to be used for the same purpose), the two statements, and subsequently the WHA, promoted the activities of tracking of financial flows for health research. Work undertaken in 2005 by the Global Forum, COHRED, the Rockefeller Foundation and country partners (governments, civil society and the private sector) have initiated country studies on financial flows for health research since the Mexico meetings. Key innovative developing countries are contributing to this effort including Brazil, South Africa and India.

Further, the Global Forum jointly with the UK Medical Research Council coorganized a meeting in London on 12–13 June 2005 to provide inputs to a meeting of the Heads of International Research Organizations of high-income countries. One of the key discussion points of the meeting was the considerable interest expressed in documenting and analysing financial flows invested in health research by the largest public sector financing institutions of the world. As a result, intensified work in this field is now under development, and is expected to be undertaken during the second half of 2005.

There is also progress with proposed studies to identify investments on health research related to MDGs 4, 5 and 6, including research on HIV/AIDS by the International AIDS Vaccine Initiative and UNAIDS. In view of the fact that this year's world health theme is 'Mothers and their Children', there is renewed interest in understanding the financial investments on child and maternal health around the world. A workshop called by the Child Survival Partnership and the London School of Hygiene and Tropical Medicine in March 2005 expressed interest in evaluating projections on potential funds required to achieve MDG 4 on child health and child survival and the research required.

Sexual and reproductive health research

There have been some activities in the field of sexual and reproductive health (SRH) research. Having approved a resolution on reproductive health in 2004, the WHA 2005 passed two resolutions related to this field. One of them is general and related to the MDGs, and the second one calls specifically for universal coverage of maternal, newborn and child health interventions. These two resolutions are welcome as this area of work has been neglected in the past, and this is being reflected in a dramatic reduction in investments for research. One of the consequences of that neglect of research on SRH is the substantial decrease in funding of the Special Programme of Research, Development and Research Training in Human Reproduction (HRP) hosted by the World Health Organization.

During the WHA 2005 a lunch seminar was organized by COMMAT (the Commonwealth Medical Trust), the Millennium Project, and the Global Forum for Health Research. The event was attended by a dozen Ministers of Health and they talked about the relevance of SRH for their health policies and their support for more attention to this area. It is expected that this field will move further ahead with the two WHA resolutions, advocacy work and the interest generated in this field by the World Health Organization's theme on 'Mothers and Children' in 2005.

Building partnerships for health research

Both Statements issued in Mexico emphasized the need for more collaborative action and stronger partnerships to address ongoing health challenges. One important development since the Mexico meetings has been the establishment of a Memorandum of Agreement between the Global Forum for Health Research and the Council on Health Research for Development (COHRED). Building on this formal agreement, the two organizations are engaging in a number of joint activities including publications, tracking of resources for health research at country level, studies of research capacity strengthening in collaboration with TDR, and operational collaboration in planning, administration and fundraising. These collaborative efforts are predicated on the recognition of opportunities for synergy through the interfacing of global and country-level perspectives, while their separate and unique identities enable each organization to provide a clearly articulated voice for its own concerns and constituencies.

Conclusions

The Mexico meetings, the *Ministerial Statement on Health Research* and the *Forum 8 Statement* are landmarks in the development of health research since the 1990 Commission

for Health Research and Development called for more attention to research. During the nine months since the Mexico meetings, substantial progress has been made to enhance and focus health research on the needs of developing countries, to contribute to the achievements of the MDGs.

Despite the progress reviewed in this document, there are important challenges still evident in promoting health research for developing country health problems. Initiatives have been launched, resolutions have been passed and programmes are being pursued. It will be only in retrospect that these efforts and initiatives will be measured in terms of their effectiveness and impact. The planned joint meeting of Ministers of Health Research and Forum 12 in Africa will review progress and define whether we lived up to the expectations that emerged from the Mexico meetings. ❑

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Achieving equity in health: the research dimension

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Rediscovering inequalities in health: a new research agenda



Article by Jumana Qamruddin (pictured), Davidson Gwatkin and Abdo S Yazbeck

After years of research, it is now widely accepted that health, nutrition, and population programmes rarely reach disadvantaged population groups effectively.[1,2] It has become evident to health sector policy-makers and the international development community that only a small proportion of government resources spent in the health sector reach the poor. For example, in over 80% of the developing countries reviewed (17 of 21) in a recent World Bank study, the best-off 20% of the population receives more or as much of the government subsidies to health services as the population's poorest 20%. On average, the benefit going to the best-off 20% is two-thirds higher than that accruing to the poorest 20% (Figure 1). Also, service coverage rates have been found to be higher among the best-off 20% of developing country populations than among the poorest 20% for essential services like basic maternal and child health care.

This paper summarizes and puts into context recent research efforts in the area of inequalities in health as well as highlighting global efforts in moving beyond advocacy to specific policy actions and recommendations. One of these efforts – the Reaching the Poor Program – is described in some detail. The paper concludes with a look forward into the directions of future research efforts in this area.

Evidence to action

The accumulating empirical evidence on the performance of health services in reaching the poor has resulted in increased work on two issues: further documentation and measurement of inequalities in health status and health service use, and the identification of strategies for reducing those inequalities.

Work on documenting health inequalities has been fuelled by the discovery that information about household assets – such as ownership of such common articles like bicycles and radios, and sources of water and fuel – can be used in place of income or consumption to assess families' economic status.[3] This has not only allowed the analysis of distribution in health outcomes and health system outputs from sources like the Demographic and Health Surveys,[1] but has also opened the door to other agencies to include asset questions in their surveys to permit distributional analysis. Over the past few years, for example, asset questions have been added by UNICEF to the Multiple Indicator Cluster Surveys (MICS) and by WHO to the World Health Survey (WHS); and distributional assessments of data from the sources have been or are being produced.

The increased evidence of inequalities has contributed to growing attention to the second issue, the identification of new strategies, as concern among policy-makers about improving health equity has grown faster than their knowledge of how to do it. This has intensified the need for solid evidence about policy and strategy options that can help find feasible solutions. The need for pro-poor policies has been further bolstered by two international initiatives, namely Poverty Reduction Strategies (PRSP) and the Millennium Development Goals (MDG) that have recentred development policy around poverty reduction, outcome orientation and reducing inequalities.

The more receptive climate to pro-poor health strategies, symbolized and reinforced by initiatives like PRSPs and MDGs, has been accompanied by a growing volume of research and publications on inequalities in health outcomes and health system outputs that sought to go beyond diagnosis to the design of remedial strategies. The dynamic nature of such activities can be seen by noting some of the more prominent ones of the last few years.

The health sector chapter in the World Bank PRSP sourcebook sought to draw together the reservoir of knowledge about the development of pro-poor strategies in health and related sectors and present it in a form readily accessible to PRSP authors.[4] Another early activity was the Global Health Equity Initiative, organized by the Rockefeller Foundation and the Swedish International Development Cooperation Agency. This produced a well-known volume on health inequalities, *Challenging Inequalities in Health: From Ethics to Action*.[5] The 21-chapter volume is a collection of studies analysing health gaps within and among countries and available tools and programmatic approaches for redressing persistent inequalities.

A more recent Rockefeller-supported health inequality research activity has been undertaken by the INDEPTH Network of demographic surveillance sites in developing countries. The INDEPTH health equity project started as a purely diagnostic effort focused on inequalities within 13 of its member sites, with populations ranging from 8,000 to more than 200,000. The volume of studies produced by this initial phase covered inequalities in both health outcomes



Figure 1: Distribution of benefits from government health service expenditures[6]

and health service use.[7] Having found much more frequent inequalities than expected, INDEPTH added a remedial focus in the second round of its project by inviting proposals for assessing service delivery strategies to reduce those inequalities. Thus far, it has funded five such assessments – all in Africa – dealing with expanded outreach programmes to encourage use of HIV/AIDS prevention and treatment services by poor families, targeted subsidies for insecticide-treated bednets, and child welfare grants to poor households.

A third Rockefeller-initiated activity, the Equity Lens Project, focused on strategy change from its beginning in the early 1990s. This project was an effort to alert the leaders of prominent global health initiatives to the emerging evidence on coverage inequalities and to encourage them to develop more effective delivery strategies. It organized and supported a wide range of presentations, literature reviews, and similar activities in cooperation with global health initiative personnel working in six areas: child health, immunization, malaria, safe motherhood, trachoma and tuberculosis. In September 2003, Rockefeller, the World Bank and the WHO concluded the project's initial phase through a consultation of health equity specialists associated with the global initiatives. A second phase, featuring field experimentation with alternative strategies for reaching the poor, was being developed at this writing.

The *World Development Report 2004*[2] is another example of an effort to call attention to, and find ways of alleviating the documented disparities in health service coverage. It summarizes the growing evidence on how public spending for education, health, nutrition, water, sanitation and electricity fails the poor in many low- and middle-income countries. The report advances a framework of accountability that recognizes three critical groups of actors (citizens, government and providers of care) and recommends policies that strengthen the accountability lines between the three groups.

The emphasis on health services by that World Development Report and other activities has recently been complemented by a focus on social and economic determinants of health inequalities by a commission established in March 2005 by the WHO. Like several of the other activities described here, the WHO Commission on Social Determinants of Health will compile evidence and propose agendas for action based on that evidence.[8] In doing so, the commission hopes to develop a 'third major thrust' that can support health system development and poverty relief by finding ways of reducing social disparities.[8]

The Reaching the Poor Program

The Reaching the Poor Program (RPP), with which the authors of this paper have been associated, seeks to extend the work begun by the groups described by going beyond the diagnoses of coverage inequalities to find ways of reducing these inequalities and improving coverage among the poor. It was initiated in 2001 by World Bank staff concerned by the emerging evidence about the existence of large health coverage disparities and the lack of clear guidance about how to reduce them.

In its effort to provide better diagnoses and point toward solutions, the RPP adopted the benefit-incidence approach (described in Box 1) for assessing and monitoring the distribution of programme benefits. However, its interest was not in benefit-incidence analysis per se; but rather in the application of this technique to the identification of better ways to reach disadvantaged groups in order to overcome increasingly well-documented disparities.

To realize this objective, the RPP has been undertaken in three phases. The first was knowledge generation, implemented by commissioning evaluation research studies identified through a competitive bidding process. The second, knowledge synthesis, was conducted through a global conference in February 2004, and the final phase, which is currently underway, is knowledge dissemination.

While not all RPP outcomes were encouraging, there were far more positive cases than expected. This principal finding provides hope that the current situation can be changed, and that health programmes do not have to be inequitable. The RPP studies also illustrate a wide variation of policies and programmes favouring the poor and therefore, the availability of multiple approaches that hold promise. This suggests that the challenge is to find the approach that works best in a particular setting.

Box 1 | The benefit-incidence approach

Benefit-incidence analysis is a technique developed over the past 20 years by public finance specialists. It is used to determine how the benefits of overall government expenditures are distributed across different economic groups. More recently, health economists have begun to become aware of the benefit-incidence approach. However, few benefit-incidence studies of health expenditures have thus far been undertaken, and outside the health economics community, the technique is still poorly known. For example, almost all public health specialists are now aware of cost-effective analysis, the economic technique used to measure the volume of health programme outputs produced by a given volume of inputs. But recent discussions with leading equity specialists in public health indicate that most have not heard of benefit-incidence analysis, the analogous technique that can determine how such outputs are distributed among poor and better-off segments of the population.

The basic approach featured in the RPP studies referred to in this paper is a version of the benefit-incidence approach that has been modified for use in the health, nutrition and population field. For example, the benefits whose distribution is assessed are usually not financial transfers but rather service outputs like clinic visits, children immunized, people reached through home visits, and the like. Also, the scope of activities covered in the RPP studies is not limited to government-provided services, as it was the original benefit-incidence work, but often deals in addition or instead with services obtained through private-for-profit or not-for-profit providers. Nor do the RPP studies often consider the net benefit of the services received, by taking into account any amounts that service recipients pay. Rather, the focus is more frequently on simple coverage differences across groups.

Examples of promising approaches identified by the studies commissioned by the RPP include:

- Contracting with non-governmental organizations (NGOs). In Cambodia, gains for the poor were especially large in districts where the NGOs were given full responsibility for service provision under contracts specifying coverage to be achieved in the population's poorest 50% as well as the population as a whole.
- Distribution of commodities through mass immunization campaigns. In Ghana and Zambia, field experiments to distribute insecticide-treated bednets through government Red Cross mass immunization campaigns were conducted. The result was a rise in overall bednet ownership from less than 5% to nearly 95% in Ghana and from less than 20% to more than 80% in Zambia. In the process, ownership differentials between the poor and better-off were eliminated in Ghana and greatly reduced in Zambia.
- Participatory programme planning. In Nepal, a field experiment was organized by a multi-agency consortium, with a participatory approach involving prospective beneficiaries in the development of adolescent health programmes. The outcome was a larger improvement among the disadvantaged than among the better-off for all three of the indicators covered: prenatal care, attended deliveries and knowledge about HIV.

In addition, presentations at the RPP conference of benefit-incidence studies undertaken by other researchers produced examples of additional approaches that showed promising results. An illustration is the Colombian government's use of an innovative technique (proxy means testing) to identify poor families who were provided with subsidized health insurance in order to lower financial barriers to service use. Another example is Mexico's PROGRESA Program, which features payments (conditional cash transfers) to poor families to use education and health services.

Future directions

The impressive growth over the last few years in health policy research focused on inequalities in the sector has significantly changed the environment for policy-makers and their development partners in two important ways. First, it is no longer acceptable to assume that public spending on health is the same as spending on the poor. Without explicit attention to inequality and monitoring, the evidence shows that benefits from health programmes will likely be captured by the better-off in society. Second, the more recent research efforts, such as RPP, show that it is possible to redirect public spending to the poor by increasing their share of benefits from public programmes in health. The fact that spending can be pro-poor, however, does not mean that it is easy to achieve this outcome. There will be a need to understand the determinants of

unequal use of health services, adapted policies to address the bottlenecks faced by the poor, and monitored to ensure objectives are met.

Efforts to generalize the positive outcomes produced by programmes that succeed in reaching the poor are at an embryonic stage and will have to overcome the result of years of little to no attention to inequality and persistent political economic factors. Three related lines of research and action appear particularly promising for the promotion of further progress against health inequalities:

- **Improving measurement.** Efforts are needed to include wealth-related questions in household surveys, and to make use of techniques such as benefit-incidence analysis standard in health programme analysis and evaluation.
- **Consistently asking 'why'.** Finding solutions to inequalities requires an understanding of why the poor do not use health services. To develop such an understanding, the use of qualitative and quantitative assessment techniques (preferably combined) will have to become a standard approach to designing policies.
- **Experimenting.** Business-as-usual has proven to be an ineffective way to reaching the poor. Field experimentation with alternative approaches is called for in order to find better strategies. ❑

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Equality in health: the case of disabled women



Article By Anita Ghai

The appreciation of the centrality of health research in the Bangkok declaration is indicative of an acceptance of the belief that any move towards securing equitable health can be successful only if it is based on sound policy planning that uses research as an essential and inseparable part of its interventional efforts. While the unparalleled economic growth of globalizing economies is celebrated, the issues facing marginalized people escape notice. The disparities amongst different groups of people have widened so much that now the question is not about the deficiencies in services or the reach of the services, but rather, who are those who do not have any access to services? Historically, certain groups have been marginalized because of their class, caste, gender, or rural-urban residence leading to a situation where a categorization of 'vulnerable groups' came into being. One vulnerable category that continues to experience this marginalization is the category of disabled people.

Disability and health: a paradoxical relationship

Disability and illness/health are often considered synonymous. In fact, people who are disabled by chronic/life threatening illnesses have had to fight the identification of disability with illness. This identification has contributed to the medicalization of disability in which disability is regarded as a personal tragedy, creating an impression that disabled people suffer primarily from physical and/or mental disabilities that medicine can and should treat, cure, or at least prevent. Disability is a constant challenge to medical practitioners, as their aim is to cure and fix the body and mind of their patients. Disability adjusted life-years (DALY), which assumes a reduced value of lives lived with a disability, reflects this medical orientation positioning them as 'burdens of society'. Research in health needs to interrogate the implication of DALY in determining allocations of public health resources. While both disabled men and women experience human rights violations, research suggests that there is a gender dimension to disability. Disabled women share with their non-disabled sisters a reality of exclusion from health services and research that is rooted in both hegemony of normality and patriarchy. Even mainstream women's literature on health care concerns has missed out on the multiple levels of oppression experienced by disabled women. If they are mentioned, it is as a 'vulnerable group' and more as an afterthought. The United Nations Convention to Eliminate all Forms of Discrimination Against Women (CEDAW) committee recently adopted General Recommendation 24 on the Right to Health. While some of the concerns of disabled women are different, major areas of health concerns and health service needs are identical to those of any woman.

First and foremost the problem lies in architectural or communication barriers. The locations of Public Health Centres (PHCs) also make it difficult for disabled women to avail themselves of health services. Furthermore, if state transport is available, it is not disability-friendly. Lack of health personnel and medicines usually makes the journey to the PHC futile.

Disability in developing countries such as India is never a singular marker. Thus it is much more difficult to access health services when there is a poor disabled girl from a low caste living in rural areas. The prevalence of impairment, particularly polio and blindness, is at least four times higher among those who are below the poverty line than those who are above it. Thus, for poor families the birth of a child with a condition or illness leading to impairment or the onset of a significant impairment in early childhood is often considered a fate worse than death.

There are many human rights violations that need to be recognized by concerted efforts so that meaningful policy imperatives can be evolved. For instance, disabled women often experience 'public stripping'. They have to stand naked in front of a number of doctors in order to get 'diagnosed' and examined. It is not uncommon to find medical checkups being performed with doors or curtains left ajar and confidential information carelessly discussed in public places. Policy-makers have to find ways of safeguarding privacy from both off-hand and deliberate infringements.

Another significant research area with definite policy implications is instances of large-scale hysterectomies on female inmates of state-run homes, labelled as 'mentally disabled'. Hysterectomies are performed to manage menstrual hygiene and avoid pregnancies in cases of sexual abuse, without the consent of the woman involved. This overt legitimization of abuse is a clear violation of the right to self-determination. One of the research priorities is to collect evidence of the extent of these violations and to inform

policies aimed at the health and well-being of women. Forced sterilization is a form of violence against disabled women. The consequences are long term and can be emotionally and physically devastating. The fact that professionals in medical settings are implicated has to be seriously attended to. Research priority should be to work out methodologies that can comprehend experiences even in the case of severe impairments.

Disabled women who have been sexually abused or assaulted very rarely receive adequate medical or psychological help to recover. For many of them, the subsequent medical treatment is like 'undergoing a second assault'. Mental health is thus another priority area of research with significant policy implications. It is imperative that disabled women are included in research on depression, suicide and other emotional problems, so that adequate intervention and support can be provided. Policy has to develop suicide prevention services, as the ones that are available are totally inaccessible. Policy should guarantee the availability of accessible, affordable mental health services or professionals who understand disability.

Another form of abuse and rights violation is forced medical treatment that collides with medical experimentation. For example, girls who are born without or with impaired limbs are forced to wear prostheses when they are still infants, while reliable research has proven that this is detrimental to their identity development and results in more harm than help.

One of the prime violations is in the area of sexuality and reproductive health

Disabled girls and women do not get the appropriate information and treatment regarding reproductive health care. Disabled girls and women rarely get information about sexuality, birth control, sexually transmitted diseases or pregnancy and motherhood from mainstream health care facilities. Society generally invalidates disabled girls and women's sexuality. Their reproductive potential is feared.

Disabled girls and women rarely get information about sexuality, birth control, sexually transmitted diseases or pregnancy and motherhood from mainstream health care facilities

Disabled girls and women need much more information on how available contraceptives affect them. Research into contraception has to look into the interactions of contraceptives with different impairment conditions and into how to best provide information that is accessible and understandable, irrespective of the type of impairment or condition. As many professionals seem disturbed by the idea that reproductive health or sexuality would be 'significant' to their disabled patients, they evade questions about sexuality or body image. In fact questions about orgasm, pain during sex, the advisability of getting pregnant, childbirth, and weight gain are often brushed off.

Physicians' tendencies to view disabled women as asexual can result in failure to investigate signs of serious conditions. Research in understanding the physician's discomfort in responding to disabled women's complaints – particularly those involving their reproductive health has shown that this is largely because of over-generalization of the primary impairment.

The policy directive is clearly saying that it is better not to have disabled children. In a country where gender ratio is problematic, disabled girls will not stand a chance

While these human rights violations need to be researched, there is fear that the development of new reproductive and genetic technologies may encourage a eugenic perspective. Selective abortion implies the affirmation of deprecating and disapproving cultural value judgments and norms. The widespread supply of prenatal diagnosis or testing as a screening method must be questioned especially in view of the context that in India, the legislation sanctions abortions if there is a 'medical condition'. The policy directive is thus clearly saying that it is better not to have disabled children. In a country where gender ratio is problematic, disabled girls will not stand a chance. Despite enormous research on sex-selection issues, disability selection is not researched. Moreover, if more health care resources are concentrated into developing new technologies, fewer resources will be available for health care.

There are instances where a person with muscular dystrophy has asked for permission to die so that organs could be donated, or parents have sought permission for 'mercy killing' their daughters as they were unable to meet the medical costs of looking after them. Allowing euthanasia reinforces the often-heard message that 'it's better to be dead than sick or disabled'. The underlying implication is that some lives are not worth living. What is worse is that such assumptions not only put disabled people at risk, they also devalue their status as human beings while they are alive.

What needs to be underscored is that life with a disability is not a disaster. The quality of life argument, which is often used against disabled people, has to be questioned. It stems out of an individual model of explaining disability without looking at the societal structures that are responsible for transforming impairment into disability. Both research and policy have to acknowledge that such directives are ultimate acts of violence that cannot be tolerated. There is a need to engage with the issues and to collect baseline information about what kinds of needed health and other services are lacking, or inaccessible, and

how they can be made disability-friendly. The inputs have to be integrated within policy to effectively deal with health care and related issues that affect the overall health and well-being of disabled people. ❑

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Gender in health research – past, present and future



Article by Piroska Östlin

'Gender inequities in health are important, because severe inequities waste human potential, erode trust, weaken social institutions, and hamper democratic functioning. Severe inequities are a deprivation of basic human rights,' reported Lincoln Chen, Stockholm, on 15 May, 2002.[1]

During the last few decades there has been an emerging recognition among health professionals – researchers and policy-makers alike – of the widespread and profound implications of gender-based inequities in health. The term 'gender' means the socially constructed distinctions between women and men in access to and control over resources and knowledge, their decision-making power in the family and community, divisions of labour and occupational segregation as well as the roles and responsibilities that society assigns to them. The concept of gender allows researchers to distinguish and comprehend the deep, but modifiable, social basis of differences between women and men apart from the seemingly obvious biological differences (sex differences). There is a growing body of scientific evidence (both quantitative and qualitative) that gender, as a socially constructed distinction, can reinforce, counteract, or work independently of biological sex. Together, gender and sex influence exposure to health risks, access to health information and services, health outcomes, and the social and economic consequences of ill-health. Recognizing the root causes of gender inequities in health is crucial therefore when designing health system responses. Without such a perspective their effectiveness may be jeopardized and inequities in health between women and men might even increase.

More recently, researchers from the health equity field called for a more systematic examination of the interaction between gender and other social factors (e.g. class, race and ethnicity) in the social patterning of health.[2,3] For example, gender and poverty often combine to create multiple barriers to the well-being of women: evidence suggests that women's lower social autonomy and structural disadvantage exacerbate their biological susceptibility to HIV and other diseases.[4–6] Health research that addresses the intersection of gender and other social stratifiers would considerably improve our ability to explain, and efficiently act upon, the mechanisms producing and maintaining inequities in health. However, the path towards this current understanding has been long and slow.

Research on sex differences in health

'Power is a key dimension in the cultural construction of medical knowledge. Medical systems frequently reproduce inequalities and hierarchies in a society by naturalising and normalizing inequalities through facts and images about the body,' said Anne C Larme, *Social Science & Medicine*, 1998.[7]

During the 19th and early 20th century, the differences between the female and male body were strongly emphasized in health research, which has been conducted primarily from a medical perspective with a strong biological orientation.[8] Differences in health between men and women have been analysed using a biological/genetic model developed within Western medicine without being aware of social, cultural and historical context. This model emphasized that biological makeup in terms of reproductive functions and physiology, and more recently hormones and genes, were of primary importance for understanding health differences between women and men. The tendency at the time was to regard biological differences as innate and unchangeable, although scientific advances have changed this perception to some extent. Women were characterized in the medical literature by hormonal cyclical instability and constitutional weakness. Ill health was seen as a more normal condition for women while good health was seen as the hallmark of the normal male body.

Less than 100 years ago, every female health problem would often be reduced, directly or indirectly, to a gynaecological disorder. Problems with the uterus and other reproductive organs were perceived to influence every other organ. Migraine headaches, heart failure, eye problems as well as mental disorders in women, such as 'hysteria' and insanity were seen as functional disturbances in the reproductive organs. The reduction of women to their reproductive functions, and the view that illness was a normal state for women led to the overemphasis of medical treatment of women. The perception of women as biologically weaker, delicate and more susceptible to being invalid, discouraged women from engaging in various activities in society on the basis of their 'fragile' constitution and 'delicate' nerves. Young girls were discouraged from entering higher education, because their energy was more needed for the development of their reproductive functions. There was a belief that since women's energy was needed for

reproduction, they remained inferior to men in terms of intellect and creativity and at a lower stage of civilization.[9] At that time the scientific community used evolutionary theories to prove that women's subordinate position was biologically determined. It is striking to see how biological differences between women and men have 'naturally' led to and justified different and unequal social status or rights for women.

Early research on gender and health

During the 1950s and 1960s it became more and more clear that biological/genetic explanatory models could not provide a complete framework for analysing causes of differences in health between women and men. Women's health researchers, primarily from the social field, questioned how research hypotheses were derived and how research results were interpreted. They called for more attention in health research to explanatory factors related to women's lives and work. The term 'gender' was introduced to separate biological sex from the social, cultural and symbolic construction of femininity and masculinity.[10] The emerging research model for studying women's and men's health was one that took into account relationships between men and women and the fact that there are reciprocal effects of biological sex and sociocultural gender.

Focus on social roles and behaviours

During the 1960s, gender roles became a central concept in research for understanding women's and men's health. Women and men were seen as having been trained in stereotypical role behaviour through upbringing and other social influences. This gives a naturalistic perspective to, for example, the gender division of labour, gender differences in lifestyle and health related habits (such as alcohol consumption and smoking), risk-taking in traffic, perception of health symptoms and health seeking behaviour.

Critics have argued that the naturalization (hence inevitability) of social roles and health-related behaviours linked to those roles in research and policy led to a focus on behavioural change at the individual level, rather than on policy change at the societal level.[11,12] For example, women with stress-related morbidity could be accused of not being able to cope with multiple pressures arising from their different roles and responsibilities as mothers, wives, housekeepers and workers. Instead of easing working women's burden through provision of day-care centres for children and introduction of more flexible working hours, they were encouraged to develop their own personal stress coping strategies for being better able to balance between different social roles. Similarly, many men may experience extraordinary pressures from unemployment and material hardship, which constrain them to fulfil their assigned role as 'breadwinners'.[13] Those who try to cope with stresses through behaviours, such as smoking, drinking or drug abuse, are accused of risking their health by their own personal choice. Thus, role theories on which research on gender and health was based tended to see both women and men as passive objects of social norms and to play down social conflicts resulting from structural inequalities and imbalance of power.

Gender in health research today and tomorrow

It is well acknowledged today, at least in theory, that good public health research and policy that seeks to understand and redress unfair disparities in health between women and men needs to analyse the complex ways in which biological and social determinants, ranging from individual to structural levels, interact. However, in reality, gender biases in health research, policy and programming, and institutions continue to create a vicious circle that downgrades and neglects gender perspectives in health. Gender imbalances in the content of research as well as in the research process are responsible.

Gender imbalances in the research context

Sen et al.,[14] identified three dimensions of imbalances in the content of current health research. The first is the slow recognition of health problems that particularly affect women. For example, violence against women – arguably the most extreme phenomenon of gender inequality – affects millions of women and has significant negative outcomes for women's physical, sexual and reproductive and mental health. In some countries up to 60% of women report having suffered physical or sexual violence or both.[15] Until recently, the magnitude and health consequences of domestic violence against women have been neglected in research.[16] The lack of research is obvious also in areas concerning menstruation and nonlethal chronic diseases that affect women disproportionately, such as rheumatism, fibromyalgia and chronic fatigue syndrome.[17]

The second is the misdirected or partial approaches in different fields of health research. For example, occupational health research and safety regulations are mainly focused on health hazards in formal employment, where men predominate. Health risks in the household, where many women work, has not been subjected to similar concern in research and for health protecting measures. In developing countries, nearly 2 million women and children die annually from exposure to indoor air pollution (caused by smoke from cooking fuels) and many more suffer from illness from acute and chronic respiratory infection.[18–20] Misdirected or partial approaches may also affect men. For example, mental health research often ignores the role of reproduction in relation to men's mental health.[21]

The third dimension of gender bias in health research is a lack of recognition of the interaction between gender and other social factors. All too often, women and men are looked upon as homogenous categories.[22] Research on gender differences in health rarely asks whether such differences vary by socioeconomic position (e.g. class, race and ethnicity). Similarly, research on socioeconomic differences

in health often ignores the analysis of how such differences vary by gender.[2] Research that successfully merged the two research traditions (gender and health; socioeconomic position and health) has greatly contributed to a better understanding of, for example, how the interaction between gender and poverty explains the social patterning of health. For example, gender and poverty often combine to create multiple barriers to the well-being of women: apart from being biologically more vulnerable due to pregnancy, poor women are also more vulnerable to morbidity from malaria than both rich women and poor men due to poorer access to quality health services and adequate nutrition.[23]

Gender imbalances in the research process

The most acknowledged gender biases result from the lack of sex-disaggregated data in individual research projects or in larger data systems (without appropriate sex-disaggregated data it is difficult even to begin gendered analyses), the lack of attention to the possibility that data may reflect systematic gender biases, and the use of methodologies that are not sensitive enough to capture the different dimensions of disparity. The gender imbalance in ethical committees, research funding and advisory bodies, and the differential treatment of women scientists have also been acknowledged as a contributing factor to gender bias in research (Figure 1).[24,25]

An equally important, but different kind of problem with methods used in medical research and clinical trials for new drugs, has been the general lack of a gender perspective and the exclusion of female participants from study populations.[26] The rationale behind the exclusion of female participants from research is that the menstrual cycle introduces a potentially confounding variable and the fear that experimental treatments or drugs may affect women's fertility and expose foetuses to unknown risk. Despite such concerns, research results based on studies of male participants are seen as universally valid and applicable to women, which is not always the case.[27]

In response to critics, efforts have been made to include more women in clinical trials and pharmaceutical research. The US Food and Drug Administration has for example, in 1993 required the National Institutes of Health to include women in all human subject research. A recent study by the US General Accounting Office reports that although women are now being adequately represented in clinical trials, the data collected is not being analysed by sex. Thus, efforts to include more women in research studies are not the solution to addressing gender bias in health research, just a weak and tentative beginning.

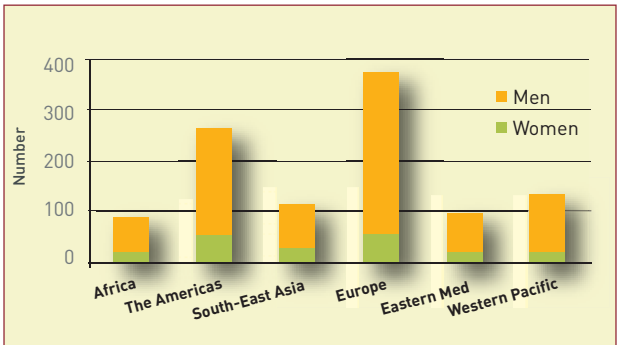


Figure 1: Membership of WHO expert advisory committees, by sex and region, 2004

Addressing gender bias in future health research

Health researchers need to focus more in future on the possibility that risk factors, biological mechanisms, clinical manifestation, causes, consequences and management of disease may differ in men and women. In such cases, prevention, treatment, rehabilitation and care-delivery need to be adapted according to women's and men's differential health needs. Not doing so may have a negative impact on the health of both women and men and gender-based inequities in health might even increase.

Physiological differences between men and women are not confined to the reproductive system and the possibility of gender differences must be considered in all areas of medical research. In addition to physiological differences that may or may not be linked to the reproductive system, research must also investigate the different experiences that underpin health-seeking behaviour, health status and access to both material and non-material resources.

Mechanisms and policies need to be developed to ensure that gender imbalances in both the content and processes of health research, discussed in the previous sections, are avoided. The prerequisites for conducting gendered health research are the collection of sex-disaggregated data that also include indicators of social position (e.g. education, income, occupation and ownership of land or homes) by individual research projects or through larger data systems at regional and national levels. Such data would allow a cross-tabulation and classification between sex and social stratifiers for a better understanding of the mechanisms behind gender disparities in health. Attention needs to be paid to the possibility that data may reflect systematic gender biases (e.g. in health-seeking behaviour) due to inadequate methodologies that fail to capture women's and men's different realities. Data managers and systems need to be sensitized to the need for basic disaggregation of data by sex and presentation of data that allow analysis of the intersections between gender and other social determinants of health. Research funding bodies should promote research that broadens the scope of health research and links biomedical and social dimensions, including gender considerations. Ethical and other review boards, editors and editorial boards should include gender experts to ensure that gender dimensions of research projects are not missed out. Medical and related journals should request that papers present data disaggregated by sex and explain observed differences adequately.

Putting a gender perspective into health research is not without cost. However, the benefits of our efforts overshadow the cost in terms of better science and more effective and equitable health policies and programmes. ❑

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Acknowledgement

I am grateful for excellent comments on the manuscript provided by Professor Gita Sen from the Indian Institute of Management in Bangalore. I have also benefited from work and discussions with staff of the Gender, Women and Health Department at WHO in Geneva and members of the Gender and Health Equity Network (GHEN).

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What works at enhancing health equity? Cochrane and Campbell Collaboration Evidence Base



Article by Vivian A Robinson (pictured), Peter Tugwell, Mark Petticrew, Elizabeth Kristjansson, Elizabeth Waters, Luis Gabriel Cuervo, Jimmy Volmink

Over the last 30 years, a number of influential individuals and agencies have called for action to enhance health equity, reduce inequalities in health and address social determinants of health. Most recently the Millennium Development Goals[1,2,3] have brought this issue to the forefront, drawing an extensive list of global organizations together to reduce poverty and related outcomes. However, unacceptable health inequities due to socioeconomic factors continue to persist in all countries of the world, for most diseases and health conditions.

Part of the solution will be the provision of appropriate policy-relevant evidence. As a result, there is growing recognition that we lack evidence needed to support equity-oriented policies. In this policy climate, national governments such as the Netherlands and the UK have developed research programmes to assess the impact of health and social policies and programs on health equity.[4] The World Bank "Reaching the Poor" initiative is an international initiative to assess the evidence that programs are indeed serving the poor by assessing the "coverage-inequality".[5]

Mexico Ministerial Summit encourages systematic reviews for decision-making

With this growing body of evidence, it is difficult to locate, appraise, and synthesize all relevant studies when making a policy or program decision. Systematic reviews based on all available evidence and conducted according to rigorous standards to minimize bias are increasingly recognized as a useful tool to inform decision-making. In November 2004, the Mexico Ministerial Summit Statement encouraged governments to promote access to reliable, relevant, up-to-date systematic reviews based on the totality of available research evidence.[6] This was in line with the recommendation that emerged during the Health conference on the Role of Science in the Information Society (RSIS) held in the context of the World Summit of the Information Society in December 2003, stressing the need for reliable evidence delivered in a timely manner and in the right format. RSIS highlighted the importance of offering accessible and up to date summaries of the evidence.[7]

The Cochrane Collaboration, founded in 1993, is an internationally recognized global initiative that promotes accessibility to methodologically rigorous systematic reviews about the effects of public health and health care interventions. The Campbell Collaboration is based on the Cochrane methods and principles, but applied to social, legal and educational interventions.[8] Both the Cochrane and Campbell Collaboration are including increasing numbers of reviews and generating tools to assist decision-makers, many of which are relevant to low- and middle-income countries through a number of strategic initiatives and developments.[9]

The Cochrane Collaboration is an enterprise that rivals the Human Genome Project in its potential implications for modern medicine[10]

However, systematic reviews have tended to focus on average effects rather than distributional effects or impact in disadvantaged subgroups. A recent analysis of a random sample of the Cochrane Library revealed that only 1% (1 out of 95) Cochrane reviews assessed differences in effectiveness across socioeconomic factors.[11] A similar assessment of all Cochrane reviews on tobacco control in youth demonstrated that none of the tobacco control reviews contained sufficient information for equity-oriented policy-making.[12]

This lack of inequality analysis in systematic reviews of the Cochrane Library is partially due to absence of information in the primary controlled trials and evaluation studies. The random survey above found that only 10% of controlled trials assessed efficacy of the intervention across socioeconomic subgroups.[11] Furthermore, a systematic review of controlled studies of tobacco control found that only 4% (1 out of 26) assessed impact of the intervention across socioeconomic factors.[13]

Cochrane Health Equity Interest Group launched to promote equity assessment

The Cochrane Collaboration has recently launched an Interest Group on Health Equity, and we are in the process of registration as the Health Equity Field. Most Cochrane reviews only assess the average or mean results of the

intervention of interest – the Equity Field will work with the 51 Cochrane Review Groups to expand their methods to include a description of equity components that are currently missing, into all their reviews. This Equity Field will also encourage the production of Campbell and Cochrane reviews on interventions that are primarily focused on reducing socioeconomic inequalities in health and/or improving the health of the disadvantaged. We will promote the incorporation of these equity aspects into the several initiatives underway to promote accessibility and use of Cochrane reviews for decision-making.

The Cochrane Equity Field will focus both on 'upstream' [impact at a community level] and 'downstream' [impact at an individual level] interventions that impact upon health and health care. For the 'upstream' interventions we will collaborate with the Health Promotion and Public Health Field (HPPH) to promote equity interests, develop methods and provide a link with field experts. For example, the Cochrane Equity Field is collaborating with the HPPH to encourage Cochrane reviews on high-priority public health topics, identified using the WHO priority-setting matrix and an expert consensus panel.[14]

Defining Disadvantage: PROGRESS

We are testing a method of collecting data on health inequality using an acronym called "PROGRESS" for measuring disadvantage, developed by Hilary Brown and Tim Evans (World Health Organization). PROGRESS stands for Place of residence, Race/ethnicity, Occupation/ unemployed, Gender, Religion, Education, Socioeconomic Status (income or composite measures), and Social capital.[15]

Empirical work is underway on the feasibility of collecting this data, and its usability and usefulness as part of five registered Cochrane reviews on the following topics: school-feeding for disadvantaged children [also registered with the Campbell Collaboration], peer support for women with HIV/AIDS, reducing inequities in the management of tuberculosis, tobacco control policies and programs and peer support for chronic disease. Preliminary criteria for demonstrating that interventions reduce health inequalities has been developed using the PROGRESS categories and is being tested in the above reviews.[15]

Register of controlled studies developed

We have established a preliminary trials register of controlled studies that assess the effect of interventions on health inequality across one or more dimensions of PROGRESS. This register is important since it is difficult to locate trials that assess effects on health inequalities due to lack of relevant indexing in the controlled languages such as MESH. We are developing sensitive and appropriate search strategies for relevant studies (led by librarian scientist Jessie McGowan).[16] This database will feed into Cochrane's CENTRAL database cascading into overviews, enhancing their exposure, and making them available for consideration in systematic reviews.

Increased use of evidence from non-randomized studies

Cochrane reviews initially focused exclusively on evidence from randomized controlled trials (RCTs). While RCTs are the gold standard for efficacy, they provide limited information about effectiveness in real-world situations where provider compliance, patient adherence, coverage and diagnostic accuracy are not ideal.[17] Furthermore, randomized trials may not be available for some topics, or they may not be the most appropriate design to address some clinical or policy questions.

Both the Cochrane and Campbell Collaborations are increasingly including evidence from other controlled studies. It has been estimated that about a third of Cochrane reviews include non-randomized controlled trials.[18] For example, the Effective Practice and Organization of Care (EPOC) review group routinely includes controlled before-after and interrupted time series studies which provide a better assessment of real-world conditions.[19] The Tobacco Group also encourages evidence from non-randomized studies; for example the Cochrane review on mass media interventions to prevent smoking in young people included not only randomized trials, but controlled trials without randomization and time series studies.[20] The HIV/AIDS review group encourages including non-randomized studies in their reviews, where no other evidence is available. For example, members of our team are contributing to a Cochrane review on the effect of legislative interventions on access to anti-retrovirals.[21] This review will include before-after studies with historical controls and interrupted time-series. Non-experimental data is also used by many Review Groups where the effects of the intervention are very rare and/or delayed such as late cancers or effects upon offspring.

Improving applicability of Campbell and Cochrane reviews to equity-relevant clinical guidelines

Clinical Practice Guidelines are recognized as an important way of informing clinicians of the best available evidence using a practical and useful format – especially for 'downstream interventions' that impact upon individuals. With funding from the Rockefeller Foundation, INCLEN (the International Clinical Epidemiology Network) Knowledge Plus Program is developing methods for equity-focused and locally relevant clinical practice guidelines. These methods include applying an equity lens to existing clinical practice guidelines, as well as developing new recommendations using a modification of the GRADE Working Group methods (led by Andy Oxman).[22]

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group began in 2000 as an informal collaboration that aims to develop a common, sensible approach to grading quality of evidence and strength of recommendations. The GRADE working group has acknowledged the importance of equity by

proposing that equity considerations be reflected in separate recommendations. The extent to which Campbell and Cochrane reviews can play a role as the source of evidence for these separate recommendations depends on the availability of equity information in reviews.

Improving applicability of Campbell and Cochrane reviews to inform policy development

It is vital that reviews focusing on interventions to reduce health inequalities are relevant ant for policy-makers. This is particularly important for 'upstream' interventions that aim to impact at the population level. The Cochrane Equity Field aims to conduct focus groups and interviews with policy-makers to assess information needs on effectiveness of interventions and policies for reducing the rich-poor gap. We have already held workshops with policy-makers at the Canadian Conference on International Health (2003 and 2004) and the World Bank "Reaching the Poor" Conference (Washington, February 2004). We are also working with the Global Equity Gauge Alliance (GEGA) to promote the assessment of the evidence-base in the selection of interventions for the Equity Gauges worldwide.

Assessing "Potential Equity Effectiveness"

One suggested application of Campbell and Cochrane reviews on interventions to reduce health inequalities is as a 'best source' of efficacy data, which can be used as an 'anchor' for the calculation of the hypothetical equity-effectiveness of interventions. The calculation of equity-effectiveness involves the application of an 'equity lens' to four factors that are known to negatively impact the efficacy of an intervention or policy in the community; (i) awareness/access/coverage, (ii) screening/diagnosis/targeting, (iii) provider compliance, and (iv) consumer adherence.[17]

This framework has already been presented at the Global Forum for Health Research's Forum 7 in 2003 by Andy Haines and the Canadian Conference on International Health in 2004 by Jeanette Vega. Jeanette Vega estimated that Direct Observation Treatment (DOTS) for tuberculosis was only 25% as effective in the poorest compared to the least poor due to inferior case detection and greater diagnostic delay. This analysis suggests that key health systems need to be strengthened to improve service delivery to the poorest communities.

Conclusions

In conclusion, the new Cochrane and Campbell Equity Field aims to build an equity-oriented evidence base to inform policy decisions, both in industrialized and low- and middle-income country settings. We will work with other global initiatives such as the Global Forum for Health Research to minimize duplication of effort and maximize impact, usability and uptake of this evidence base. This initiative represents a major acknowledgement by the Cochrane and Campbell Collaborations of the importance of assessing the effects on health equity of health, legal, social and educational interventions. ❑

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Country perspectives and responses to health challenges

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National rural health mission: reaching the needy



Article by Anbumani Ramadoss

Health research during the 20th century has helped evolve effective strategies for the prevention of disease and the promotion of positive health. It has also shown that poverty and illness are intertwined: morbidity and mortality are higher among the poor. The *World Development Report, 1993* indicates that the magnitude of poverty is an important macro-level determinant of health status.[1] Death, disability or prolonged illness leads to debt and consequent poverty. Positive health is a critical contributor to economic productivity.

Over the years, India has achieved significant improvement on the various health indices. The crude birth rate (29.9 per 1,000 in 1991; 25.0 per 1,000 in 2002) and crude death rate (9.8 per 1,000 in 1991; 8.1 in 2002) have declined significantly. Infant mortality rates have continued to fall from 134 per 1,000 live births at the time of India's independence, to 64 per 1,000 live births in 2002 and expectation of life at birth has increased from 51.7 years from 1986–1991 to an estimated 64.8 years for the period 2001–2006. In terms of drinking water, 95% of rural habitation has now been covered with potable drinking water. These aggregates, however, mask the differentials that stem from poverty and inequities.

The infant mortality rate and under-5 years mortality is higher among the marginalized sections of the community like the scheduled castes (SCs) / scheduled tribes (STs), and higher in the SCs/ STs living in rural areas as compared to those living in urban centres. The proportion of children underweight was 53.5% in the SCs and 55.9% among the STs, compared to the national average of 47% in 2000. A woman from the poorest quintile of the population, despite being more vulnerable to health problems, is less likely to be attended by a medically trained person at childbirth than the better-off mother from the richest quintile of the population. A tribal mother is about two times less likely to be attended by a trained medical person at delivery. Children below 3 years among STs and SCs are twice as likely to be malnourished than in other groups.[2] Gender inequality compounds the effect of poverty on health. Among the disadvantaged, women are even more marginalized. Among the poor, they are the poorest. According to the National Family Health Survey-II (NFHS-II), a female child is 1.5 times more likely to die before reaching her fifth birthday as compared with male offspring. The declining female to male ratio for children, which declined from 945 girls per 1,000 boys in 1991 to just 933 girls per 1,000 boys in 2001, is another indicator of the low social status of women. Factors that limit access to health care for poor women are time constraints, intra-household resource allocation and the locus of decision-making with regard to health care, as well as legal and sociocultural constraints. The impact of gender on health may be seen in terms of overwork, hazardous and poor nutrition, mental illness, vulnerability to domestic violence and stigmatization due to health problems. The combined effect of gender inequality and poverty produces ill-health and inter-generational transmission of poverty through the undernourishment and overwork of pregnant and lactating women.

Out-of-pocket expenditure on health care, as a percentage of earning capacity, is higher for the poor. The poor spent 12% of their income on health care compared to 2% in the case of the rich. Ill-health is also a reason for indebtedness among the poor. Between 1986 and 1996, the proportion of those sick and not availing themselves of treatment for financial reasons increased from 15–24% in rural areas and from 10–21% in urban areas. The richest 20% of the population utilized public health facilities almost three times more than the poorest quintile.[3] Private health care facilities are more likely to be concentrated in the more developed areas thereby further limiting access to health care by the poorer sections of the population.

The absolute number of poor, which remained almost stagnant during the 1970s and 1980s declined significantly in the latter half of the 1990s, from 320 million to 260 million. At the national level, the incidence of poverty has declined from 36% in 1993–1994 to 26% in 1999–2000. In rural areas poverty incidence was 37.37% in 1993–1994, compared to 27.09% in 1999–2000.[4]

National Rural Health Mission

Recognizing the importance of equity in health services to achieve economic and social development, the Prime Ministry of India launched a National Rural Health Mission (NRHM) on 12 April 2005.[5]

Goal of the mission

The goal of the mission is to improve availability and access to health care for those living in rural areas – the poor,

women and children by enabling community ownership and strengthening of the public health system for efficient service delivery, enhancing equity and accountability, and promoting decentralization. The 73rd Constitution Amendment Act, 1992 conferred legal and constitutional status on the Panchayati Raj Institutions (PRIs) and paved the way for a system of participatory self-governance, aimed at ensuring political empowerment of the poor, marginalized and oppressed sections of the population. Under the Act, PRIs are envisaged as instruments for the establishment of a democratic decentralized development process, through the people's participation in decision-making, implementation and delivery of services central to the living conditions of the people.[4] The NRHM envisages a major shift in the governance of public health by giving a leadership role to the Panchayati Raj Institutions in all matters relating to health at the district and sub-district levels. To enable efficiency in health service delivery, the NRHM envisages integration on all ongoing vertical programmes in the domain of health and family welfare like the various national disease control programmes, RCH II and the integrated disease surveillance project. This will also enable the mainstreaming of Ayurveda, Yoga, Unani, Siddha and Homeopathic (AYUSH) systems of medicine and address issues related to the other significant determinants of health, like sanitation, nutrition and safe drinking water.

The NRHM envisages a major shift in the governance of public health by giving a leadership role to the Panchayati Raj Institutions in all matters relating to health at the district and sub-district levels

The NRHM covers the entire country, with special focus on the 18 states where the challenges of strengthening inadequate public health systems are the greatest. An outlay of Rs 67,130 million (approximately US$1,492 million) has been provided for this purpose during the period 2005–2006. The mission adopts a synergistic approach, by integrating health with nutrition, sanitation, hygiene and safe drinking water.

Core strategies of the NRHM

- Decentralized village and district level planning and management. A provision of restricted funds to the tune of Rs 10,000 (US$222) has been made for each sub-centre. Funds would also be provided, in a phased manner, to states covered under the Empowered Action Group for district planning.
- Appointment of Accredited Social Health Activists (ASHAs) to increase the outreach of health systems to the village and household levels. Envisaged as an educated female community level volunteer, there will be one ASHA for every 1,000 population with provision to relax these norms for hilly and tribal areas. She will be responsible for awareness-building about village health rights, the implementation of various national health and family welfare programmes at the village level and for providing first contact minimum health care, together with appropriate referrals. Payment for services, which will be linked to performance, will be met from funds under the various national health programmes.
- Strengthening of the public health delivery infrastructure, particularly at the village, primary and secondary levels. The Indian Public Health Standards (IPHS) have been set to ensure a package that includes availability of specialist services at Community Health Centres (CHCs), establishment of Rogi Kalyan Samitis to improve accountability and establishment of norms for infrastructure, laboratory equipment, blood storage facilities and drugs. Funds for strengthening of CHCs will be provided in a phased manner to each district.
- Mainstreaming AYUSH systems of medicine, which are indigenous to the country.
- Improving managerial capacity, to enable better organization of health systems and effective service delivery.
- Augmenting evidence based planning and effective implementation, through improved capacity and infrastructure.
- Promoting the non-profit sector in order to increase social participation and community empowerment.
- Promoting of healthy behaviours.
- Improved intersectoral convergence.

Supplementary strategies

- Regulation of the private sector to improve equity and reduce out-of-pocket expenses.
- Fostering public-private partnerships.
- Re-orientation of medical education.
- Introduction of effective risk pooling mechanism and social health insurance to raise the health security of the poor.

The Maternity Benefit Scheme integrates cash assistance with institutional deliveries and entails early registration of pregnancies, early identification of complications, provision of at least three antenatal care and post delivery visits, and referral and provision of referral transport to pregnant women

In order to reduce the maternal mortality ratio and infant mortality rate of women living below the poverty line (BPL), the NRHM has initiated a Janani Suraksha Scheme by bringing within its ambit the erstwhile Maternity Benefit Scheme. The scheme now integrates cash assistance (Rs 700 per beneficiary, approximately US$16) with institutional deliveries and entails early registration of pregnancies, early identification of complications, provision of at least three antenatal care and post delivery visits, and referral and

provision of referral transport to pregnant women. The strategy for implementation of this scheme involves operationalization of 24-hour PHCs to provide basic obstetric care and first referral care to provide emergency obstetric care. Funds will be provided (Rs 1,500 per case, approximately US$23) for specialist care from the private sector, if this is not available at government health institutions. The benefits will be extended to all pregnant women belonging to BPL families who are 19 years or older, for up to two live births in the ten low performing states.

With adequate resources, fiscal and otherwise, as envisaged under the mission for improving access and availability of quality health care services to those who need it most, it is hoped that India will be able to reduce the equity gap created by poverty and the unequal distribution of resources. ❑

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Health research: reducing poverty and improving health in South Asia



Article by Mohammad Nasir Khan

Poor people live without fundamental freedom of action and choice that the relatively better off in society take for granted. They often lack adequate food, shelter, education and health, deprivations that keep them from leading the kind of life that everyone values. They also face extreme vulnerability to ill-health, economic dislocation and natural disasters.

Huge disparities exist in health between rich and poor in the world, and between rich and poor within developing countries. Poor health is closely associated with poverty. Across and within countries, differences in income can account for as much as 70% of variance in infant mortality.[1] The poor are most vulnerable to ill-health and have the least means to combat it. The case for investing in health has been further strengthened by a growing body of evidence, which shows that better health contributes to greater economic security and growth. Better health reduces poverty, and reduced poverty improves health. Table 1 illustrates the wide differentials that exist between countries and different regions of the world for various health indicators.

Over the past 30 years, developing countries have made remarkable progress in raising average income, reducing infant mortality, increasing life expectancy and boosting adult literacy. Despite these achievements, poverty remains a paramount challenge for national governments, as well as for the international development community. In most of the developing regions the number of poor people has been rising since the 1980s. Today, more than one out of five people around the world are living in conditions of extreme poverty (little more than US$1 a day).[2]

Regions of the World	Under-five mortality rate per 1,000 live births (2001)	Infant mortality rate per 1,000 live births (2000)	Maternal mortality rate per 100,000 live births	Prevalence of TB per 100,000 population (2001)
Developed regions*	9	8	20	23
Developing regions**	90	63	440	144
Northern Africa	43	39	130	27
Sub-Saharan Africa	172	106	920	197
Latin America and the Caribbean	36	29	190	41
Eastern Asia	36	31	55	184
South-central Asia	95	70	520	218
South-eastern Asia	51	39	210	108
Western Asia	62	51	190	40
Oceania	76	66	240	215

* Means high income countries as defined by the World Bank.
** Means low- and middle-income countries as defined by the World Bank.

Table1: Regional disparities for selected health indicators

South Asian nations are at the crossroads of economic and political progress, but are still facing severe problems of underdevelopment. Available data illustrate that while some macroeconomic indicators have improved over the years, disparities between rich and poor have steadily increased. A quarter of the world's population live in South Asia but their annual contribution to global production is only 2%, their share in world trade is a mere 1% and about half of them are living below the poverty line with limited access to health care and other essential basic services.[3] Despite impressive gains in two important health indicators – life expectancy and infant mortality – there is increasing evidence that these benefits have not spread equitably across all socioeconomic groups in the past decade. In the past decade no South Asian country has spent more than 1% of its GDP on health as compared to global averages of 2–5%, and with one exception none has spent 2% of its health budget on health research.[4,5]

Poverty is no longer contained within national boundaries, it has become globalized, it travels across borders without a passport in the form of drugs, diseases, pollution, migration, terrorism and political instablity[6]

Failure to diminish poverty has become a threat to all countries, rich and poor. As Mahbub ul Haq has said, 'Poverty is no longer contained within national boundaries, it has become globalized, it travels across borders without a passport in the form of drugs, diseases, pollution, migration, terrorism and political instability'.[6]

People living in poverty are generally malnourished and have inadequate shelter, with little or no access to basic social services. In many instances the poverty of means and access is also associated with the poverty of hope and despondency. This may in turn lead to inaction and paralysis in terms of lateral thinking. Poverty and ill health are interlinked and have a major impact on the economic situation and well-being of an individual in any society. This is particularly true in lower income countries and for the absolute poor, due to the vicious circle of poverty and ill-health. There is a close link between poverty and inequity (relative poverty), and the poverty of means, hope and imagination.[7]

It has been argued that the horrific disease burden of the poorest countries is a fundamental barrier to economic improvements for the world's poorest people. Consequently, although health is a valid end in itself, the main reason for seeking to improve the health of poor people is as an investment to facilitate economic growth. The WHO advocates a broad response to poverty and health that includes focus on specific diseases, efforts to promote pro-poor health systems and measures that address broader determinants of health and initiatives, which promote cross-sectoral actions, e.g. in education, social protection, etc.[8]

Like the WHO, other organizations include broad responses to issues of health and poverty in their policy statements. For example, the World Bank sees health primarily as an essential asset for economic growth but includes a focus on a pro-poor health care system and a health environment as a means to promote health.[1] The Asian Development Bank (ADB) sees health as the key to human capital and goes beyond responses to specific diseases including emphasis on pro-poor health systems, environmental health and the broader determinants of health. Similarly, the African Development Bank (AfDB) sees health in terms of human capital. The European Commission sees work on strengthening health as increasing human capital. The UK Department for International Development (DFID) also sees health as a mediator of economic growth and advocates for a broad social sector response. The World Summit for Social Development recognized the need for social development if economic policies were to succeed. The Bill and Melinda Gates Foundation focuses its Global Health Program on targeting the diseases that impose the greatest burden on the poorest countries and those conditions that are associated with poverty. Strategies to achieve this include health system reform, extending primary health care, health promotion and disease prevention, investment in water, sanitation, housing, safety at work and gender equity, etc.

Lush and Walt argue that any focus on the diseases of the poor (major infectious diseases) must also consider social factors, e.g. insecurity and inequalities as, 'better health does not depend simply on medicines, doctors and health services'.[9] This view has been adopted by a number of international agencies. For example, the Rockefeller Foundation argues that measures promoting public health are unlikely to be effective in promoting the health of poor people if they restrict them from participating in decisions that affect their health. For interventions to be successful, they argue, people must be able to negotiate their own inclusion into health systems and demand adequate health care. Other writers argue for a broad approach to public health, which focuses on reducing social and economic deprivation. Such a view challenges the recent 'neo-liberal' trend, which has increasingly seen health as the responsibility of the individual, as 'the determinants of health are increasingly located at the global level'. The broader view on poverty and health has also been discussed in the People's Health Assembly (PHA), however, it relies not simply on seeking to address the diseases which affect the world's poor, but asking a series of 'but why' questions relating to why these problems disproportionately affect the world's poor.

The UN Secretary General in his address to the General Assembly in 2001 stated: 'the biggest enemy of health in the developing world is poverty'. The Millennium Development Goals (MDGs) declaration has placed poverty reduction at the centre of intensified development.[10]

Selected examples of success from South Asia

The discovery of Oral Rehydration Solution (ORS) by the IDDCRB to prevent the disastrous outcomes of diarrhoeal diseases based on simple logic and simple solutions has saved millions of lives all over the world. I believe there is an ORS-like solution for most diseases. However, this will only happen if our researchers appreciate and look for such simple and practical solutions.

The innovative work being done and evidence produced by the Bangladesh Rural Advancement Committee and the Grameen Bank, which provides easy credit to the poor in Bangladesh, the Self-employed Women's Association, and the Maharashtra Employment Guarantee scheme in India, the Samridhi Programme in Sri Lanka, the Basic Minimum/Development Needs (BDN) Program in Thailand, Pakistan, Iran and Jordan, that addresses poverty through integrated income generating schemes, are a few of the programmes based on sound research that have been success stories. The BDN approach, coupled with advancement of primary health services, is found to be particularly effective in reaching vulnerable groups and improving their health. What is needed is to collate and synthesize this available knowledge and disseminate it to other populations to improve their health as wealth.

Health research has suffered from an overall lack of funding and from a huge discrepancy between the allocations of research funding and the diseases or conditions that account for the highest global disease burden expressed as, 'the 10/90 gap'[11]

A number of other studies have made considerable advances in the understanding of poverty and ill-health at the individual and community levels. The health of the individual is now linked to that of the community, and this has allowed the development of a social model of health and novel approaches to health action beyond biomedicine.

Suggestions and conclusion

One of the critical roles of health research is to ensure that measures proposed to help break the vicious circle of ill-health and poverty are based on evidence, so that the resources available to finance them are used in the most efficient and effective way. Despite this critical role, health research has suffered from an overall lack of funding and from a huge discrepancy between the allocations of research funding and the diseases or conditions that account for the highest global disease burden expressed as, 'the 10/90 gap'.[11]

Sound macroeconomic policies and stable economic growth are essential for sustained investment in health. Health and economic growth are inherently linked. Rising incomes are necessary, but not sufficient for improved health. They have to be accompanied by social development policies focused on the underprivileged. The experiences of many Asian countries have shown that improved health has contributed to economic growth in several ways. Most significantly, the gains from investment in health are relatively much higher for the poor, especially poor women and indigenous people. The bottom line is that health is a fundamental goal of development as well as a means of accelerating and sustaining it.[12]

Yet the health sector is still not accorded due priority in the overall development agenda. It is viewed as a sectoral programme that only 'consumes' resources. It is not seen by many policy-makers as a central pillar in the development process. What is needed is a change in the mind-set and strong political will to assign health its due place in developmental and political agendas.

The policies and strategies in the social sector, including health, need to focus on poverty reduction, as poverty is one of the main causes of ill-health. Poverty reduction programmes must selectively target women and the vulnerable. The countries that have been successful in reducing poverty and improving the health of their people did so through policies that distributed the economic gains with adequate attention to improvement of human capital. Acceleration of economic growth and development of human capital reinforce each other. However, it has been underscored that while there is a link between poverty alleviation and economic development, this is not automatically assured and uncontrolled development may actually increase inequity by disproportionately increasing benefits to the rich.[13]

Another cardinal requirement is to ensure that our health systems are sustainable and socially relevant. There is an urgent need to do research, which minimizes difficulties in transferring promising products to the developing nations and ensure that new technologies are sensitive to local sociocultural needs, are affordable and work efficiently and effectively in the local setting. In addition, we must build on and make the best use of the vast reserve of indigenous knowledge and practices. Good governance at all levels is of course imperative for sustainable development and in order to meet the needs of the poor and vulnerable groups.[14]

As equity is linked to health research, which is a powerful instrument for development, there is a need to invest in the health of all people and reduce inequities that constrain economic growth and human development. In addressing these objectives, health research holds even greater promise than it did a decade ago, as the application of knowledge increasingly underpins global development. One of the important findings from recent work on inequity and poverty is that without focused attention to the poor, development of interventions may actually increase inequity in the medium term.[15]

A key element in ensuring that health research indeed becomes an 'essential link to equity in development' is creating a dynamic link between research and policy. Strengthening the linkages between policy and research

requires an understanding of the key components of their interface: research and policy processes, voices of stakeholders, mediators to help link the two processes, research products, and the larger context of decision-making and research.[16]

The most common approach to linking research to policy has been to produce good research and disseminate the results to the intended users. This relies on the assumption that decision-makers will always be receptive to relevant and useful information and make ready use of it once it is available. Good quality research on policy-relevant issues, with well-packaged and well-targeted products can succeed in informing decision-making processes. However, my experience as health minister over the last few years has made me aware that most of the research conducted is neither policy-relevant nor of any benefit to the poor. There is hardly any critical analysis of the already available information and existing knowledge, and mostly what is published in peer reviewed journals is for 'peers' and not for the poor or policy-makers. The weakest link in use of evidence was and remains limited absorption capacity of most health ministries in developing countries.

From a research-to-action point of view, funding for research plays an important role in determining the extent of the linkage between the research and decision-making processes. Some research-funding agencies play crucial roles in mediating between these processes, especially influential external donors. Even when research funds are derived from national sources and the demand for research is high, countries still do not always make financial resources readily available for research institutes.

For every country that wants to achieve the MDGs, the assumption to begin with should be that they are feasible and can be achieved, unless technically proven otherwise. To prove otherwise, we need evidence based on science, which is fully appreciative of local needs and takes into account sociocultural sensitivities. For many South Asian nations, the goals are indeed ambitious, but they could still be achieved if there are honest efforts by all parties to improve governance, promote peace, involve the private sector and genuine commitment to invest in health and health research. That said, without a quantum leap in health research allocations, strengthening health (research) systems, and trust in the research results for improved management decisions, achieving the MDGs, reducing poverty and improving health in South Asia will remain a distant dream. ❑

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Achieving equity through reform of the health sector in Egypt



Article by Mohamed Awad Tag El Din (pictured), Emam M Moussa and Ahmed M Shelbaya

During the 1980s and 1990s, the political environment in Egypt was ripe for the government to engage in undertaking major transformations aimed at social justice and poverty alleviation. Initial efforts focused on economic development, but by the mid 1990s, it was clear that in order to reduce poverty and achieve social equity, it was necessary to attend to social development issues, including health sector development, with programmes and policies to address the poor and their needs.

For health professionals and those responsible for the management of health care delivery, it was necessary to identify objectively and scientifically the strengths as well as the weaknesses within the system as it stood. Indeed, the existing health system had its strengths, but also suffered from serious deficiencies. It was a paradoxical system of obvious inequity. On the positive side, it performed well in terms of physical access (95% of the population were within 5km of a medical facility), it was an extensive health infrastructure of physicians, clinics and hospitals and was cost-efficient and effective in some basic public health matters (high immunization levels, lowering the fertility rate and clean water for most of the population). On the negative side, the health system suffered from serious deficiencies that resulted in diminished health outcomes, as well as geographic, income and gender inequities with regard to access, use, cost and outcomes, poor value for money, poor quality and clinical effectiveness and lack of financial sustainability.

There was an urgent need for scaling up, providing access, increasing utilization and ensuring equity. It was imperative that the system be reformed to address the needs of the whole population, particularly the underserved, the poor and the vulnerable. Otherwise, the poor were at risk of slipping deeper into poverty and the entire development process risked being undermined.

No attempt to reform the health sector could be made without evidence-based policies that address the needs of a key constituency, namely the underserved, the poor and the vulnerable. Evidence-based policies and programmes had to target this group, if the government were truly serious about development in Egypt.

The Health Sector Reform Programme was thus an attempt to put research into practice. The challenge for the health sector was to develop a new kind of evidence base that distinguished between an understanding of the primary causes of morbidity and mortality vs one that provides an evidence-based understanding of and approach to the relevant social, political, economic and institutional structures that would ensure that all people, at both local and national levels, have access to health interventions. Essentially, the programme aimed to reduce the unjust inequities in accessing quality health care experienced particularly by the underserved and vulnerable.

This article will first explain the important role research has played in the development of the various successful models of family health in Egypt. Secondly, it will describe the challenges faced with regard to capacity development in health policy and systems research. Finally, it will consider recommendations for addressing these challenges.

Towards a health sector reform programme that addresses poverty through research

If governments are serious about development, especially in the developing world, health should be given a higher priority than it currently has in relation to other development focal areas. At present, most developing countries give health low priority on their development agendas. This is reflected in the total government expenditure on health. If governments are serious about health then they should not detach it from its context. 'Health is a social, economic and political issue and above all a fundamental human right.'[4]

It was imperative that the system be reformed to address the needs of the whole population, particularly the underserved, the poor and the vulnerable

Accordingly, any health sector reform programme should address the social, economic, institutional and political arenas in which it is embedded. But unless policies and programmes are built on evidence-based information, we risk adopting unsound policies or falling hostage to preconceptions about the source of the problem, which

happens all too often in our part of the world.

Research and evidence-based policies for health-sector reform in developing countries, with their focus on the underserved, the poor and the vulnerable, need to be oriented toward the reduction of inequities of all sorts in access to health care, for example, those related to income, geography and gender.

In the case of Egypt, policies and programmes for reforming the health sector were oriented towards the underserved, the poor and vulnerable, through the elaboration of a Family Health Model concept. The strategy of empowerment of the family unit was one of the means of achieving development and reform in general. Through research, the different factors (see Figure 1) influencing the equity of distribution of an effective, efficient and sustainable high quality health care service to the poor were studied. Pilot models for addressing them in three governorates were developed, evaluated and then redesigned in preparation for rolling out the successful modules to other governorates.

Understanding how to strengthen health systems and to reform them required careful conceptualization of the nature of health systems, how they change over time and how that change can be managed

Understanding how to strengthen and reform health systems required careful conceptualization of the nature of health systems, how they change over time and how that change can be managed. This, in particular, involved consideration not only of issues such as financing, formal structures and clinical activities, but also of features such as values, leadership and relationships.

Currently the work on health sector reform in Egypt has reached different stages of development, depending on what aspect of reform is considered (see Figure 2). In terms of service delivery, the family health model has emerged from being a concept or idea to a model that was first piloted in three governorates (Alexandria, Menoufeya and Sohag). It is now being rolled out in 26 governorates. Institutional restructuring (ensuring development of the different functions and roles of the different health care institutions, as well as management development) and financial reforms (ensuring the separation of the financing function from the regulatory role and the provider role, as well as ensuring sustainability of a high quality effective and efficient health care service) are still in the pilot stage.

Both theoretical and practical work related to the refinement of the service delivery model is continuing, including revisions to the definition of the basic benefits package (BBP), the development of means testing and exemption mechanisms for the poor, strategies for elevating the status of family health practitioners within the health sector and attracting physicians to this practice, improvements in rational drug use, strategies for quality improvement and accreditation, etc. Despite ongoing refinements, the model has progressed well into the implementation stage (see Figure 2).

While these refinements continue to be debated, the Ministry of Health and Population (MoHP) needs to take thinking and practical work about reform beyond the BBP and service delivery models – where most of the practical progress in Health Systems Research (HSR) has been made to date – and seriously engage in work related to two other sets of issues (see Figure 1 for the different functional relationships involved in the process of reform that depend on research for conversion of concepts and ideas to planning-modelling-measuring-piloting and rolling out).

- Firstly, how to restructure the different health care institutions in order to assume their specific roles of regulation of services, delivery of service and financing of services, together with management development of these institutions.
- Secondly, how to finance family health models as they are replicated in other areas, and how to reform financing of the health sector more generally, including reconsiderations of health insurance modalities, reallocation of funds within the public sector, improving efficiency within the public sector, and developing ways in which the public sector can collaborate and work directly with the private sector. These are complex and sensitive issues, where work is largely at the research, modelling and planning stage, and some of it is still at the conceptual stage (see Figure 2).

It was imperative that the MoHP and its donor partners make funds available for research to put together the multidisciplinary approaches of political science, economics, law, and so on, in order to cater to the reform needs addressing the underserved, the poor and the vulnerable.

The nature of the health policy and systems research that was performed in the MoHP, and the areas of work that the Ministry has engaged in have included:

- knowledge generation to improve how the Ministry organizes itself to achieve health goals, including how to plan, manage and finance activities to improve health;
- roles, perspectives and interests of different actors in this effort;
- empowerment of the family as a unit, where individuals in the family are empowered with regard to decisions related to their health and ability to hold those who provide the care accountable. Empowerment of poor clients to play a more central role in health system design and operation;
- establishment of techniques that would identify the underserved and vulnerable upon which a targeting

policy should be based. Within that aspect the role of research has proved vital in the development of a tool.

The proposed methodology combines both the individual and macro-assessment techniques identifying those in need of subsidy and allocation of health resources to achieve equity, whether vertical or horizontal. Eligibility could vary by region dealing with the challenge of the absence of a system that captures incomes. A tool was developed based on proxy means testing for the underserved, the poor and the vulnerable, with the aim of increasing health care coverage.

Research on health sector reform was thus able to contribute to sound, socially relevant and ethically acceptable guidelines for more effective, efficient and

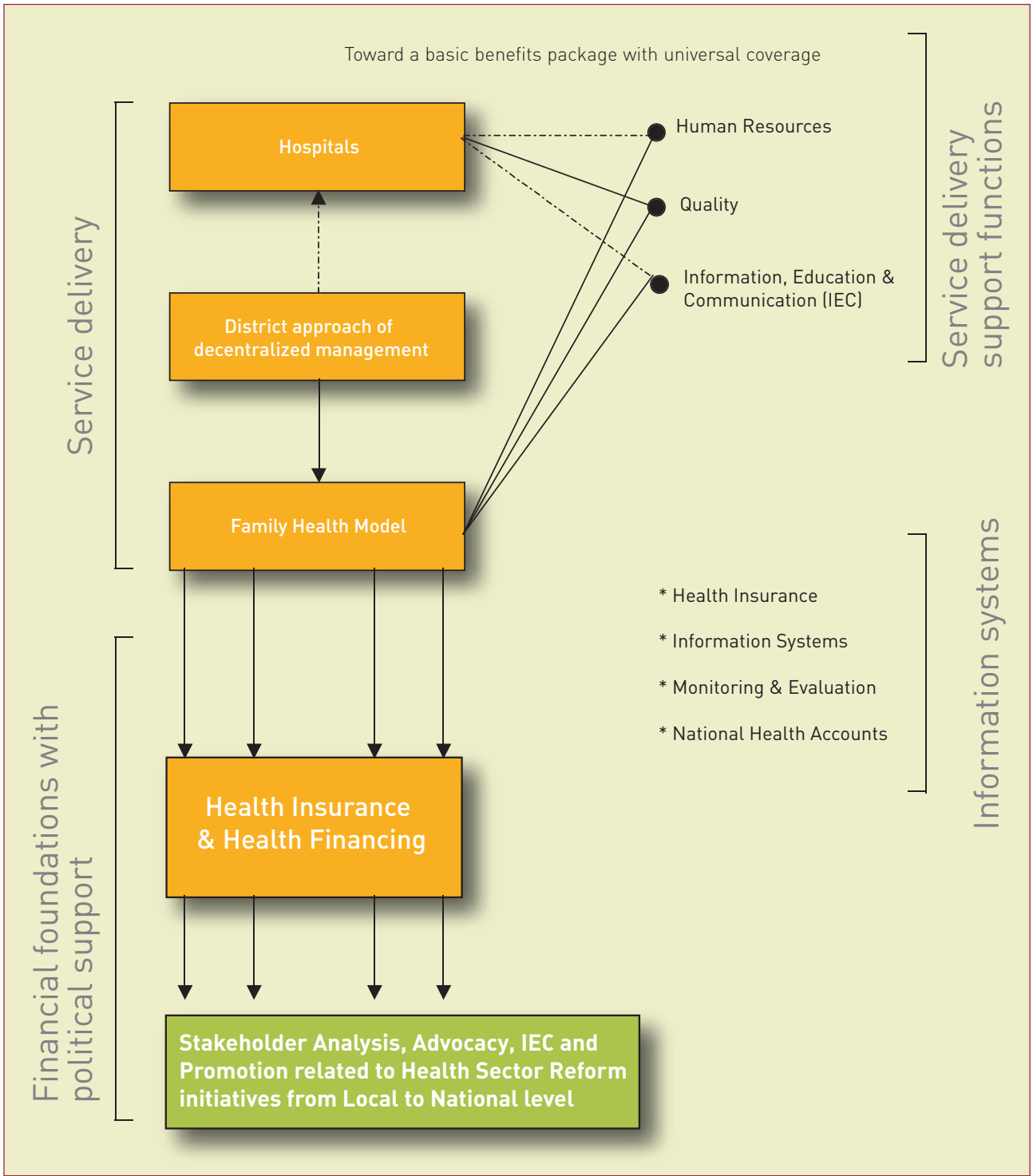


Figure 1: Functional relationships of the different factors affecting health systems research

sustainable health policies and systems that would benefit the underserved and the vulnerable.

Challenges and constraints

The role of health research in the development and achievements of the Egyptian reform programme is unquestionable. Without evidence-based research, the ideas and concepts of reform would have stood still at that stage without evolving towards implementation and roll-out. However, in spite of the achievements certain factors presented constraints and challenges regarding the role of health research and thus were of concern to the reform programme:

The dichotomy of policy (formative) activities and implementation and the flaw in policy-making

One of the main constraints faced by many government institutions in developing countries is the unclear boundary between policy formulation that is dependent on sound evidence, and research and implementation. Leaders in such institutions are under pressure to deliver fast. The pressure comes from within or even from donor agencies that are output oriented. In such cases implementation sometimes supersedes policy development and adequate research.

There is also the challenge for the health community of developing a new kind of evidence base that distinguishes between an evidence-based understanding of the primary causes of morbidity and mortality vs one that provides an evidence-based understanding of and approach to the social, political, economic and institutional structures that would enable societies locally, nationally and globally to ensure that all people have access to health interventions. In short, this means opening up a key line of inquiry, analysis and evidence building that begins with the social and political determinants of health and health care – and recognizes the deep political and global nature of the worldwide effort to reach the Millennium Development Goals.

Lack of a mechanism for routine researcher/policy-maker dialogue

Unfortunately, as there is no mechanism for routine researcher/policy-maker dialogue, our efforts to bridge the research/policy divide are often personality dependent. Another problem is that of engaging policy-makers with research, due to the absence of a system that ensures the continuous feed of research to policy-makers and guarantees its use. Information systems and technology are not ends in themselves, but rather means that enable the economic, effective and efficient attainment of the Ministry's central mandate: to enable a more effective institutional management framework. Ministries should work on strengthening the generation, management and use of health information.

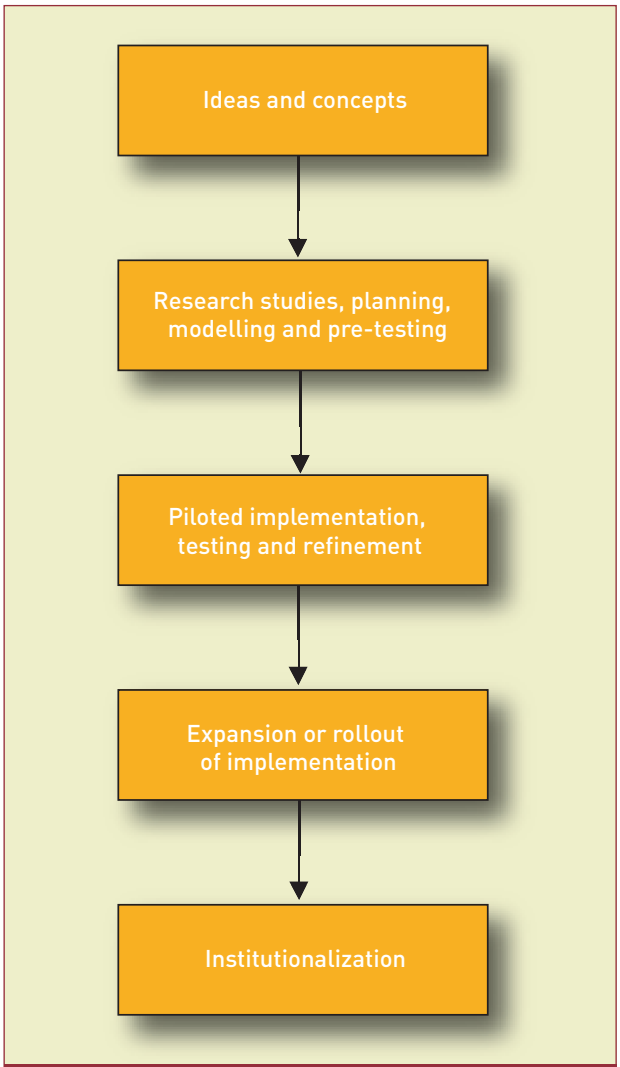


Figure 2: Health sector reform process from conceptualization to realization

Insufficient investment and national capacity for public health and health systems research

Increasingly, the MoHP located the crisis in the shortcomings of health systems. The weaknesses of health systems have now become a primary obstacle to meeting the Millennium Development Goals.[7] Even though the amount of resources pooled for the production of evidence-based information is unclear, it is obvious that there is a mismatch between evidence-based information and policy decision-taking.

The lack of a long-term financial commitment to build health systems research poses numerous challenges for health systems development and thus to address the needs of the underserved, the poor and the vulnerable.

Lack of indicators and priorities addressing the poor and which are measured periodically

It is not enough to have public health research that simply incorporates epidemiological evidence. We must move into compiling new types of evidence related to policy,

programmes and implementation that specifically address the underserved, the poor and the vulnerable. Accordingly, all the indicators and monitoring schemes ought to be oriented towards achieving these goals.

Where do we go from here? Recommendations

Health needs to be a central priority for governments if they are to embark on an ambitious journey of development. Accordingly, the MoHP had to build a research agenda and body of evidence to address the political and social determinants of health and translate them into implementation agendas.

As part of that agenda the MoHP took on the task of quantifying some of the most important risks to health and assessing the cost effectiveness of some of the various measures taken to reduce these risks. The ultimate goal is to guide stakeholders towards investing in priority research areas related to lowering threats to health and relieving poverty.

Ministries of health should thus act as a compass for all stakeholders by:

- increasing public awareness of priority areas related to lowering health risks;
- improving programme effectiveness through research and evidence-based programmes;
- providing policy analysis;
- Improving decision-making within the ministry of health, among other ministries and agencies, as well as individuals involved in public health action
- mobilizing technical and material resources towards serving health research and finding evidence-based solutions towards achieving equity.

Accordingly, in order for ministries to act as a guide to stakeholders on where to put their resources for health research, they ought to invest in:

1) Identification of focal areas for health research action

In order to identify national health objectives, we have to identify focal areas. Identification of the focal areas is based on the following criteria:

- science-based criteria – based on scientific analysis, research and reliable data, which identify the problem of concern (epidemiological, economic, political, analysis of cost effectiveness);
- preventive and health promotional (or health promotion-oriented) – in the sense that preventive and health-promoting interventions and actions will have a significant impact on the prevalence of focal areas;
- people and majority oriented – the focal areas chosen should reflect a real science-based risk to the population and their health status;
- of greatest priority and realistic – reflects the greatest health impact, the highest prevalence or risk, or can achieve the greatest benefit for the population (based on scientific evidence as opposed to subjective speculation).

2) Identify achievable measurable national health objectives

It is recommended that the approach of ministries (and government in general) should focus on reaching the underserved, the poor and the vulnerable. Thus, objectives should be established whose achievements target the poor.

3) Rallying the identified stakeholders around the objectives

Programmes should be put in place for guidance: mapping the way forward; helping stakeholders to see what the most appropriate and most cost-effective measures are, which can be taken to reduce at least some risks and promote a healthy life for the population. Emphasis should also be put on communicating risks clearly and openly to the public, and of creating an atmosphere of trust and shared responsibility between the government, the public at large and the media.

4) Supporting the activities of stakeholders[8]

The role for rallying stakeholders around investing in health research should not stop there, but move towards:

a. Building capacity
b. Training
c. Networking
d. Mapping target groups
e. Policy analysis
f. Information, education and communication (IEC)

5) Monitoring progress towards objectives

It is also imperative to monitor the resources being put into health research and its impact on the announced goals of reduction of poverty and achievement of equity.

As mentioned earlier, 'health is a social, economic and political issue and above all a fundamental right'. If we accept this definition, we as health professionals and as officials responsible for the health of our nations, especially the underserved, the poor and the vulnerable, our health policies and programmes have to incorporate all of the factors affecting their well-being.

As developing nations, we can afford to waste neither our limited resources nor precious time before addressing the development needs of our societies. Health research is the gateway to saving our limited time and resources. Health research means sound information and information means power – an element we desperately need for our citizens. ❑

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Fora, policies and systems for maternal mortality in Ecuador



Article by César Hermida

Scientific health knowledge becomes meaningful only if it is endorsed by health systems and provided for the benefit of the entire population. In Ecuador, where social and health sectors are not treated as priorities, the process of setting up health research priorities began by organizing health fora to discuss policies and corresponding systems in order to empower the health research field. The experience of Ecuador, using the example of maternal mortality (MM), is addressed in this article.

Cairo, Beijing, the Millennium Summit and The Global Forum for Health Research were all grounded in a framework of equity. This international framework provided the actors in the Ecuadorian health sector with the political tools for the construction of a Health Policy, a National Health System (NHS), and particularly a National Policy for Sexual and Reproductive Health and Rights. Learning from the Global Forum, a National Health Research Forum and a National Congress for Health and Life have recently been organized. They contributed to the development of health policies and systems to improve equity in Ecuador, contributing to the reduction of poverty. Health fora were organized to communicate research results about determinants related to ethnicity, social class and age, to debate proposals, learn from each other, produce conclusions and define policies at national level. Access to health knowledge and corresponding services is a priority. Therefore, the sector plays a leadership role in reducing poverty by improving political empowerment and enhancing the interaction between health and other human rights.

The Sexual and Reproductive Health and Rights Policy was discussed at 11 workshops around the country and eventually approved during the Second Congress for Health and Life.[1] One urgent matter was to address the problem of MM. This challenge was presented as a research priority at the Forth National Health Research Forum.[2]

Based on the results of these fora and the implementation of new health policies, a process has been launched to reduce MM in Ecuador, drawing from three key vulnerability factors: the socioeconomic situation of the majority of the population; the low quality of health services; and the lack of training and commitment of human resources.

Research is based on local and national data raised by the Maternal Mortality Surveillance System (MMSS) including information on women dying at reproductive age (10–49 years) and within these data, maternal deaths.

Intervention and training are based on findings and focused on three criteria: maternal decision to go to services, transport to reach them, and quality within the Essential Obstetric Care Centres (EOCC) at the local level.

National policies for health research and sexual and reproductive health and rights

Once the National Health Policy, with a wide approach, was defined, the NHS rests on all private and public health services institutions, from local level in the hands of County Health Councils to a national context in the hands of the National Health Council. Policies for Health Research and Sexual and Reproductive Health and Rights (SRHR) approved at National Health Fora are constructed through the National Health Council. From among them comes the example of MM, the main components of which follow.

Research component of maternal mortality

The main component of the NHS is the MM Reduction Plan that includes: MMSS, EOCC, the Maternal and Infant Free Services Program and eventually both the promotional and intercultural approach based on a collective health services network.

The MMSS as a research component is about local and national data on all the deaths of women aged 10–49 years, identifying within these maternal deaths, and data processing and analysis at all levels, with corresponding reports. Then come interventions and training based on the findings.

Research and national data

Maternal mortality is the 'death of a woman during pregnancy or during the 42 days following the end of it, independently of place and pregnancy duration, due to any cause related to or aggravated by pregnancy or its attention, but not for accidental or incidental causes'.[3] Today the 42-day period is considered for 'direct' causes and a '1 year' period for 'late' or indirect causes. The concept of 'any cause'

brings into question the concepts of accidental or incidental, and underscores the need for better research into problems such as depression, suicide and *inter alia*, maternal deaths.[4]

Among the eight Millennium Development Goals (MDGs), number five is about 'improving maternal health', with a target of reducing 'by three quarters, between 1990 and 2015, the maternal mortality ratio'. There are two indicators for this goal: one relates to the 'mortality ratio' and the other to 'proportions of births attended by skilled health personnel'. Maternal mortality is an acute public health problem in poor countries and, as a health services indicator, it is very important to show both the epidemiological problem (age, gender, ethnic, socioeconomic and other differences), and the quality of health services.

Maternal mortality is measured with a well known 'ratio' having as a numerator maternal deaths and as a denominator the number of live births (per 100,000). How many maternal deaths are there in Ecuador compared to almost none in a developed country? How wide are the differences with regard to age, ethnic and socioeconomic groupings within the country? As the Director General of the United Nations Population Fund (UNFPA) put it, 'this is simply outrageous because we know how to prevent these needless deaths'.[5]

Maternal mortality ratio in Ecuador

A key problem in Ecuador is the inconsistency in the data on

MM ratio*	Year	Source
130 (adjusted)	1997	Maternal Mortality in 2000. Estimates developed by WHO, UNICEF and UNFPA.
74	1997-1999	OPS: Situación de Salud en las Américas, Indicadores Básicos 2001. Cited in OPS/OMS Estrategia Regional para Reducción de la Mortalidad y Morbilidad Maternas, 26ª. Conferencia Sanitaria Panamericana.
130 (adjusted)	2000	UNICEF, The State of the World's Children, 2004.
130	2000	Maternal Mortality in 2000 WHO, UNICEF, UNFPA
92	1993/2001	OPS/OMS, PRB, UNFPA, y otros. Género, Salud y Desarrollo en las Américas.
74.3	2001	Evaluación Común de País, Ecuador. Naciones Unidas, Quito, 2003.
97.0	2001	OPS/AIS: Iniciativa Regional de Datos Básicos en Salud; Sistema de Información Técnica en Salud. Washington DC, 2003. Cited in OPS; Equidad de Género y Salud en las Américas a comienzos del siglo XXI.
160 (registered)	1985 to 2002	UNICEF, The State of the World's Children, 2004.
81.1	2002	OPS/OMS: Situación de Salud en las Américas, Indicadores Básicos, 2004.

* Per 100 000 live births

Table 1: Maternal mortality ratio in Ecuador, international sources, 1997 to 2002

Year and source	Ratio (5)	Goal and general recommendations:	Specific recommendations:
1990 (1) (1986-94)	159	Target for 2015: 39.25, feasible.	Support research process, starting year 2005, pertaining to deaths of women in fertility age and MM, with participation of Local, Provincial and National Maternal Mortality Committees. Intervention and training based on three criteria, permanent quality control of Essential and Completed Obstetric Care Centres.
1994 (2) (1990-94)	114.82	Recommendations: Strengthen new National Health System. Research, intervention and training with participation and support of Local, Provincial and National Health Councils.	
1999 (2) (1995-99)	60.54		
2003 (3) (2000-03)	60.11		
2004 (4)	67-147		

Sources: 1) National Maternal and Infant Survey (ENDEMAIN 1994)
2) National Institute for Statistics and Census (INEC)
3) INEC (with late registration of live births)
4) National Maternal and Infant Survey (ENDEMAIN 2004; 1999 Survey did not measure MM). Mean 2004: 107 Per 100 000 live births.

Table 2: Trend of maternal mortality ratio, goals and recommendations in Ecuador, 1990 to 2003

Year	Indicator of PHS (%)	Indicator of LCS (%)	National	Lowlands	Highlands	Amazon
1990	58.2					
1995			**76.8**	**82.0**	**72.5**	**52.2**
1991-1995	53.57					
1998			**78.7**	**86.3**	**69.0**	**61.7**
1999			**77.5**	**84.0**	**70.1**	**-**
1996-2000	71.2					
2001-2002	73.25					

Table 3: Trend of deliveries occurring at (professional) institutional health centres by Production of Health Services, 1990 to 2002, and Life Conditions Survey, 1995 to 1999, in Ecuador

MM (see Table 1). The trend of the MM ratio in Ecuador can be seen in Table 2, where ENDEMAIN 944 and 2004 were based on the method of 'living sister' interviews. INEC data for 2003 include late registration of live births in denominator. Reaching the target 'to reduce, between 1990 and 2015, MM by three quarters', seems possible.

For the indicator 'proportions of births attended by skilled health personnel', Table 3 shows the trend – reaching the target of 80 % by 2015 seems possible.

Differences within the country

A greater number of mothers are dying at home or in transit in the highland provinces with the highest indigenous population and within health services in the lowlands. Pichincha and Guayas, where the largest cities are located, are the provinces with the most problematic indices (see Table 4).

Provinces	Total MDHO 1999 to 2001	% MDHO	Total TRMD 1997 to 2003	% TRMD	% Population
Carchi	10	1.9	20	1.5	1.3
Imbabura*	7	1.3	72	6.0	2.8
Pichincha*	101	19.6	283	24.0	19.7
Cotopaxi*	10	1.9	37	2.6	2.9
Tungurahua*	10	1.9	41	3.3	3.6
Bolívar*	7	1.3	33	2.6	1.4
Chimborazo*	13	2.5	79	5.9	3.3
Cañar*	11	2.1	33	2.5	1.7
Azuay*	15	2.9	77	6.3	4.9
Loja*	14	2.7	61	4.8	3.3
Esmeraldas**	18	3.4	90	6.7	3.2
Manabí**	47	9.1	66	5.5	9.8
Los Ríos**	19	3.6	42	3.3	5.3
Guayas**	190	36.8	161	13.9	27.2
El Oro**	22	4.2	44	3.5	4.3
Sucumbíos*	8	1.5	24	2.0	1.1
Orellana*	2	0.3	10	0.6	0.7
Napo*	1	0.1	19	1.4	0.7
Pastaza*	6	1.5	4	0.2	0.5
Morona*	3	0.5	17	1.3	0.9
Zamora	0	0	10	0.5	0.6
Galápagos	0	0	2	0.1	0.2
Total	**514**	**100 %**	**1226**	**100 %**	**100 %**

P % Percentage of national population, Census 2001.
* Provinces with most indigenous population.
** Lowlands. Esmeraldas is the province with the most Afro-descendent population

Table 4: Maternal deaths at hospital outcomes and total registered maternal deaths by provinces in Ecuador, 1997 to 2003

Other findings

From the total registered maternal deaths (TRMD), the main causes in Ecuador are hypertension (36.9%), haemorrhage (24.8%) and abortion (8.8%). From maternal deaths at hospital outcomes (MDHO), the origins are delivery and post partum (25%), abortion (14.5%), hypertension (14.1%) and haemorrhage (12.4%).

Total registered maternal deaths shows that 14.3% of the deaths are adolescents under 19 years of age, while MDHO shows this group represents 14.4%.[7]

Statistical problems

Two important statistical problems were identified: the lack of up-to-date information for the numerator (differences between TRMD and MDHO), and for the denominator (live births).The first is the contradiction of having more MDHO than TRMD in 1999 (Table 5). The explanation is that doctors' diagnoses at TRMD are changed by the codification person, or by the doctors themselves when they make a different diagnosis in RMD. There is some duplication in the registration of deaths. However, the exact amount is difficult to discern. Although diagnoses could not been aggregated, the total in Table 6 shows that real MM ratio is somewhere between the ratio by TRMD and by 'total'. It is also important to know that MDHO is 44.9% of the total and 77.5% of TRMD.

The second statistical problem is the denominator: 28% of live births involve late registration, including 12% in the following year.

Conclusions

In the last couple of years, fora gave Ecuadorians a health policy, a health research policy, a sexual and reproductive health and rights policy, and the NHS, which has recently been constructed through a broad approach and is already approved in law.

The Ministry of Health, leading the National Health Council, is building a system where the MMSS is an example of a local and national research process, with interventions and training based on findings. Reports from local, provincial and national committees are presented to corresponding health councils of the NHS. Interventions and training include the Permanent Quality Control Program with clinical supervision in a subsystem called the Integrated System of Essential Obstetric Care (ISEOC). At the local level, all these programmes include the participation of local committees of users and other civil society organizations.

It is expected that research will clarify major causes or determinants of deaths, related with three criteria: lack of decision (maternal or from relatives) to seek health services; lack of transportation to reach them; and lack of quality care within the EOCC, leading to the planning of interventions and corresponding training. As UNFPA Director General advised: 'To close the gap women need: family planning, antenatal

Diagnoses/year O0	1999 MDHO TRMD	2000 MDHO TRMD	2001 MDHO TRMD	2002 MDHO TRMD	2003 MDHO TRMD	Total MDHO TRMD
Abortion	**31**	**22**	**22**	**20**	**15**	**110**
O1	16	20	11	16	6	69
Hypertension	21	30	22	17	25	115
(Eclampsia O15)	84	77	75	43	58	307
O2						
Others from pregnancy	**9**	3	**9**	3	**8**	**32**
O3-O4	1	3	3	3	6	16
Pregnancy and fetal	**38**	26	**42**	**31**	**27**	**164**
O6-O7	19	26	24	5	15	89
Complications and	23	17	24	18	12	94
Haemorrhagy	54	61	35	26	24	200
O80-O92						
Delivery and post	**81**	**43**	5	**9**	7	**146**
partum complications						
O85-O92						
Sepsis y embolia						
O9	20	19	10	9	10	68
Others	15	12	21	13	11	64
Total	15	26	29	47	20	137
	218	153	145	111	105	**732**
	209	232	187	149	139	916

MDHO, Maternal Deaths at Hospital Outcomes
TRMD, Total Registered Maternal Death
Contradictory data in bold
Source: INEC, 10ª, ICD

Table 5: Maternal deaths at hospital outcomes and total registered maternal deaths by diagnoses in Ecuador, 1999 to 2003

Maternal Deaths Year	TRMD	MDHO	Total	Live births, (including estimated late registration)	MM Ratio per 100 000 live births TRMD	MDHO	Total
1999	209	218	427	339,786	61.50	64.15	125.65
2000	232	153	385	332,359	69.80	46.03	115.83
2001	187	145	332	323,303	57.84	44.84	102.68
2002	149	111	260	308,220	48.34	36.01	84.35
2003	139	105	244	299,619	46.39	35.04	81.43
Total	**896**	**722**	**1,548**	**Total 1,603,287**	**55.88**	**45.03**	**96.55**

Source: INEC

Table 6: Estimated maternal mortality ratio by total registered maternal deaths and maternal deaths at hospital outcomes in Ecuador, 1999 to 2003

and post-natal care, skilled attendants at birth and emergency obstetric care. Because these basic reproductive health services are not more widely available, accessible and affordable, more… women die each year from complications of pregnancy and childbirth. Universal access to reproductive health services would save women's lives and the lives of their children, and allow us to achieve key Millennium Development Goals'.[8]

Family planning is closely related with awareness and permanent quality control of health services, that is to say EOCC at county level. The EOCC are the building blocks of the NHS, providing antibiotics, oxytocics, anticonvulsivants, placenta extraction, residual products extraction, endouterine manual absorption, and vaginal delivery service, at county level, and caesarean section and blood transfusion at the provincial level.

At present all phases are being developed, although it is difficult to know how long it will take to establish a consistent NHS, including MMSS and ISEOC, with corresponding interventions and training. Big problems, such as a lack of consistent information demonstrated at the national level, have yet to be solved, but at least regular fora, policies and systems now exist as pathways to solving health problems as significant as MM. ❑

César Hermida was the General Coordinator of the National Forum for Health Research from 2002 to 2004 in Ecuador and Vice Minister of Health from 1998 to 2000. Mr Hermida holds a Masters Degree in Social Medicine from the London School of Hygiene and Tropical Medicine and is the author of many books and articles on health research and health services management.

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United States investment in global health research



Article by Mary Woolley (pictured), Stacie M Propst and Emily T Connelly

Poverty and inequity take a costly human and economic toll in our world. As demonstrated by the outpouring of response to the victims of the December 2004 tsunami, Americans are attuned to and deeply concerned about the health and well-being of people facing critical challenges. American concern is not, however, limited to disaster response. Research!America's public opinion surveys[1] show that large majorities of Americans favour having the United States invest considerably more dollars to improve health and quality of life worldwide as well as at home. Majorities of Americans also favour translation of research to facilitate more rapid and cost-effective health care, and they strongly support elimination of health disparities in order to speed cure, treatment and prevention of disease, disability and injury for all people. In this article we examine the question: What will it take to translate these and similarly positive American attitudes and expectations into increased support for global health?

The challenge

Transforming positive public opinion into action is a task familiar to advocates. The history of advocacy campaigns in the United States provides ample evidence that when public interest and support are rallied to a cause, decision-makers will act. The doubling of the budget for the National Institutes of Health (1999–2003) and the passage of the Americans with Disabilities Act are recent examples.

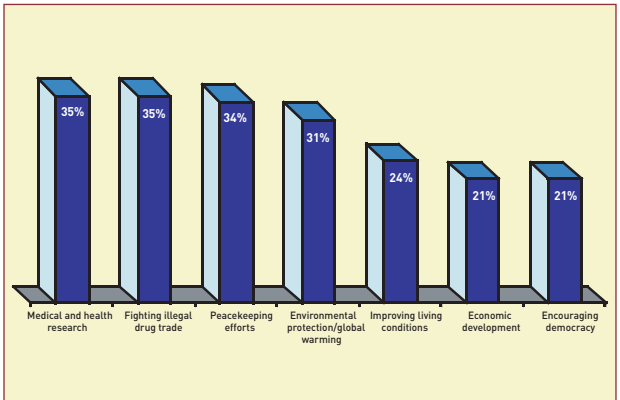


Figure 1: Health research is a top priority

Greater investment by the United States in global health and global health research would quickly become a reality were the American public to expect and demand it. Based on our public opinion research, as well as our experience in public outreach and advocacy for medical and health research, we believe that dramatically increasing United States investment in global health is an attainable goal. We caution, however, that the task of unifying and activating sufficient stakeholders to convince decision makers of the importance of increasing the United States commitment to globally oriented health research and service is a complex process requiring bold leadership, sufficient resources and sustained effort.

What we know about current investment in global health research

More and more prominent groups and individuals are speaking out about the United States' under-investment in meeting the challenges of ill-health, poverty and inequity around the world. From Bono to Bill Gates and Angelina Jolie to Jeffrey Sachs, influential people are voicing concern and putting their organizations and resources – intellectual, financial and otherwise – to work in support of their convictions.

As US leaders are encouraged to step up to the challenge

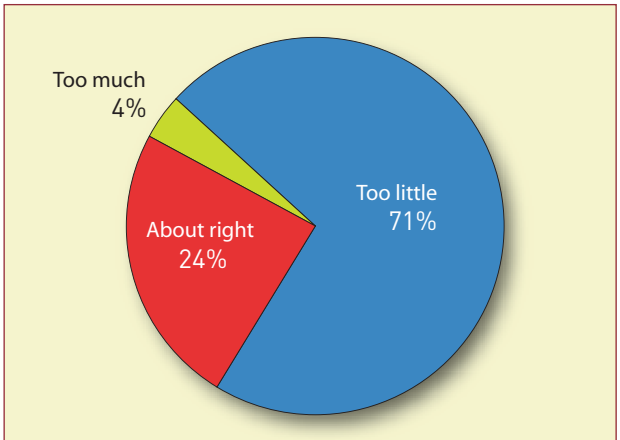


Figure 2: Most Americans think the United States spends too little on health research

Source of Funding	Global Health R&D
Pharmaceutical Industry [3,4]	2,929
Biotechnology Industry (2001) [5,6]	2,600
National Institutes of Health [7]	2,987
Centers for Disease Control and Prevention [8]	24
U.S. Agency for International Development [9,10]	338
Department of State [11]	10
Department of Defense [12,13]	61
Foundations and Independent Institutions [14,15]	505
Total	**9,454**

US $ in millions

Table 1: Estimated United States investment in global health research and development in 2003

of truly improving health on a global scale, it is necessary to identify the current investment level. It is difficult to obtain reliable data on what the United States is currently spending on global health. To meet this need, the Global Health Policy Research Network of the Center for Global Development has organized a working group of experts to publish a policy report in 2005 describing how to build an effective global health resource tracking system.[2] Although the recommendations are not yet finalized, early communications indicate that the parameters of this proposed resource tracking system will not include a plan for tracking global health research expenditures.

Initial estimate of United States investment in global health research

With our experience in tracking aggregate United States health research expenditures, Research!America is well positioned to produce a reasonable estimate of the United States overall investment in global health research. With support from The Ellison Medical Foundation, Research!America has, for the first time, compiled data on United States' investment in global health research (Table 1).

Our estimate shows that the United States invested approximately $9.5 billion in global health research in 2003. That amount is about one-tenth of the annual investment in all health research in the United States,[16] and in addition, amounts to less than one cent of each dollar spent on health costs in the United States each year.[17]

The estimated United States investment in global health research includes expenditures by industry, the federal government, academia and independent institutions. Industry provides more than half ($5.5 billion) of the total investment. Pharmaceutical and biotechnology companies internally conduct and externally fund research designed to benefit developing nations. In addition, they provide access to medicines, methods of disease prevention, training for health care professionals, and health care and research infrastructure. These are valuable contributions, but are not included in our analysis as research.

The National Institutes of Health (NIH) is responsible for much of the United States government's $3.4 billion investment in global health research. The areas of research at the NIH applicable to global health include emerging infectious diseases, HIV/AIDS vaccine development, international HIV/AIDS research, infant mortality/low birth weight, tuberculosis and vector-borne diseases. The Department of Defense also invests a significant amount in research, with $61 million focused on HIV/AIDS and infectious diseases such as malaria, dengue fever, meningitis and haemorrhagic fevers. The Centers for Disease Control and Prevention dedicates $24 million of its Global Health Strategy monies to research. The Department of State and the United States Agency for International Development are more focused on diplomatic and humanitarian efforts. USAID spends $338 million on global health research and the Department of State invests a very small percentage of its budget at $10 million.

The role of independent institutions and foundations in global health has increased significantly in recent years, especially with the establishment of the Bill & Melinda Gates Foundation. In 2003 alone, the Gates Foundation distributed $577 million in grants for global health. Of this total, $322 million was invested in global health-focused research.[15] For the many other private investments in global health research, we relied on data gathered and reported by the Foundation Center.

We regard our analysis of investment in global health research as a good first approximation; however, additional

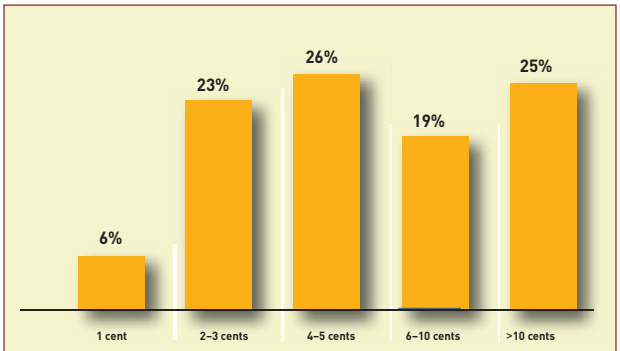


Figure 3: Americans think the United States should spend more on global health research

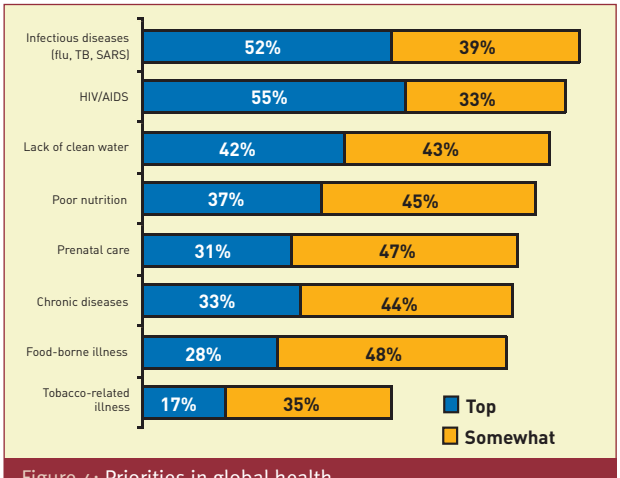


Figure 4: Priorities in global health

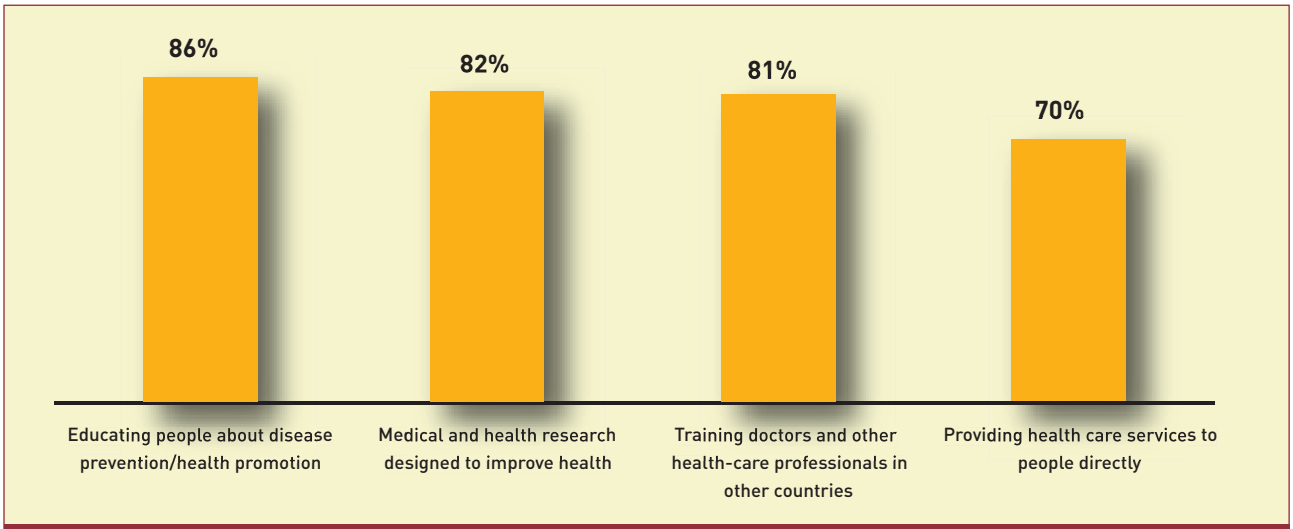


Figure 5: Disease prevention is a priority

work is required to permit regular, systematic data collection and reporting on total United States investment in global health, including global health research. This is an undertaking that we urge stakeholders in global health to support. Without reliable data on the current state of investment in global health, decision-makers will not easily be persuaded to substantially increase the investment.

What we know about United States public attitudes on investment in global health

As an additional aspect of our Ellison-supported work, Research!America commissioned a national public opinion poll designed to assess attitudes toward global health and global health research. Conducted by Harris Interactive between 30 March and 16 April 2004, this poll is similar in methodology to polls commissioned by elected officials and the media, and thus familiar to those two important target audiences.[18] Public opinion polling is much less familiar to researchers and health professionals because neither is steeped in political processes. An effective advocacy campaign will include a component designed to familiarize stakeholders with the value of public opinion.

"In this and like communities, public sentiment is everything. With public sentiment, nothing can fail; without it nothing can succeed."

PRESIDENT ABRAHAM LINCOLN

Americans can identify the leading causes of death for both rich nations (heart disease, cancer) and for poor and developing nations (malnutrition, infectious diseases): 71% say they are at least somewhat familiar with the health problems facing the world today. A very high proportion (90%) is concerned about the world's health problems. When asked to prioritize how the United States government spends money around the world, Americans think medical and health research is as high a priority as fighting the illegal drug trade and peacekeeping efforts (Figure 1).

A majority of Americans (71%) believe that the United States is spending too little on research designed to improve health around the world and think significantly more of each government dollar should be invested (Figures 2, 3). Americans think that research on infectious diseases and HIV/AIDS, along with disease prevention, health promotion and training health care professionals, should be a leading investment priority (Figures 4, 5).

For more than 10 years, Research!America has tracked consistently strong public support for the United States to maintain its leadership role in medical and health research (Figure 6). Furthermore, Americans say they are willing to pay for more research! Of Americans, 67% say they would be willing to pay $1 more each week in taxes if they were certain that it would be spent on additional medical research (Figure 7). Americans also consistently support research to understand and eliminate health problems that disproportionately affect people with lower incomes and minorities (Figure 8). It is clear that Americans are not only interested in their own improved health, but also in better health for all people.

This initial measure of American opinion on global health will only be strengthened when tracked over time. Keeping a finger on the pulse of public opinion in an ongoing fashion is essential to developing and delivering effective messages about the value of increased investment in global health and global health research.

Moving from positive grassroots attitudes to increased investment: a case history

A brief case history is instructive. Ten years ago, a group convened to launch an ambitious drive to double the budget of the NIH over five years. The scientific case for such an increase had been well established[19] and public opinion had been demonstrated to be strongly supportive,[20] but there

were significant barriers to achieving the goal. At the time, the United States economy was struggling; there was a budget deficit, caused in part by Operation Desert Shield/Desert Storm;[21] President Clinton was not a vocal champion of the NIH; and Congressional champions, while outspoken, amounted to only a handful. Many members of Congress, and virtually all of the American public, were unfamiliar with the NIH.[22] Meanwhile, interested stakeholder groups were oriented to requesting very modest increases for research and, as the overall budget scenario became gloomier, apt to work against one another by pitting one kind of research against others.

Over time, sitting and former members of Congress convinced stakeholders to deliver on the promise of better health. Research!America played a leadership role in the resulting, multi-year campaign to double the NIH budget. Years of work, including extensive public opinion polling nationally and in states of key members of Congress, development of key messages, ongoing analysis of investment in medical and health research, informed, aggressive in-person lobbying at the local and national level, earned and paid media attention and the all-out commitment of thousands of members of voluntary health organizations, led to the first of what became five years of successive 15% increases to the NIH budget, moving it from $13.6 billion in 1999 to $27.2 billion in 2003.

Building a new alliance for global health

Drawing on the lessons of the NIH budget doubling experience, as well as those of other advocacy campaigns, we suggest that stakeholders in global health and global health research come together to set an informed and ambitious goal agree upon unified messages and empower and equip large numbers of messengers to deliver those messages systematically. A commitment to regular public opinion polling is essential to delivering successful messages to decision-makers. Simultaneously, additional work should be undertaken to refine the investment estimate and to develop compelling economic and human interest messages concerning the value of this investment. Global health can and should be aligned closely to other public interests, for example, strong interest in eliminating health disparities, providing broader access to health care and overcoming poverty. Self-interest, national interest and global interest can be aligned. Like people everywhere, the American public values health and wants research to succeed.

"The United States is arguably the world's best, in terms of understanding health, the public health infrastructure and the research that drives innovation; but to date we have not fulfilled our ability to put our know how and our compassion to work to improve the lives of people everywhere. Better health is something we must summon the will and the way to export globally."

THE HONORABLE JOHN EDWARD PORTER, MEMBER OF CONGRESS 1980–2001, CHAIR OF RESEARCH!AMERICA BOARD OF DIRECTORS

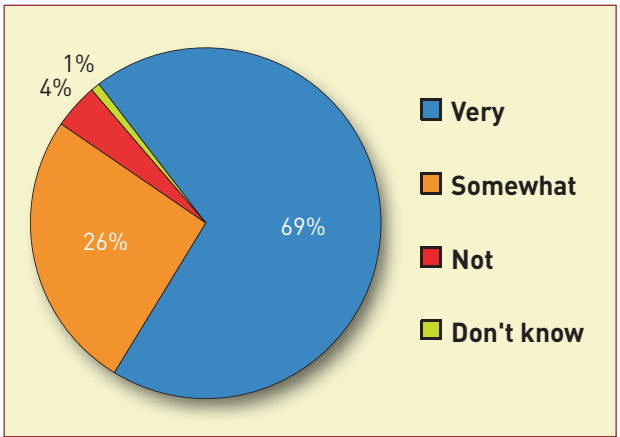


Figure 6: The United States should be a global leader in medical and health research

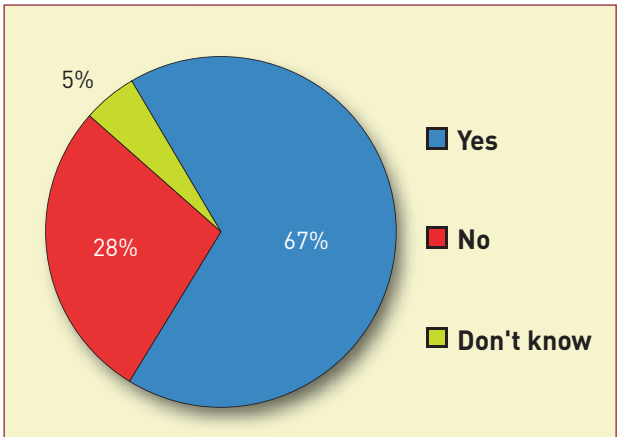


Figure 7: Americans willing to pay more taxes for medical

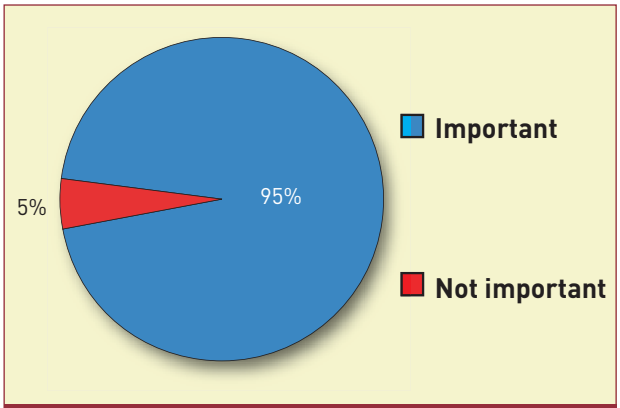


Figure 8: Importance to eliminate health disparities

The costly toll of poverty and ill-health across the globe is undeniable. Excellent illustrations exist that demonstrate the value of lives saved and economies assisted by shoring up research capacity, the public health infrastructure and health care delivery around the world. In the 1960s and 1970s, the World Health Organization led a global effort to deliver the smallpox vaccine worldwide. This campaign

resulted in the eradication of smallpox in 1977, a disease that infected an estimated 50 million people each year just 25 years earlier. Thailand's '100% Condom Program,' which promoted condom use among sex workers and other high-risk groups, is another global health success story. Thanks to the programme, Thailand had 80% fewer new cases of HIV in 2001 than in 1991 and has prevented nearly 200,000 new cases.[23]

In developing a case for greater United States investment in research to improve health globally, a well-organized alliance of stakeholders must boldly commit to making these success stories come alive for Americans and their leaders.

Our experience tells us that accurate investment data can be developed, compelling messages framed, effective leaders engaged, cohesive alliances forged and positive public opinion translated into decision-maker response. It is time for the community of stakeholders to commit to audacious advocacy for global health – from grassroots to global. ❑

Acknowledgements

We thank The Ellison Medical Foundation for generous support of the development of the first United States global health research investment estimate and the attitudinal research to measure American support for more research to enhance health globally.

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Setting and implementing a health research priority agenda in Brazil



Article by Reinaldo Guimarães (pictured) and Leonor Pacheco Santos

A number of models and methods for setting health research priorities have emerged in the last 10 years, the majority of them emphasizing conceptual and methodological aspects. Several international health research agencies, academic institutions and individual researchers developed tools and methodologies for health research priority setting, like burden of disease analysis, the five-step process, the combined approach methodologies, etc. In spite of some progress, the debate about priority setting, particularly at the national level, is more open than ever before.[1,2]

Equal consideration has to be given not only to setting priorities, but on how to implement these priorities in actual programmes and projects. This brief report describes how this was accomplished in a middle-income developing country, in a relatively short period of time, given adequate political and financial support.

The Brazilian health system was modified after the 1988 Constitution, due to an extensive health reform based on proposals set out during the Eighth National Health Conference (1986). The basic principles guiding the new Unified Health System (SUS) are: decentralization; comprehensive care (promotion, protection, early diagnosis, damage prevention and rehabilitation); universal coverage and access; equity; and community participation.

A landmark of the system is community participation, guaranteed by a network of more than 5,000 municipal health councils, 27 state health councils and the national health council (NHC), involving about 100,000 people in this voluntary work. In these councils four social sectors are represented: clientele (50%); health providers plus health managers (25%); and health workers (25%). Most of the decisions about health care at the three levels have to be approved by the health councils, such as budget, construction of health facilities, implementation of health programmes, etc.[3] The participatory process reaches its summit during the National Health Conferences: the last one, held in December 2003, involved about 300,000 people in the three levels: municipal, state and national. National Health Conferences are a landmark in the Brazilian health system; besides the 12 general conferences held so far, thematic conferences are also organized to deal with more specific issues, such as science and technology (S&T).

In 2002, nearly 4,900 research groups were involved with health research in Brazil, with 18,000 researchers (11,000 of whom have a PhD). These figures correspond to between 25% and 30% of the total research effort in Brazil (National Research Council [CNPq], 2002).

A preliminary estimation of the resources applied in health research between 2000 and 2002 showed an annual mean of US$288.3 million. From the suppliers' side, public sector accounted for 51%, private for-profit sector for 42% and external financial resources for 7%.[4]

The need to focus health research as high priority at the national level has been pointed out on the international scene over the last 10 years, as described before. However, much has been said about the need to do it, but not so much about how to actually do it. The processes are equally important as, if not more than, the results attained. The political process to guarantee an adequate and wide consensus is not an easy task, especially if one wants to involve not only small scientific committees, but broaden the horizons to the community at large.

The setting of a comprehensive agenda for priorities for health research in Brazil has been a stepwise process. It started in June 2003, when the Ministry of Health (MoH) appointed a Technical Advisory Committee, composed of 20 distinguished scientists and health policy-makers. This group, in consonance with the National Health Council Subcommittee on Science and Technology, proposed the 20 sub-agendas in Figure 1 to account for the specificities and the breadth of the health research field.

The second stage was the identification of research

Infectious and parasitic diseases	Demography in health
Chronic diseases	Health systems and policies
Mental health	Work in health and health education
Violence, accidents and trauma	Health, environment, labour and bio-safety
Women's health	Health technology assessment / health economics
Child health	Food security and nutrition
Elderly health	Communication and information in health
Indigenous peoples' health	Bioethics and ethics in research
Risk factors (health promotion)	Clinical research
Epidemiology	The Industrial health complex (drugs, vaccines, equipments, diagnostic devices, etc

Figure 1: Sub-agendas to account for the specificities and breadth of the health research field

priorities for each sub-agenda. This occurred in a national seminar on November 6–7, 2003, which convened 408 professionals, among health researchers (68%) and health policy-makers/health-care providers (32%). Separate seminars were held previously to set research priorities in two subjects for which calls for proposals were planned for 2003 ('dengue' and 'violence, accidents and trauma'), with the participation of 102 people. The final number of specialists involved in the entire process was 510. The spectrum of experts involved biomedical, clinical and public health researchers, as well as health policy-makers and health-care providers at the municipal (county), state and federal levels.

The meeting was organized in groups of 15–25 people for each of the sub-agendas. Rapporteurs were appointed among the MoH staff and logistical support was provided so the process of proposal writing was as interactive as possible. At the end of the two-day meeting the proposals were immediately made public to all participants. For each of the 20 sub-agendas, 15–40 priority topics were proposed.

The next step was to submit it to a formal public consultation on the MoH website for a period of 45 days, aiming to broaden the consultation reaching health workers and the community at large.[5] During this period 1,900 people registered online to have access to the document. A total of 360 comments and contributions were received, analyzed, published and made available to be discussed during the conference. All versions of these documents were saved for further consultation.

The First National Conference of Science and Technology in Health was held in 1994, and although it represented a breakthrough, its organization did not allow ample participation. However, some of the proposals set forth during the conference, like the creation of a Secretary of Science and Technology at the MoH, were made effective by the new government in early 2003.

The Second National Conference of Science, Technology and Innovation in Health, held on July 25–28, 2004, was an initiative of three ministries: Health, Education and Science and Technology. During the preparatory phase, which lasted about 100 days, 307 towns and 24 states (out of 27) organized their local level conferences, involving around 15,000 people. From the state conferences 360 delegates were appointed for the national phase. In addition 120 delegates were appointed by the education sector and 120 by the science and technology sector, most of them health researchers, coordinators of graduate programmes, university hospital managers, representatives of the major scientific societies, etc.

To the national plenary sessions, 644 participants attended from the health, education and science and technology sectors: 431 voting delegates and 213 invited people and observers. Among the 431 delegates, 299 represented the health sector (146 health system users, 82 health workers and 68 health policy-makers). Among the health system users, 35% represented the local, state and national health councils, 24% community associations, 19% patient associations, 5% workers unions and 17% others. Among the health professionals 27% represented professional associations, 18% workers unions, 17% state and municipal health secretariats, 12% the local, state and national health councils and 26% others.

The science and technology sector was present with 62 delegates: 34% science and technology policy-makers and representatives of scientific associations, 11% from health research institutions, 6% from universities and 15% others. The education sector had 70 delegates: 55% from universities, 13% from health research institutes, 6% science and technology managers and 26% others.

The two main themes of the conference were: (a) national policy for science, technology and innovation in health; and (b) the priority agenda for health research. After three days of intense debates and deliberations, the two documents were approved. The conference was a challenge for both scientists and community leaders – never before had these social actors made such effort to speak a common language, to interact in such depth and to discuss openly their points of view, sometimes conflicting.

After taking into consideration the comments and suggestions from the state conferences, the original National Policy document was expanded from 98 to 108 items, some research topics were added to the agenda and three other sub-agendas emerged with their corresponding detailed research topics: (a) oral health; (b) health of afro descendents; and (c) health of the disabled.

All versions of the above documents were saved for further consultation. Our effort was to overcome the problem, noted for most countries, that the crucial intervening steps leading to the selection of research priority areas and topics are not fully documented, leading to problems of reliability and credibility.[1]

Currently, the health research agenda is ruling the application of the MoH's financial resources for research and development. As stated before, implementing these research priorities into programmes and projects was the major goal. Immediately after the conference the MoH, through its Science and Technology Department, launched eight public calls for proposals in areas outlined in Figure 2. As a result 1,379 proposals were received, analyzed and 344 projects were financed.

Another large programme, named Research for the SUS was developed in partnership with the 27 State Secretariats

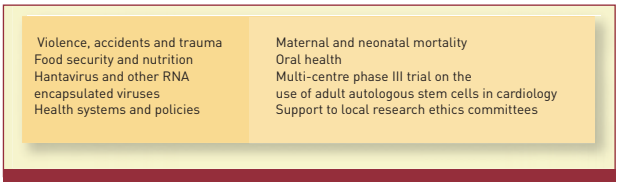


Figure 2: Eight areas were outlined by the MoH Science and Technology Department following the conference

of Health and State Agencies for Research Support. The funds were decentralized to the state agencies, which in turn disbursed a complement (from 10% to 50% of the MoH funds) and run the state level calls for proposals. For five states the call was launched in July, for 13 in September/October and for the remaining nine in November/December. So far, 400 proposals have been received, as not all deadlines have been reached. At present the projects received are in the process of analysis.

The MoH also supported some projects belonging to the sub-agenda of the Health Industrial Complex. Among them, several deserve mention the development of some vaccines prioritized by the National Immunization Programme, diagnostic devices for tuberculosis (TB) and hepatitis C virus (HCV), NAT tests for HIV, monoclonal antibodies related to blood transfusions and clothing factors by recombinant technology. The partnership with the Brazilian Cochrane Initiative in order to strength an evidence-based process of technological incorporation to the SUS also deserves mention.

In 2004, a budget of about US$25 million was committed to the Department of Science and Technology for health research support. It was wholly disbursed and an important point is the operational cost of running the programme. Out of our total budget the amount spent directly financing research corresponded to 97.6%.

It should be mentioned that the majority of the financing operations described was performed with technical advice and operational aid of two federal research financing agencies, namely the National Research Council (CNPq) and the National Bank of Technological Development (FINEP).

Adding this research portfolio to the one initiated in 2003 – nine projects of the Brazilian Tuberculosis Research Network, 11 projects of the National Research Taskforce in Dengue and 140 projects in the Research for SUS programme, we consider that we have started a process to reposition the MoH in the Brazilian effort for health research. The remaining challenge is to make these first steps permanent and sustainable. It is helpful to outline some particular lessons that we learned:

- Our experience suggests that the agenda setting follows a 'TripleHelix' logic with a permanent compromise among three rationales: the managers/providers, users and researchers, all of whom should be taken into account.
- Towards a fair balance between technical basis and political consensus. The less complicated the political consensus, the stronger the technical basis, and vice-versa. However, the goal ought to be strength for both.
- Technical basis is a global matter. Political consensus is a local one. For a given technical basis globally assumed as good, it will have as many pathways to consensus building as there are countries exercising the agenda's construction process.
- Prioritizing the priorities – the broader the agenda's scope, the looser the definitions for priorities. For a specified programme, an isolated problem or a small geographic region, a priority agenda can be quite a simple tool, capable of being self-applied. But when the target is a whole country, especially a large one, the picture changes. Independent of the technical approach involved, the agenda assumes huge complexity with a great number of choices. This issue raises the question of prioritizing the priorities, and the leadership of the national health authority is mandatory.
- The sanitary landscape changes and thus setting an agenda is a process of permanent construction. It can hardly be considered a finished piece of work. ❑

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Turning knowledge into health benefits for the poor



Article by Alastair Ager[1]

Developing new knowledge through research has an increasingly central place within the UK Department for International Development's (DFID) work towards the goal of poverty elimination.[2] But does an increasing pool of global knowledge inevitably bring benefits to the world's poor? DFID strategy sees an increasing level of investment in research – up to around US$80 million in the health field in the current year – but also increased attention to the manner in which research effort is focused.

There are three key issues that have shaped DFID policy in promoting research effort for maximum impact on health equity and poverty: funding mechanisms; links to policy and practice; and capacity development. Each of these areas' structures can work to either strengthen or weaken the impact of new knowledge on the health of the poor. How can we make sure that the new knowledge we gain is of maximum benefit to the poor?

How can we make sure that the new knowledge we gain is of maximum benefit to the poor?

Funding mechanisms

It is clear that funding mechanisms shape research agendas, and research agendas determine the focus of new knowledge. If we are concerned to ensure that knowledge is maximally relevant to the needs of the poor we need to examine the appropriateness of funding mechanisms for this purpose. In recent years there has been increased recognition, for instance, that market mechanisms alone are insufficient to enable the development of essential medicines for poor people. It was recently estimated that less than 1% of global health research funding is directed at developing new interventions for diseases predominantly impacting on the poor.[3] DFID, as a development agency with a commitment to science as a key tool for poverty elimination, has thus seen this area as a key focus for investment.

Product Development Public-Private-Partnerships (PD PPPs) are mechanisms that bring together public and private sector expertise and finance to develop effective health interventions that are accessible to the poor. They are focused in translating discoveries of basic science into the development of new products, and making these accessible in the situations where they are needed. The management of such a 'product pipeline' requires deep engagement with scientific innovation, commercial and clinical skills in managing a 'portfolio' of potential products, and close working with the wide range of stakeholders (including clinical trial sites, regulatory bodies, manufacturers and distribution channels) required to get an effective product into the field. This wide participation of stakeholders – generally with a significant representation from developing country scientists, governments and NGOs – potentially provides a channel for funding that ensures access both to the best of global science and to individuals and institutions within countries most significantly impacted by the relevant disease. DFID – along with other funders in this area – is currently engaged in analysis of the approach of different PPPs, seeking to identify the best means of approaching the above 'ideal' of integrating scientific rigour, commercial acumen and 'pro-poor' impact.

The impact on the poor of new knowledge in this area is potentially immense. As part of its overall commitment to address AIDS, DFID has to date committed investment of over $100 million in research into new preventive technologies regarding HIV inflection, including work on vaccines and microbicides. Studies have estimated the



Picture 1: New health knowledge can bring great benefits to the poor



Picture 2: Linking research into policy and practice is crucial

impact of introducing a microbicide of 60% efficacy could prevent nearly one million HIV infections per year if used consistently. As well as being an intervention very much under the control of women, microbicides are relatively easy to use and are thus an accessible technology for most potential users.

Another major example of DFID seeking to structure research funding in a manner that maximizes potential benefit to the poor is the 'untying' of DFID research funding. 'Untying' is the process of procuring services on the basis of the maximum benefit to the beneficiary, rather than with respect to the interests of the supplier. DFID has sought to lead the way in 'untying' of aid monies, such that contracts are only awarded to British companies when the goods and services supplied by them (be they vehicles, equipment or whatever) are clearly the 'best deal' for the beneficiary.

Studies have estimated the impact of introducing a microbicide of 60% efficacy could prevent approaching one million HIV infections per year if used consistently. As well as being an intervention very much under the control of women, microbicides are relatively easy to use and are thus an accessible technology for most potential users



Picture 3: Building sustainable research capacity is a key goal for Africa

Similarly, calls for DFID bilateral research funds are now open to institutions from throughout the world. The excellence of proposed work, and its potential impact on the lives of the poor in the developing world, are the key criteria. For example, funds have recently been granted to the University of Cape Town – in competition with applications from throughout the world – to lead an innovative research programme consortium examining interventions for promoting community mental health. Given the excellence of British science, significant funds are still allocated to British research institutions. However, in most cases this is on the basis of demonstrably strong partnership with institutions within the developing world. The centrality of research institutions from the South in taking forward the health research agenda of the South is critical in ensuring the ultimate impact of research on the health of poor people in the South.

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Links to policy and practice

DFID has become increasingly aware that the traditional model of research dissemination (principally through publication in peer review journals) has failed to have significant and sustained impact on policy and practice. In a recent review of health research programmes funded by DFID, wide variation in the effectiveness of researchers in demonstrating clear impact of their work on policy and practice was noted. Those demonstrating greatest influence were marked by: a strategic approach to communication and influence; a direct engagement with policy-makers; and a preparedness to 'translate' research findings into a form that could be utilized by policy-makers and practitioners.

As a result, DFID now encourages a very purposive strategy of policy influence for the work it funds with, from this year, 10% of funding for research programme consortia now expected to be directed to specific communication activity. DFID has employed communication 'specialists'

(Researchers) demonstrating greatest influence were marked by: a strategic approach to communication and influence; a direct engagement with policy-makers; and a preparedness to 'translate' research findings into a form that could be utilized by policy-makers and practitioners

The Ministries of Health in Kenya, Uganda and Tanzania have come together to propose a mechanism for the synthesis and communication of health research conducted within these countries to inform the development of evidence-based health policy in the region

with the principle goal of communicating the key findings of commissioned research to relevant users. This involves support ranging from electronic access to journals for developing world academics, through the commissioning of abstracting services accessible by policy-makers, to the production of a 'radio soap opera' communicating key health messages to communities in Africa.

The Regional East African Community Health (REACH) Policy initiative[4] is an example of an initiative that addresses the local demand for research as well as its effective supply. The Ministries of Health in Kenya, Uganda and Tanzania have come together to propose a mechanism for the synthesis and communication of health research conducted within these countries to inform the development of evidence-based health policy in the region. Such structures – very much reflecting the thinking of the Ministerial Summit on Health Research in Mexico in 2004 – offer a very promising strategy to maximize the impact of new knowledge on the health of poor people.

The 10/90 gap of research investment in health problems of the developing world, is commonly mirrored by a 10/90 imbalance in the South-North distribution of relevant scientific expertise.

Capacity development

Both of the above issues point to the centrality of capacity development in seeking to ensure that knowledge gain brings direct benefits to the poor. As we come to see health research as a key part of the wider agenda of development for countries of the South, we must acknowledge that the means of production of new knowledge is key in determining its ultimate impact on the poor. In these terms, capacity development may still occasionally involve such means as making doctoral training opportunities available in 'northern' institutions, but in general, and far more fundamentally, it will focus on the establishment of strong research institutions to drive knowledge development in the South. The vision for the future must be North:South (and South:South) institutional relationships based on the genuine reciprocity of interest and expertise that has characterized North:North institutional links for decades.

For this vision to become a reality, however, there is clear need for sustained investment. The 10/90 gap of research investment in health problems of the developing world, is commonly mirrored by a 10/90 imbalance in the South-North distribution of relevant scientific expertise. It is for such reasons that the Commission for Africa has called for investment in Centres of Excellence that become African regional hubs of research and development of genuinely global significance.[5]

It is also the basis of planned investment by DFID – in collaboration with the Wellcome Trust – in research capacity strengthening initiatives in Kenya and Malawi. Building upon existing capacities, the goal is to establish a research infrastructure that, as well as contributing to global scientific knowledge, relates such knowledge increasingly closely to the national health policy needs and secures sustainable national institutions that can recruit and retain skilled and knowledgeable researchers.

New vehicles for new knowledge

Growing awareness of the potential value of science and technology in driving and supporting development has recently propelled the field of global health research into significant profile. The potential value of new knowledge is clear. But to make sure that new knowledge is of maximum benefit to the poor we need to look carefully at how research is funded, communicated and institutionalized. All stakeholders in the field of global health research who share the vision that the overriding priority for new knowledge is its benefit to the poor need to explore new vehicles fit for this purpose. ❑

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Task Force on Health Systems Research: a research agenda to help attain the MDGs



Article by Andy Haines

Recent evidence suggests that many low-income countries are unlikely to achieve the Millennium Development Goals (MDG) health targets by 2015[1,2] and that those countries furthest away from the targets are least likely to make significant progress. Increased resources for health are essential, but in addition there is a growing consensus that 'a primary bottleneck to achieving the MDGs in low-income countries is that health systems that are too fragile and fragmented to deliver the volume and quality of services to those in need'.[3] Although further basic research is needed to develop better interventions, the full implementation of existing interventions would, for example, reduce child mortality by around two thirds[4] and maternal mortality by around three quarters.[1]

Many of the barriers to scaling up effective interventions are common to a range of global programmes addressing priority health problems. Reviews of programmes focused on child health, maternal health, HIV/AIDS, malaria and tuberculosis (TB) in a range of countries have identified a number of health system challenges to delivering effective and affordable interventions (Table 1). At the same time, the many approaches to organizing and delivering services have not been adequately evaluated, and so the evidence base for strengthening health systems in low-income countries is weak.

This knowledge deficit prompted Tim Evans, Assistant Director General of the World Health Organization, to convene the Task Force on Health Systems Research (members are listed at the end of this article). Its primary aim was to develop an agenda for health systems research, which, if addressed, would support the attainment of the MDGs. This article is a condensed version of the report that was submitted to the WHO in March 2005.

The process of developing a research agenda

The Task Force, which was formed in December 2003, consulted widely with a diverse group of stakeholders. Its thinking was also influenced by analyses of health system constraints to achieving the MDGs[3,5,6] and previous work aimed at identifying priority research topics on health systems.[7] With inputs from WHO staff and other experts, a tentative research agenda was developed comprising 12 topic areas that were intended to cover the important barriers to improving health systems performance (Table 2).

- lack of demand for interventions at the individual and community level
- policies that do not support the use of effective and affordable drugs
- multiple uncoordinated actors (public and private sectors) who have different priorities and modes of working
- underdeveloped service management capacity
- competition between programmes
- inefficiency and/or inequity in financing and resource allocation
- weak health information systems
- limited availability and suboptimal performance of human resources

Table 1: Health system challenges to delivering effective and affordable interventions

Global influences: effects of global initiatives and policies on health systems

The Task Force then undertook a consultative process involving several WHO regional meetings, an article in *The Lancet*,[8] a presentation at the Ministerial Summit on Health Research in Mexico[9] and the extensive circulation of the preliminary research agenda using email discussion lists. Reflecting on the feedback that was received, brief templates were prepared for each proposed topic addressing the following questions:

- What is the problem and why is it important?
- What is known and what is not known?
- What research is needed and how would it help?

In addition to these 12 topic areas, a number of broader issues are essential to factor into any attempt to move the health systems research agenda forward – equity, systematic

Financial and human resources:
- Community-based financing and national health insurance
- Human resources for health at the district level and below
- Human resources for health at the national level

Organization and delivery of health services:
- Community involvement
- Equitable, effective and efficient health care
- Approaches to the organization of health services
- Drug and diagnostic policies

Governance, stewardship and knowledge management:
- Governance and accountability
- Health information systems
- Priority setting and evidence-informed policy-making
- Effective approaches for intersectoral engagement in health

Global influences:
- Effects of global initiatives and policies (including trade, donors and international agencies) on health systems

Table 2: Suggested topics for health systems research

reviews, methodology, networking, funding and evaluation.

The central importance of equity

The 'inverse care law', initially put forward over 30 years ago, still applies today: 'the availability of good medical care tends to vary inversely with the need for it in the population served'.[10] The MDGs address inequities between nations, but there are also major health inequities within nations that need to be addressed.

For example, in a recent review of 56 developing countries, death rates were nearly twice as high, on average, among infants and children in the bottom economic quintile of the population compared with the wealthiest 20%.[11] The opposite trend was found in disparities with respect to access to health systems – the better-off generally fared far better than the disadvantaged. Gender is also a significant contributing factor to inequities in health within many nations, both because health systems may not deliver services appropriately to cater for the needs of women and because women suffer more from the effects of poverty in many societies.

Any health systems research agenda, therefore, needs to address explicitly how to reduce the socioeconomic differentials in access to effective health care, which may be compounded by political and cultural factors. In recognition of the central role of primary health care in achieving the MDGs by reaching vulnerable and disadvantaged populations, many of the priority topics have a strong focus on the research that is required (at the global, national and local level) to strengthen this essential component of health systems in less-developed countries.

More systematic reviews required

Although primary research is needed to fill in the knowledge gaps that are highlighted in the 12 templates, it is also essential to map out the relevant research that has already been undertaken. Systematic reviews of each of the topic areas are a necessary prerequisite to commissioning new research and will ensure there is no unnecessary duplication of pre-existing work. By synthesizing all relevant existing knowledge, a systematic review reduces bias and the role of chance, and thus provides a more precise estimate of the strength of the evidence.

More systematic reviews of topics relevant to health systems in the developing world are required. Only a few of the reviews that have been completed by the Cochrane Collaboration's Effective Practice and Organisation of Care Group[12] are from low- and middle-income countries; and although their numbers have been rising, in 2003 only 8.2% of the Cochrane Collaboration's reviewers were from developing countries.[13]

There are a number of challenges in undertaking reviews of health systems topics including: the publication of many reports in the grey literature; the frequent lack of clear descriptions of complex interventions; and the frequent changes to the governance, financial and delivery arrangements within which interventions are delivered. Nevertheless, they can provide useful information for researchers and policy-makers and should be supported by donors, international agencies and national governments.

Making research valid and transferable

Rigorous health systems research requires contributions from many disciplines, including epidemiology, biostatistics, health economics, sociology, anthropology and policy analysis. Both qualitative and quantitative research methods have important roles to play. In some circumstances, interventions can be evaluated using randomized trials – particularly cluster trials where the unit of randomization may be communities or health facilities – but such opportunities are often missed.

Many research questions, however, cannot be addressed by randomized trials – for example, because they may be system-wide in their scope. Other approaches, such as controlled before-after studies and interrupted time-series analyses, need to be considered, as well as process evaluations to better understand how and why interventions work or do not work as intended. Participatory action research has the potential to elucidate constraints to success of interventions and improve the performance of health staff.[14]

Recommendations for the improved design and reporting of non-randomized and randomized studies have been published and should be followed.[15,16] Contextual factors are generally thought to be important effect modifiers, but are often poorly described by researchers, making it difficult to determine why a particular intervention or policy has been effective or ineffective. Better descriptions and more attention

to assessing the influence of contextual factors on the local applicability of research in general and of systematic reviews in particular is needed.[17]

Fostering research networks

Health systems research requires multicountry collaborative networks to develop priorities, improve methodological approaches, undertake primary research and systematic reviews, and strengthen research capacity. There are three main arguments that support the need for larger and more widely applicable research programmes.

Firstly, as has already been highlighted, many aspects of health policies and systems are heavily influenced by the local context. Multicentre and multicountry studies are important because they permit a specific intervention to be studied in contexts that can be both similar and different, allowing conclusions to be drawn on the dependence of the outcome on the context.

Secondly, some strategic issues are driven by global or supra-national influences, such as the impact of global trade negotiations on the movement of health personnel, the spread of private health insurance companies, and access to essential drugs. Thus health systems research needs to take into account global influences on health systems and to incorporate a global perspective about research on issues that may be subject to such influences.

Thirdly, health systems research capacity is as yet limited in almost all countries. It is an interdisciplinary endeavour that demands not only technical expertise, but also expertise in relating to and working with policy-makers and other decision-makers in developing research agendas, conducting and interpreting research, and supporting action based on the findings. While training plays an important role in developing research capacity, expertise also has to be built 'on the job', by doing research.

Bridging the gap between researchers and the users of research

In order to facilitate the uptake of research findings, it is important to bridge the gap between the producers and users of research.[17,18] Networks should also provide the opportunity for decision-makers to interact with each other and with researchers in order to identify common problems, issue calls for priority research, and define critical needs from a policy development perspective. Such networks will allow for both producers and users to be better informed of the needs of the other group and promote joint approaches to key issues requiring research.

The European Observatory on Health Systems and Policies provides one model for a support function for public policy-makers that could be adapted for low- and middle-income countries.[19] The secretariat for such an entity could take responsibility for identifying topics for systematic reviews, developing actionable messages for policy-makers from such reviews, and promoting interactions between researchers, policy-makers, and other stakeholders.

Allocating more funds to health systems research

Few resources are spent on research directed at health systems issues. Recent estimates suggest that only about 0.017% of health expenditure in less-developed countries is devoted to such research.[20] At a time when substantial sums are being made available for the purchase of effective interventions and the development of new drugs, vaccines and other products, it is essential to channel more resources to address the preparedness of health systems to deliver these interventions.

The ongoing evaluation of the Integrated Management of Childhood Illness (IMCI) programme gives an indication of both the likely scale of resources required to evaluate a major international health programme and the potential benefits of doing so. The evaluation, which began in 2000 and will take 7 years to complete, will cost approximately US$10 million.[21] The research completed to date includes a major cluster trial of the IMCI strategy in Bangladesh, which showed substantial improvements in the quality of care for children in first-level facilities and a more than three-fold increase in the use of such health facilities for the care of sick children.[22] It also indicated aspects of care where further improvements were needed to capitalize on the full potential of IMCI, such as low rates of referral among children with severe illness sent to local hospitals. The evaluation will ultimately provide data on the impact of IMCI on mortality and on IMCI's cost-effectiveness. A smaller study in Tanzania showed improvements in the quality of care and possible improvements in mortality with similar or lower costs in two intervention districts compared with two districts that served as controls.[23]

The experience with IMCI suggests that a programme of research on a major international public health priority topic might cost $10–20 million depending on the questions addressed and the scope of the research. Such costs are very modest in relation to the overall costs of implementing major programmes and have the potential to represent an excellent return on investment. Without such research the lessons from failed and successful implementation will not be learnt and disseminated. Doubling the current annual health systems research expenditure of $134 million[20] seems a reasonable aspiration in the near term: it is equivalent to a small proportion of the funds committed by the Global Fund to Fight AIDS, TB and Malaria (around $3 billion) or the US President's Emergency Plan for AIDS Relief ($15 billion requested).

The Mexico Statement from the Ministerial Summit on Health Research, which took place in Mexico City in November 2004, urges developing countries to implement the recommendations of the Commission on Health Research for Development, which has stated that at least 2% of national health expenditures and at least 5% of external

donor funds for health should be invested in research and capacity building. The statement also calls for governments to allocate adequate funds to support health systems research in order to address priority questions.[24] If the Mexico Summit recommendations were followed for low-income countries, a total of $407 million would be available for health research –$278 million from internal funds and $129 million from external funds (using 2002 data). For low- and middle-income countries, the total would be $2,082 million – $2,022 million from internal funds and $60 million from external funds.[25] Therefore, if acted on, the recommendations should be sufficient to fund necessary health systems research while still providing sufficient funding to support other categories of health research.

Moreover, ensuring that relevant research is accepted as a legitimate call on additional funds of perhaps $50 billion annually – which will become available in the event of the launch of the proposed International Finance Facility[26] – would provide a new source of funding for the governments of low-income countries to commission such research.

Committing to evaluation

Making the case for urgent investment in research to evaluate the major programmes now being rolled out to deliver interventions for priority diseases seems the most promising strategy for scaling up health systems research in the near term. Such research not only meets the operational needs of programmes but also capitalizes on the opportunities to compare different approaches to the delivery of effective interventions.[27]

It will be important, however, to ensure that the opportunity to investigate cross-cutting health systems issues relevant to a number of programmes is not lost, otherwise there is a danger that the overall benefits to public health of such programmes will be less than anticipated. This could result, for example, from competition between programmes for limited health personnel or inefficiencies resulting from the introduction of parallel drug delivery and training programmes.

At the moment, there is no mechanism to ensure that the opportunities for research are capitalized on with a view to improving implementation of priority interventions and programmes. Research funds are not made available routinely alongside global health programmes. And although the Global Fund will support research in-country to improve the likelihood of implementation, there is no way to facilitate the development of appropriate research proposals where research capacity is lacking or policy-makers are indifferent to the opportunities for generating health systems research knowledge and linking that knowledge to action.

There is little likelihood that such research will arise spontaneously. Therefore funds must be made available for experienced researchers to work in very close cooperation with those developing, managing and delivering services to ensure that relevant research questions are addressed in a methodologically appropriate fashion.

The sources, management and mechanisms for the disbursement of such funds are matters that will require considerable discussion among stakeholders. Nevertheless, the WHO can play a key role by ensuring that such research takes place and that the findings influence policy and practice. It can, for example, make a commitment that all of its own priority programmes will be accompanied by a rigorous programme of evaluative research (as was undertaken by the IMCI programme). In addition, the WHO can work with other international agencies, bilateral donors, and major NGOs that fund and implement health programmes to develop a code of practice to ensure that evaluation is built in at the beginning of such initiatives and that there is a commitment to be guided by the evidence that emerges as a consequence.

Conclusions

Health systems research is essential to reduce our collective uncertainty about how to achieve the MDGs and to provide a basis for well-informed decisions and actions through which the findings of such research can be implemented. There are opportunities to initiate substantial research programmes by collective action among research funding bodies and by ensuring that major programmes focused on specific diseases or target groups incorporate the evaluation of impacts.

There are some early indications that the work of the Task Force and others has succeeded in drawing attention to the importance of health systems research and that the global health research community will respond to urgent calls for action. For example, the WHO is assessing the feasibility of establishing a major new programme on health systems research that will build on existing initiatives such as the Alliance for Health Policy and Systems Research. The Task Force believes that the best way the proposed WHO programme could catalyse health systems research and generate support is through commissioning adequately funded projects and programmes that illustrate to policy-makers the benefits of such research. It should also focus on supporting member countries to take coordinated action to strengthen health systems research within countries and, especially, across countries. Such a programme could also play a role in regularly reviewing the research agenda outlined by the Task Force in the light of changing health priorities and challenges.

Finally, the WHO Advisory Committee on Health Research has an important role to play in monitoring progress towards the achievement of the broader recommendations that have been made by the Task Force. Only a decade exists before the target date for the MDGs in 2015. It is now a matter of urgency to ensure that health systems become the focus of national and international efforts to improve capacity to deliver effective interventions in an equitable fashion to those who can benefit.

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The Task Force wishes to acknowledge with thanks the excellent editorial assistance from Joanne McManus and contributions from many WHO staff and other individuals who responded to the consultation. This paper represents the views of the Task Force and not the official policy of WHO. ❑

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Innovation systems and global health



Article by Richard T Mahoney

For a long time, there has been controversy about the relative values of research and development (R&D) on new technologies for health and of the identification and implementation of best policies for national health systems. Proponents of expanded support for R&D argue that only through new and improved technologies will it be possible to address effectively some of the greatest health problems facing poor people worldwide. Investment in research today will pay off by helping people more effectively than current technologies, and will help the long-term. New real scientific advances last for a long time. Only with safe and effective vaccines will it be possible to control AIDS, malaria and tuberculosis (TB). Those who support focus on policy argue that very significant progress could be made in controlling disease today with existing technologies and known policies. Money spent on research that may not pay off for decades could be allocated to known interventions that would save lives today. For example, malaria might be largely controlled in Africa with the widescale availability of bed nets and advanced therapies. In this article, I propose a framework for decision-making that could help resolve this controversy or at least make it easier to reach better decisions.

Life is complex

The problem with both these views is that they represent an incomplete appreciation of the world and how it works. Specifically, the arguments do not take into account the way in which innovation occurs. R&D cannot lead to new products used by people who need them without interacting with a very large number of players in institutions, governments and the private sector. Product innovation is a complex process involving numerous failures, feedback loops and changing collaborations. How are health research priorities set? What are the regulatory barriers? What is the impact of intellectual property regimes? Conversely, imaginative and potentially effective policy innovations cannot work without addressing a complex web of complementary and competing forces. How do governments allocate funds for health? How do civil service systems work? What is the effect of corruption on hiring staff and allocation of resources? How are the prices of needed drugs and vaccines determined?

The bad news then is that, as with most important things in life, the answer to the question of the relative priority of R&D and policy is, itself, complex. There are no easy answers. A simple calculation of DALYs will not suffice because a DALY calculation cannot account for the probabilities of an intervention actually being undertaken in the way modelled by the computation. What about changes in the epidemiology of diseases caused by extraneous factors, e.g. general economic development? An estimation of the potential future cost of a vaccine cannot account fully for rapid changes in technology or for the arrival of a new low cost manufacturer or for the interplay of intellectual property (IP) concerns. Pointing to the success of a model health delivery programme in one country does not ensure that the same model will work in other countries or even in other regions of the same country. What about changes in leadership, climate, road networks, education systems, and so on? Documenting one successful public-private collaboration in R&D probably does not mean that the same kind of collaboration will work for other companies and other public sector partners. What about changes in market priorities, research capabilities, level of scientific maturation of the field, regulatory issues and IP concerns?

Need for greater clarity

It is important to find a way to address this complexity. Despite the continuing dismay at the low level of resources for health compared with documented needs, it is clear that resources have been increasing over the last several years. New funds have been made available for: R&D such as for product development partnerships (PDPs) for AIDS, TB and malaria; procurement of needed antiretrovirals (ARVs), TB drugs, antimalarials and bednets; and programme delivery such as polio eradication. Even more exciting, it seems that the world's major countries are prepared to make available substantially increased funding for health in developing countries. The International Finance Facility (IFF) is only one of the most promising new ideas. It could result in the availability of billions of dollars of new resources for health in developing countries. There are several developing countries – Innovative Developing Countries – that are rapidly gaining the ability to innovate in health.[1] These countries include Brazil, China and India.

Thus, we are at an important crossroads in global health. Will we have the wisdom and foresight to develop rational

priority-setting systems that will help guide the effective allocation and deployment of these new resources? Failure to do so could be catastrophic. Prime ministers and ministers of finance may conclude that health is a black hole into which money can flow endlessly with no measurable impact, or worse, with a few things getting better while others get substantially worse. Or less dramatically, will those who hold the purse strings be faced with a squabbling global health community unable to articulate a clear vision of the future or how to achieve it?

A possible source of clarity

What do we do in the face of open and vocal disagreement about resource allocation, an inability to grasp the complexities of global health and the opportunity for new resources? As is often the case, it may be worthwhile to look to at other disciplines for answers. In the 1970s, Japan emerged as a major economic and technological powerhouse that overtook many other developed countries in the global economic scene. Leaders in developed countries appreciated the need to understand this new innovative capability of Japan and provided funding to a number of industrial and development economists, social scientists, and individuals who study the evolution of science and technology to try to figure out what was going on. The goal of these leaders was to find new ways to address the need to compete in a rapidly changing world where science and technology and economic policy were critical. Perhaps the foremost thinker in the work that followed was Chris Freeman of the Science and Technology Policy Research Unit at the University of Sussex, who coined the term 'national system of innovation'.[2] Freeman's work catalysed a whole field that has now become more generally known as 'systems of innovation'.

Studies on systems of innovation[3] show that there are certain essential elements for success in innovation including the development of networks of institutions concerned with various determinants of innovation so that appropriate attention can be paid to each of the determinants. A second insight is that innovation is not a linear process proceeding, in the case of health, from laboratory bench to bedside, but rather is a complex three-dimensional system where there are frequent feedback loops, failure, and unexpected sources of progress.[4] A third insight obtained from innovation studies is the centrality of private companies – firms. In market economies, virtually all products, and certainly most vaccines and drugs, are produced and sold by for-profit companies. An essential element of success for PDPs is this understanding of the centrality of firms in innovation. In sum, the major contributions from innovation studies are a more sophisticated understanding of the roles of: networks; complexity; and firms. The study of systems of innovation teaches that only by understanding the requirements for networks, for managing complexity, and for working with firms is it possible to understand how to develop, introduce, and deliver effectively existing and new health technologies for the poor. For an excellent recent review, see Dantas (2005).[5]

The three components of innovation systems

Networks: The development of health technologies requires effective collaborative networks among laboratory scientists, clinical investigators, production scale up specialists, health systems specialists, health systems professionals, IP managers, regulatory experts and many other professionals. These individuals are never found in one organization, but rather in various organizations in both the public and private sectors. In order to bring a product to those who need it, it is essential to build functioning networks linking each of these organizations and areas of expertise. For example, products must be designed and tested from the earliest stages of development with the needs of regulatory authorities in mind and this requires networking of diverse kinds of expertise. Intellectual property management requires additional networking. A product will not be used if it is not bought by someone. Therefore, it is essential to include future purchasers – global funds, national governments, hospitals and the private sector – in planning for the use of new or existing technologies.

Complexity: Innovation systems studies have identified the need to deal with the issue of complexity discussed above. Innovation systems studies have documented that it is not possible to predict with any level of certainty the development path that a product will follow from conception to wide scale use. For health technologies it is clear that there will be multiple failures along the development and introduction pathway requiring a return to the laboratory, or to the clinic, or to the prototype production facility, or to the policy think tank for further refinement and improvement. For example, it is not possible to predict with any level of certainty the IP that a developer will have to use from the beginning to bring a product to users. In almost every instance the lead product developer will find the need to obtain rights to new IP during the development process and may also find that IP that appeared to be of value early on is no longer of value. Another element of complexity is that IP is not simply patents. It includes trademarks, clinical data, trade secrets and know-how. Therefore the space of IP management is extraordinarily complex and requires professional input of a very high calibre. Unfortunately the public sector has not developed or employed such individuals on a routine basis. There is a tremendous need for capacity building and for identification of best practices to ensure that inventions arising from public institutions that are relevant to global health are developed in a way that ensures they can reach people in developing countries who need them most. The Centre for Management of IP in Health R&D (MIHR) is seeking to address this need.

The Firm: Within the last 20 years the public sector has

		R&D	National distribution systems	International distribution systems	Manufacture to high standards	IP management	Regulatory
Stage I:	Public						
Early product development	Private						
Stage II:	Public						
Phase 1–3 trials to licensure	Private						
Stage III: Introduction and	Public						
post-introduction	Private						

Table 1: Framework for innovation for a PDP (Product Development Partnership)

clearly identified the need to develop new health technologies to address the problems of the poor in developing countries. It has recognized, in addition, that the only way it can succeed in bringing products to the marketplace is to work with private sector, i.e. firms. In market economies, firms seek to obtain a return on investment for those who take risks by investing in those companies. Investors look for various ways to minimize risk and to maximise return on investment. Thus whether there is a concern with R&D or with policy, it is necessary to be concerned with the role that firms play in development, manufacture and distribution of health technologies.

Determinants of innovation

The teachings of innovation systems studies are of great value and need to be applied to health. We have developed a framework that could be of use in seeking to deal with issues of networking, complexity and the role of the firm (Table 1). First, we define a determinant of innovation: A field of endeavour that comprises a distinct and definable set of skills and resources necessary, but not sufficient for health innovation. In family planning, a determinant of fertility is female literacy. The more education a woman has, the fewer children she is likely to have. Governments seeking to reduce population growth can help achieve their goal by increasing education for girls and young women. But a focus on female literacy alone will not be successful in reducing fertility. For innovation in health, we identify the six determinants:

- R&D in the public and private sectors.
- Ability to manufacture new health technology products to high standards.
- National distribution systems in both the public and private sectors.
- International distribution systems including supply through international organizations such as UNICEF, the operation of global funds and trade among countries.
- Systems to manage IP for countries and organizations.
- Systems for drug and vaccine regulation to achieve safety and efficacy.

From the innovation literature, we find that determinants of innovation are dynamically linked.[6] Progress overall requires progress in each determinant. For example, a programme that narrowly focuses on R&D of a new vaccine without also paying attention to how the product will be used in individual developing countries is unlikely to succeed. The relative emphasis accorded to each determinant will vary by programme, country, or organization, but each determinant must be considered.

We propose that these six determinants are inclusive, i.e. they span all of the determinants that are involved in health innovation. If a programme effectively addresses all six determinants, it is very likely to succeed. More important, if it fails to address one or more of the determinants, it is extremely likely to fail.

The six determinants are the key elements of building or implementing any programme related to health innovation.

- A programme concerned with capacity building in health should take into account all six determinants. What new capabilities are required in R&D, domestic distribution, international supply, manufacture, managing IP and working through the regulatory requirements?
- A mid-sized developing country wishing to introduce a new antiretroviral for AIDS will want to address each of these questions. What kind of monitoring will be required (a research question)? How big is the local need? Where to buy or obtain the product from? What are the IP and regulatory issues?
- A PDP focused on new drugs against TB will have to address each of the determinants. Such a plan is clearly laid out by the TB Alliance (www.tballiance.org). In particular, the PDP will have to sort out how it will work with private companies with respect to each of the determinants – that is why PDPs have often been called public-private partnerships. Table 1 illustrates the framework for PDPs.
- A country seeking to develop a comprehensive policy for financing health innovation will have to address each determinant. How much should be allocated for R&D? How much for promoting a national distribution? How much for regulatory oversight?

A unifying framework

We see the old argument in which the 'R&D crowd' and the 'policy crowd' face off against each other as representing incomplete and counterproductive views of the world. R&D is only one determinant of innovation. Developing national health delivery systems is also only one determinant. Both groups should begin to discuss how best to allocate limited,

but hopefully growing resources among six determinants of innovation that are dynamically linked. If they have not filled in all of the cells of Table 1, they have not done a complete job of assessing the challenges of improving health.

Only by addressing all six determinants of innovation in a mutually supportive way can we effectively address the components of innovation: complexity, networking, and the role of the firm. We are all part of a system of innovation. To the extent we set up false trade-offs, we only detract from achieving our goals.

Health is too important to be held back by parochial views of the world. We need a unifying framework around which all can rally and thereby work toward a common purpose. ❑

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The critical role of genomics in global health



Article by Peter A Singer (pictured), Archana Bhatt, Sarah Frew, Heather Greenwood, Deepa L Persad, Fabio Salamanca-Buentello, Béatrice Séguin, Andrew D Taylor, Halla Thorsteinsdóttir, Abdallah S Daar

Innovation in science and technology has significantly contributed to medical advances and has consequently had a large impact on public health. The benefits of this progress, however, have yet to be equally shared globally. Millions of people in developing countries continue to face health challenges that no longer burden the industrialized world. With pandemics such as HIV/AIDS plaguing countries in sub-Saharan Africa, life expectancies in this region are 40 years and falling – nearly half of those in developed countries. This immense disparity in global health equity is perhaps the greatest ethical challenge of our time.[1] To help address this challenge, the Canadian Program on Genomics and Global Health, based at the University of Toronto, has identified three overarching questions:

- Which genomics-related technologies are most likely to improve the health of people in developing countries?
- How can developing countries harness these technologies for health development?
- What can industrialized countries do to assist developing countries?

The goal of addressing these questions is to strengthen the critical role of genomics in global health.

The potential contribution of genomics to the United Nations MDGs

The causes of global health inequities are complex and have received renewed international focus as a result of the United Nations (UN) Millennium Development Goals (MDGs). As part of a year 2000 commitment to reduce poverty and strengthen sustainable development, all UN members adopted the MDGs and established task forces to assist developing countries in achieving them. The recent report from the Task Force on Science, Technology and Innovation (Task Force 10) titled, *Innovation: Applying Knowledge in Development*, has stressed that one key underlying factor of global health inequity is knowledge, particularly of science and technology. UN Secretary General Kofi Annan supports this view and has stated that: 'no nation can afford to be without its own (science and technology) capacity.'

One tool in the science and technology toolkit is the field of genomics, or the powerful new wave of health-related life sciences energized by the human genome project and the knowledge and tools it is spawning. In 2001, the Canadian Program on Genomics and Global Health conducted a foresight exercise to demonstrate the role that genomics and biotechnology can play in global health entitled, *Top 10 Biotechnologies for Improving Health in Developing Countries*. The study identified the primary genomics-related biotechnologies that can help reduce disparities in global health equity. The top three rankings were: molecular diagnostics; recombinant vaccines; and vaccine and drug delivery.[2]

In our role as the Genomics Working Group of Task Force 10, we responded to recent international attention on global health with our report, *Genomics and Global Health*. The report maps the top ten biotechnologies identified in our foresight exercise against the MDGs, to demonstrate the potential utility of genomics-related technologies in meeting some of these goals, namely: promote gender equality and empower women; reduce child mortality; improve maternal health; combat HIV, malaria and other diseases; and ensure environmental sustainability.[3] A complete table of these goals and the corresponding genomic technologies can be found in Table 1.

What industrialized countries can do to assist

One of the major conclusions of the *Genomics and Global Health* report encourages the creation of a Global Genomics Initiative (GGI). With strong representation from the developing world in a partnership between industry leaders, citizens, academics, non-governmental organizations and government officials, the network could serve as a governance mechanism at the global level to ensure the effective application of genomics to worldwide challenges.[4] Consequently, this global network initiative could share and promote the health and environmental benefits being created through genomics-related technologies worldwide, potentially contributing significantly to improving health and development outcomes in developing countries.

The formation of a GGI could also promote partnerships between industrialized countries and the developing world. We are currently exploring the extent to which Canadian

MDG	Statistics/Facts	Biotechnology to Address MDG
Goal 3: Promote gender equality and empower women	In 2001, 57% of HIV cases in sub-Saharan Africa were women. Average HIV infection rates in teenage girls are five times higher than those in teenage boys	• Female control over STD transmission protection • Vaccine and drug delivery
Goal 4: Reduce child mortality	About 11 million children die before reaching their fifth birthday	• Molecular diagnostics • Vaccine and drug delivery • Recombinant vaccines • Female control over STD transmission protection • Nutritionally enriched GM crops • Combinatorial chemistry
Goal 5: Improve maternal health	Over 500,000 maternal deaths per year	• Molecular diagnostics • Vaccine and drug delivery • Recombinant vaccines • Female control over STD transmission protection • Nutritionally enriched GM crops • Combinatorial chemistry
Goal 6: Combat HIV, malaria, and other diseases	HIV/AIDS, malaria, and tuberculosis are responsible for more than 6 million deaths worldwide	• Molecular diagnostics • Vaccine and drug delivery • Recombinant vaccines • Female control over STD transmission protection • Bioremediation (using living organisms to degrade / transform hazardous organic contaminants) • Sequencing pathogen genomes • Bioinformatics • Enriched GM crops • Combinatorial chemistry
Goal 7: Ensure environmental sustainability	5 million deaths per year can be attributed to waterborne diseases	• Bioremediation

Source: Genomics and Global Health: A Report of the Science and Technology Task Force of the United Nations Millennium Project. Toronto: University of Toronto Press, 2004.

Table 1: Genomics and related technologies can support the MDGs

small- to medium-sized enterprises (SMEs) in the health and environmental biotechnology sectors create partnerships within developing countries. In particular, this research is focusing on the interlinking of two innovating firms through research, technology development and marketing partnerships (see Figure 1 for a diagram of the partnerships).

A global genomics network could also provide a forum for sharing good practices. In February 2004, Canadian Prime Minister Paul Martin stated that: 'our long-term goal as a country should be to devote no less than 5% of our research and development investment to a knowledge-based approach to develop assistance for less fortunate countries.' This remarkable commitment projects Canada as the first industrialised country to set a specific research and development target to address developing world challenges. The challenge now is to provide the policy research that will encourage other industrialized countries to follow Canada's example. For example, a 5% commitment by the European Union and the United States would result in an additional $9.3 billion and $14.1 billion devoted to developing country challenges, respectively.

The role of diasporas in a global economy was also recently highlighted by the UN Task Force on Science, Technology and Innovation. Given the diversity of Canada's immigrant population, particularly from the developing world, this country is fertile ground for studying diasporas. We are also currently exploring the role of diasporas in global partnerships to allow developing countries to benefit from their emigrant populations. Through an empirical qualitative study involving interviews with skilled Canadian professionals working in the life sciences who have immigrated from developing countries to Canada, we are aiming to understand how diasporas can contribute to science and technology innovation in their country of origin and other developing countries.

The role of developing countries in improving global health

The *Genomics and Global Health* report identified that developing countries must be key actors in using genomic-based technologies to address local health needs. We conducted a 3 year empirical case study of the health biotechnology innovation systems in seven developing countries that have built up capacity in the health biotechnology sector: Cuba, Brazil, South Africa, Egypt,

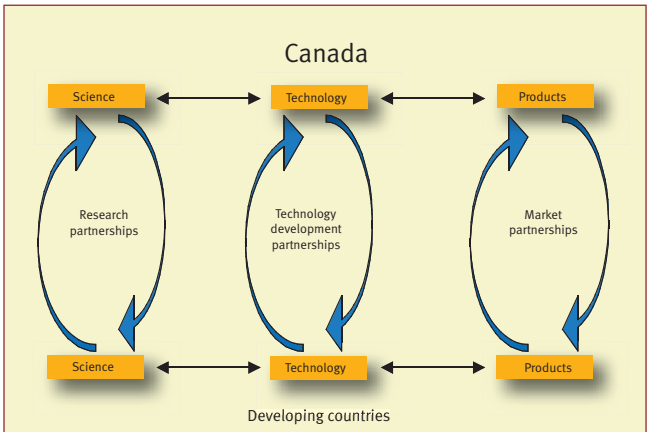


Figure 1: The fluid relationship between science, technology and products in Canada and developing countries

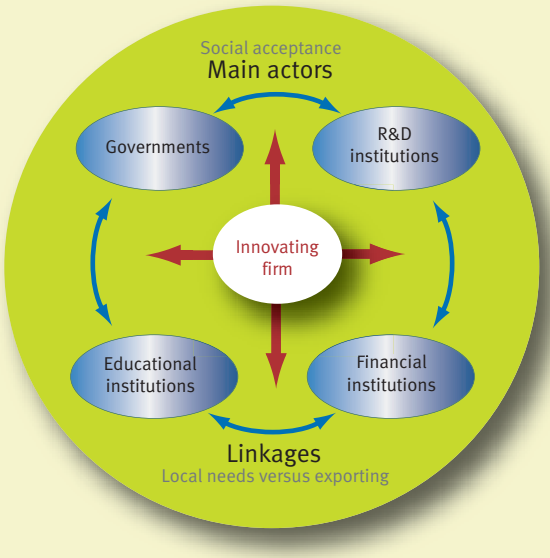
India, China and South Korea (refer to Figure 2 for a schematic model of the focus of our study – the roles of the main institutions in the innovation process). The results were published in a *Nature Biotechnology* supplement titled, *Health Biotechnology Innovation in Developing Countries*. As a result of this analysis, we identified lessons learned that might help other developing countries embark on fostering their own indigenous health biotechnology sector, and developed recommendations on how to harness genomics and biotechnology to develop local capacity and ultimately improve health in developing countries.

The study identified many key factors involved in each of the success stories, such as the focus on the use of biotechnology to meet local health needs (see Table 2 for a listing of the major findings). For instance, South Africa has prioritized research on HIV/AIDS, its largest health burden, and developments are underway for a vaccine against the strain most prevalent in the country. Egypt is responding to its insulin shortage by focusing its research and development efforts on the drug. Cuba developed the world's only meningitis B vaccine as a response to a national outbreak, and India has reduced the cost of its recombinant hepatitis B vaccine to well below that in the developed world. Publications on health research in each of these countries follow the same trend of focusing on local health needs.

Political will is another important factor for establishing a successful health biotechnology sector, as long term government support was integral in all seven case studies. In efforts to promote development of healthcare biotechnology, governments have developed specific polices, provided funding and recognition for the importance of research, responded to the ongoing challenges of brain drain and provided biotechnology enterprises with incentives to overcome problematic economic conditions. Close linkages and active knowledge flows are imperative as well. Where in some countries (such as Cuba) strong collaboration and linkages yielded successful health biotechnology innovation, lack of these factors in other countries like China, Brazil and Egypt have partially diminished innovation efforts. Many of the countries have begun to actively encourage close collaboration and linkages to further develop national science and technology innovation. Defining niche areas, such as preventative vaccines, emerged as another key factor in establishing a successful health biotechnology sector. Some countries have also relied on their competitive advantages such as South Korea's focus on bioinformatics to capitalize on its extensive knowledge in information technology.

Our study identified private sector development as essential for the translation of health biotechnology knowledge into products and services. South Korea significantly surpassed all other countries in this respect, with policies in place to assist technology transfer and allow university professors to create private firms. China has also promoted enterprise formation, converting existing research institutions into companies. To further explore the role of the private sector, we are conducting research that examines how the domestic health technology sector in developing countries contributes to addressing local health needs, and what policies or practices could make that contribution more effective as private sector development has the potential to improve both health and economic performance. Together, this research can be used to provide heads of state and science ministers in developing countries with specific guidance and good practices for implementing innovation policies that utilize the strengths of both the public and private sectors in developing and implementing health technology to address local health needs.

The recent UN Commission on Private Sector and



Source: Thorsteinsdóttir H, Quach U, Martin D, Daar AS, and Singer PA. Promoting global health through biotechnology: An exploration of health biotechnology innovation systems in developing countries. Nature Biotechnology 2004; 22: DC3-DC7.

Figure 2: Schematic model of the roles of the main institutions in the innovation process

Brazil
- Focus on developing a strong science capacity
- Promote linkages and exploit existing strengths in disparate fields
- Exploit local biodiversity for health
- Gain access to key actors

China
- Provide long-term government support
- Attract expatriate professionals
- Ensure that biotechnology development goes hand-in-hand with regulation
- Leverage large population base

Cuba
- Ensure long-term governmental vision and policy coherence
- Promote domestic integration to spur innovation
- Capitalize on international linkages
- Tap into national pride

Egypt
- Focus on health needs
- Gain access to key actors
- Take advantage of international linkages

India
- Leverage strengths when cultivating linkages
- Meet international standards
- Use competitive advantage
- Pay attention to the regulatory environment

South Africa
- Focus government policy on public health needs
- Exploit both indigenous knowledge and science-based innovations
- Develop local R&D infrastructure for self-reliance

South Korea
- Create a mix of small and large firms
- Exploit existing competitive advantages
- Go global

Source: Thorsteinsdóttir H, Quach U, Martin D, Daar AS, and Singer PA. Conclusions: promoting biotechnology innovation in developing countries. Nature Biotechnology 2004; 22: DC48-DC52.

Table 2: Lessons learned from case studies

Development, chaired by Paul Martin and Ernesto Zedillo, emphasized the important role of the domestic private sector in order for developing countries to progress. In their 2004 report, *Unleashing Entrepreneurship, Making Business Work for the Poor*, the Commission highlighted how the managerial, organizational and technological innovation in the private sector, particularly the small and medium enterprise segment, can improve the lives of the poor by empowering citizens and contributing to economic growth. The work of the UN Commission also emphasized the lack of knowledge about best practices, and the need for more sustained research and analysis of what works and what does not when attempting to harness the capabilities of the private sector in support of development.

Conclusion: the role of science and technology in global health equity

Genomics-related technologies have the potential to improve the health of millions of the world's poor, and as such play a significant role in reducing the global health equity gap.

However, a view that extends beyond genomics and biotechnology is required in order to truly harness the potential of science and technology to improve global health. Other fields such as nanotechnology and regenerative medicine can also have a large impact on increasing global access to health care. Nanotechnology, for example, currently offers a cheap alternative to current diagnostic tests through the lab-on-a-chip, a microfluid device that can test for numerous diseases at a time.[5] Regenerative medicine also has tremendous therapeutic potential: autologous bone marrow stem cells are currently being tested in patients for treatment of heart disease,[6] a promising development in light of the dramatic increase in levels of cardiovascular disease in developing countries.[7] The benefits of genomics and biotechnology are already being felt in developing countries. As we have illustrated with genomics and biotechnology, discussions of global health equity should extend to other areas in science and technology in order to harness their potential for improving health in the developing world. ❑

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Pharmacogenetics and geographical ancestry: implications for drug development and global health



Article by Abdallah S Daar (pictured) and Peter A Singer

Genomic variation will contribute significantly to improving the health of people in developing countries. We need to explore the nexus between pharmacogenetics, genotyping projects in developing countries, and the evolution of the pharmaceutical industry in both the developed and developing worlds. Here, we argue that, for the foreseeable future, we should focus not on boutique 'personalized' medicine, but on carefully defined differences between populations and ethical ways of using emerging genomics knowledge to develop drugs and improve health.

On 30 September 2004, Merck announced the worldwide withdrawal of Vioxx (rofecoxib), a multi-billion-dollar blockbuster analgesic drug, because of cardiovascular complications in those who took it for more than 18 months. It was the biggest ever withdrawal of a prescription medicine in the United States and wiped US$26.8 billion off Merck's market value that day. Was the worldwide withdrawal necessary? Or could Vioxx be resuscitated for selected populations?

Suppose that Merck had data to show that it was only individuals of north European ancestry who were affected by the adverse effects. Theoretically, Merck could still market Vioxx, with adequate warning labels to alert those people who were likely to be affected. Imagine that Vioxx was not just another analgesic, but for example, a powerful antiretroviral or another life-saving drug that was needed by, but unaffordable to, people in developing countries. Even if the drug was safe only for Indians and Han Chinese, that would constitute a market of over 2 billion people. Merck could license Indian and Chinese companies to manufacture such a drug for their own local markets. Merck's loss would be mitigated and pharmaceutical companies and patients in the developing world would benefit.

The completion of a good quality draft of the sequence of the euchromatic portion of the human genome was accompanied by a commentary in *Nature* in which the future of genomics was compared to a house.[1] The question we ask here is: who will live in that house? Is it only the 700 million or so people in the United States and Western Europe, or will the rest of the 6 billion people who live mainly in the developing world also be able to find room there? In this article we make two related arguments: first, that pharmacogenetics has significant relevance to the health of people in developing countries; and second, that for this benefit to be realized, we need to take into account not just differences between the genotypes of individuals, important as they are, but the differences in genotypes between different population groups.

We begin by identifying examples of how emerging knowledge about genetic and/or genomic variation is beginning to affect the pharmaceutical industry, and how pharmacogenetic strategies can be used to increase efficiency, cut costs, reduce adverse effects and increase the efficacy of drug-development pipelines. We document the trend towards using population-group genotypes in drug development and regulation, and discuss the implications of genetic differences that underlie variation in drug responses and disease susceptibility between population groups. We highlight emerging genotyping studies that are being undertaken in various regions of the developing world, and, if the vision materializes fully, the possible role of haplotype mapping in simplifying and reducing the cost of genotyping populations, potentially helping developing countries to benefit from knowledge of genetic diversity between populations. Finally, we explore how developing countries specifically will benefit from these new trends. We argue that pharmaceutical companies in developing countries will be able to harness pharmacogenetic principles and the knowledge of local genotype patterns to stimulate their industries, cut costs and generally improve the health of their populations.

Emerging industry trends

Pharmacogenetics itself is not a new discipline – it has been around for about 50 years (Box 1).[2] What is new is that advances in genomics, particularly in methodology, have allowed us to merge pharmacogenetics with pharmacogenomics, improving our ability to identify the genetic causes of diseases and search for new drug targets. Today, several major pharmaceutical companies have teams that focus their research on the intersection between genetics, genomics and drug development, and some are already beginning to take genomic variation into account in

their drug-development pipelines. Although the idea of focusing clinical trials on subgroups of individuals is not new – stratification by disease subtype has always been a goal of medical research – the use of genetics in this context is new.[3]

Pharmacogenetics has so far had little impact on healthcare in general, or on the pharmaceutical industry in particular. This is partly because pharmacogenetics has been thought of mainly as having boutique-style 'personal' applications that are unlikely to be relevant to the majority of people, particularly those in developing countries. We believe that this is about to change both with the adoption of pharmacogenetics per se, and because genetic differences between population groups – in addition to differences between individuals – will be taken into account. The stimulus for the adoption of these complementary emerging trends in the developed world, and particularly in the United States, will come from regulatory changes, litigation and patient demand based on accumulating scientific evidence of the validity of the pharmacogenetics approach (see the BiDil example below). In addition, there will always be market-based incentives if entrepreneurs identify an opportunity.[4]

The role of regulation in driving pharmacogenetics is best demonstrated by the recent actions of the United States Food and Drug Administration (FDA). The FDA has become a proactive advocate of pharmacogenetics and pharmacogenomics.[5] A few years ago it approved alosetron hydrochloride (Lotronex, GlaxoSmithKline) for irritable bowel syndrome, but the drug was quickly withdrawn voluntarily by GlaxoSmithKline because of adverse reactions. However, because of its efficacy, patients and physicians fought for Lotronex's return, and it was reapproved by the FDA in 2002 under restricted market terms. Now GlaxoSmithKline is studying the relationship between adverse events and genetic profiles as part of FDA-imposed post-marketing commitments.[6]

In January 2003, the FDA called for greater scrutiny of data from subpopulations, asking drug testers to use the racial categories specified by the Census Bureau, to ensure consistency when evaluating potential differences in responses to drugs.[7] This is illustrated by a compelling example: a few years ago, the FDA rejected a fixed-dose combination of isosorbide dinitrate and hydralazine (now known as BiDil, NitroMed) because its efficacy in treating heart failure could not be demonstrated statistically in a clinical trial in the general population.[8] When it was tested exclusively in 1,050 self-identified African-American patients who had experienced heart failure,[9] the results of this double-blind, randomized clinical trial were so impressive that in July 2004 the trial (which was endorsed by the Association of Black Cardiologists) had to be stopped for ethical reasons; there was a significantly higher mortality rate in the placebo group than in the group given BiDil.[10] BiDil is now expected to be approved by the FDA in early 2005, as the first ever 'race-specific' therapy.[11]

The role that litigation might play in driving the adoption of pharmacogenetics is illustrated by the Cassidy versus SmithKline Beecham case. This Pennsylvania class action suite alleged that SmithKline Beecham failed to warn doctors and the public that its vaccine against Lyme disease could trigger immune arthritis – an untreatable degenerative disease – in people who carry the HLA DR4+ marker, nearly a third of the United States population. Although both pre-marketing and post-marketing analyses by federal agencies have failed to confirm any increased risk from the vaccine, it was removed from the market in February 2002 as a result of plummeting sales that probably resulted from the controversy that surrounded the lawsuits.[12]

A number of pharmaceutical, biotechnology and genomics companies are now turning to pharmacogenetics in their 'personalized' medicine programmes, which are most relevant for the wealthy in the developed world. Some companies are prospectively collecting and analysing samples from clinical trials to identify predictive SNPs. However, they are having difficulty in obtaining phenotypic data (for example, that relates to adverse effects) to link to information from DNA samples, and some companies are now working with the FDA to develop appropriate data-mining tools for clinical trial data. In the long term, it is perhaps more relevant to people in developing countries that pharmaceutical companies are on the lookout for genetic subgroups that could identify new targets for therapeutic drugs. Pfizer, for example, is particularly interested in hypertension-related genes in African Americans, and in diabetes-related genes that could account for the high rates of the disease in both Asian Indians and Native Americans. AstraZeneca is also looking for population differences in drug response in its clinical trials. If a drug were found to have a 'profound effect' on a particular subpopulation, AstraZeneca would label and promote it accordingly, and 'if a population doesn't benefit, that could end up on the label too'.[13]

Ancestry and phenotypic differences

Studies in population genetics have revealed a great deal of genetic variation within racial or ethnic subpopulations, but also substantial variation between the five main racial groups, which are based on continental ancestry. This variation has been demonstrated in three ways[14]: first, ancestral tree diagrams carried out using population genetic data from indigenous groups consistently show that Homo sapiens have major branches that correspond to the five main groups. Second, clusters that have recently been inferred from multilocus genetic data and other studies coincide closely with groups that are defined by self-identified race or continental ancestry.[15,16] Third, low-frequency alleles are more likely to be race specific. Race-specific variants are particularly common among Africans, who have greater genetic variability than other racial groups, but more low-frequency alleles.[14] For observed phenotypic differences, self-identified race and continental ancestry often have relatively high predictive power compared to self-identified ethnicity. It is therefore likely that racial or

ethnic categories will continue to be useful as long as such categorization 'explains' variation that is left unexplained by other factors.[15]

We must, however, be cautious as to how the results of such studies are interpreted and used.[17] We need a detailed understanding of each of the racial groups that are chosen for study, because the races that comprise the human species are far more heterogeneous than was previously thought. For example, individuals living in sub-Saharan rural Africa have close to 100% of what are called African alleles, whereas African Americans living in the United States show about 26% Caucasian admixture.[18] Some groups (for example, African-American, Caribbean and Panamanian populations) are likely to show a large degree of allelic diversity, whereas other groups (for example, sub-Saharan Africans, Inuits and Finns) are less genetically diverse. Old Amish individuals share more alleles than do individuals in other populations because they marry within their own community and as a result have a higher-than- average incidence of inborn errors of metabolism,[19] as do some Arab consanguineous communities. Due to founder effects and enforced segregation, Ashkenazi Jews also share a large number of alleles.

A recent meta-analysis by Ioannidis et al. showed that genetic variants that are associated with disease predisposition might often have similar effects across racial groups.[20] However, in an accompanying commentary, Goldstein and Hirschhorn[21] point out that meta-analytic studies of this type are plagued by methodological concerns, and that the results presented by Ioannidis et al. do not mean that people from different parts of the world will, on average, have the same genetic predispositions to disease and will respond to medicines in the same way. It is well known that allele frequencies of functional variants often differ substantially among groups that have different geographic ancestries. For example, of 38 polymorphisms that have been associated in at least two studies with a given drug response,[22] two-thirds have significant allele-frequency differences between African Americans and Europeans, and many of the differences are substantial (see Box 1).

Box 1 | Drug response variation among individuals and populations

During the past 50 years of pharmacogenetic research,[42] we have learnt that variation between individuals that is influenced by genes and other factors is relevant to the efficacy of all drugs. We now know that metabolic enzymes are affected not only by SNPs (of which the human genome contains more than 10 million), but also by other genomic variation, such as gene duplications and deletions, mutations in regulatory genes, and probably by recently described large-scale copy number variations.[43,44] Increasing numbers of relevant polymorphisms are being discovered. Most relevant to our discussion, we also know that the frequencies and distributions of harmful and protective polymorphisms vary greatly between human populations.[22,34,35]

Given all of the above, it is valid to study traits that are predominantly expressed in specific populations.[46] Such studies might provide a molecular basis for population differences in drug-metabolizing enzymes (for example, cytochrome P450,[47,48] sulfotransferases[49,50] and methyltransferases,[51] transporters (such as ABC1)[34,52], receptors (such as adrenergic receptors)[3,47] and other factors that are involved in differential drug responses and disease susceptibility. Many of the population-group differences that are documented are likely to have important medical and public health implications.[10,53,55]

Genotyping in developing countries

Although it is true that many developing countries are beset by poverty, a lack of clean water, diseases that are difficult to control, illiteracy and poor governance, it can be argued that they are the ones most in need of emerging scientific and technological knowledge that might ameliorate their situations, by reducing costs and the adverse effects of drugs. At present, drugs that are tested on general populations in Europe and North America, and that are sometimes licensed on the basis of efficacy in only 30% of the subjects, are sold in developing countries without any idea of how effective or safe they are, and certainly without any regard for the local frequencies of genomic markers.

Therefore, it is not surprising that several developing countries are starting their own genotyping projects. For example, India and Thailand are both embarking on SNP-genotyping studies. Hosted by the Genome Institute of Singapore, an important regional initiative has recently brought scientists from China, India, Indonesia, Japan, Korea, Malaysia, Nepal, the Philippines, Singapore, Thailand and Taiwan to establish the Human Genome Organization (HUGO) Pacific Pan-Asian SNP Initiative, which is expected to begin in the middle of 2005. The goal of this initiative is to uncover the breadth of genetic diversity and the extent of genetic similarity within Asian populations. This information will form the basis for future studies in genomic medicine focused on Asian populations. Data from the Pan-Asian study will provide a platform for researchers in Asia to study why some populations seem predisposed to certain diseases, or do not respond to certain drugs. Cost reductions and new technologies are opening up the study to all researchers, including those with less well-developed research infrastructures.

Asia is not alone in such initiatives. Mexico has a newly-created, well-funded, federally-mandated Institute of Genomic Medicine, headed by Gerardo Jimenez-Sanchez.[23] Genotyping the Mexican populations is one of its top priorities.

Haplotype mapping

The relatively recent discovery of the haplotype structure of the human genome, and the effect that this has on SNP

inheritance, could help to simplify and reduce the cost of genotyping. When the International HapMap project is completed it might be possible to use just 300,000–600,000 tag SNPs to define the most significant genetic variation. Genotyping just a handful of these carefully chosen SNPs in a chromosomal region may be enough to predict the remainder of the nearby common SNPs.[24]

The HapMap itself does not define the genetic diversity of subgroups, but provides a useful framework to facilitate this. It will provide a resource, but not all of the answers. A cutting-edge example of the use of haplotype mapping to understand an association between complex disease and genetics is the work of the International Multiple Sclerosis Genetic Consortium (IMSGC). This example is relevant to our discussion of the value of genotyping for understanding diseases of subpopulations that have geographical ancestry in developing countries. Recognizing that multiple sclerosis (MS) is a complex genetic disorder, the IMSGC is setting out to define the most significant genetic variation that is associated with MS. By making use of the economic advantages that are provided by the emerging HapMap, as well as the falling costs of genotyping, the IMSGC expects to be able to cover the entire genome at high resolution.[25] The consortium is also taking advantage of the observation that some groups are more prone to MS than others. It has long been known that African Americans have half the risk of developing classical MS compared with European Caucasians, and that sub-Saharan Africans rarely suffer from this condition. Providing that environmental influence is discounted, this indicates that it is the genetic contribution of Caucasians in African Americans that is responsible for the higher risk of MS in African Americans than in sub-Saharan Africans. By studying African Americans who have MS and identifying the genetic components that they have inherited from their European ancestors, the IMSGC hopes to identify regions of the genome that carry MS-susceptibility genes.

Through its value in drug development and its identification of populations that will respond favourably to a particular drug, pharmacogenetics will probably have an impact on global health, especially on neglected infectious diseases such as malaria, tuberculosis and HIV/AIDS.[26] In the section below, we focus on specific ways in which drug development in, and for, developing countries will benefit from the recent trends discussed above.

Opportunities for developing countries

Only 16 of the 1,393 new drugs that were marketed between 1975 and 1999 were registered for diseases that predominantly affect people in developing countries, and three of those were for tuberculosis, which is not restricted to developing countries.[27] In the future, pharmaceutical companies in the developed world will have to pay more attention to developing countries. There are at least two trends that will drive this change.

First, there is the need to gain deeper insight into the genetic basis for variable drug responses. As demand for drugs that are tailored to specific genotypes increases, pharmaceutical companies will increasingly depend on selling their products to segmented markets. Therefore, a deeper knowledge and cultivation of a wider and more extensive market outside North America and Europe will eventually be very important to them. If done correctly, this will in turn benefit people in developing countries. For pharmaceutical companies worldwide, developing countries are not only potentially huge markets for drug therapeutics, but are also depositories of important human genetic diversity. Understanding this diversity is valuable because it better defines those population subgroups that will benefit more from a particular drug than others, and allows the detection of side-effects that might not be seen in populations that are mainly Caucasian. It can also help to ascertain disease predisposition. It will therefore be increasingly important to include non-Caucasian populations in clinical trials. The interest by Pfizer and AstraZeneca in the genetics of African- American and Asian-Indian subgroups living in the United States to help to identify drug targets will probably not be adequate to satisfy the need for harnessing global genetic diversity. Genotyping studies of various populations from around the world will therefore become valuable.

As demand for drugs that are tailored to specific genotypes increases, pharmaceutical companies will increasingly depend on selling their products to segmented markets. Therefore a deeper knowledge of a wider market outside North America and Europe will become important to them

Second, pharmaceutical companies in developing countries are themselves poised to make significant gains on the global market.[28] Big pharmaceutical companies can choose to view them as rivals to be thwarted or, alternatively, as companies with which to form mutually-beneficial partnerships. For pharmaceutical companies in developing countries, pharmacogenetics might present an opportunity, especially if they learn to harness our increasing knowledge of the link between population genomic variation and health. It is true that internal economics limit the ability of many developing countries to capitalize on their genetic configurations. However, it could well be argued that, with annual per capita healthcare expenditures as low as US$10–15, developing countries are the ones that have the greatest need of more cost effective healthcare strategies. This will enable these countries to not waste drugs on people who will not respond or who will be harmed, and to understand the genetic basis of disease predisposition, particularly of those diseases such as HIV/AIDS, which disproportionately affect people in developing countries and impose enormous burdens on their societies.

Although medical exploration in developing countries can expand the genetic diversity of people who take part in clinical trials that lead to drug development, pharmaceutical companies that attempt to harness this valuable genomic resource will not succeed unless they work closely with the authorities in developing countries, they act ethically, they are willing to share benefits, and they form partnerships with local researchers and local pharmaceutical companies. Developing countries will not cooperate if they feel that the benefits will go to others and that they are being used merely as instruments to that end. Clearly, the populations studied will also need to consent.

Drug resuscitation

In a recent review, Allen Roses described the potential useful applications of prospective efficacy and risk pharmacogenetics for drug development pipelines.[29] He observed that new drugs that are withdrawn for safety reasons (and, by extension, for their lack of efficacy) in phase IIA clinical trials by commercially-driven pharmaceutical companies will probably not be used for other segments of the population, because they would no longer be protected by patents. This might be the case for big pharmaceutical companies in the developed world, but it does represent an opportunity for pharmaceutical companies in developing countries to license these compounds and develop them, both for their local populations and for other people in the developing world who are either not genetically predisposed to the adverse effects or for whom efficacy can be demonstrated to a greater extent. This idea of 'resuscitation' of useful drugs for different populations is also, of course, applicable to post-marketing drug withdrawals, as we proposed for Vioxx.

Another example is fosmidomycin, which is a natural antibiotic that was originally developed in the 1970s for bacterial infections, but was not commercially developed by its Japanese owners

Indeed, it may now be time for incentives to be developed for just such drug resuscitations, perhaps in the form of public-private partnerships. Examples of drugs that have not been developed commercially in developed countries, but that are useful in developing countries include ivermectin, which has been given as a gift by Merck to patients in the developing world who are suffering from onchocerciasis (see online link The Story of Mectizan). Another example is fosmidomycin, which is a natural antibiotic that was originally developed in the 1970s for bacterial infections, but that was not commercially developed by its Japanese owners, the Fujisawa Pharmaceutical Company. In the late 1990s, a potential target for fosmidomycin was identified in the partial genome sequence of the malaria parasite.[30] Tests on mouse malaria confirmed the high level of efficacy of this drug, and fosmidomycin was rapidly tested in humans in Gabon. It has since been developed at very low cost, and is now part of the limited anti-malarial armamentarium that is at our disposal.[31] A very relevant example that is based on pharmacogenetics and geographical ancestry is BiDil. BiDil could have been discarded because it did not have demonstrable efficacy when tested on a mixed population of patients in the United States. However, having been tested specifically on African Americans, it has been resuscitated for that population, and is obviously now of interest to Africans who share their geographical ancestry with African Americans.

The increasing numbers of public-private partnerships that are dedicated to finding treatments for major diseases of the poor, such as the Medicines for Malaria Venture, may contribute to this trend, as will the investment of US$275 million that the Bill and Melinda Gates Foundation has put into the Grand Challenges in Global Health programme.[32] The Institute for One World Health, a United States-based organization, aims to do something similar by identifying promising drug and vaccine candidates, developing them into safe, effective and affordable medicines, and then forming partnerships with companies and organizations in the developing world to manufacture and distribute them. The Drugs for Neglected Diseases Initiative is working along similar lines. Their models have not specifically taken into account genetic diversity, but with increasing knowledge, this might become a factor to consider in their surveys of drugs that are unlikely to be made commercial by big pharmaceutical companies.

Unexpected benefits

The compounds discovered in the research and development laboratories of developing countries may be of greater interest to big pharmaceutical companies if they can be tested in selected minority subpopulations in developed countries. For example, compounds that are found to be effective in Asian Indians in India might be of interest to United States pharmaceutical companies to market to the significant population of Asian Indians in the United States. Conversely, drugs developed by smaller companies in the developed world for their minority populations could become useful for people in developing countries: NitroMed, which developed BiDil for African-American patients, might want to partner pharmaceutical companies in developing countries to test and market the drug in sub-Saharan Africa.

The increasing numbers of drugs that will need to be tested clinically on segmented populations will put further pressure on the already grossly over-burdened capacity to perform clinical trials, particularly in the United States. The large number of clinical trials being carried out in the United States at any one time is already increasing pressure to test these drugs in developing countries.[33] This will drive the trend to partner with pharmaceutical companies and organizations that carry out contract research in developing countries. A

beneficial outcome of such partnerships will be that the drugs being tested might be marketed locally in developing countries in addition to the minority population of interest in the developed country. Furthermore, the results of clinical trials of drugs developed in the developed world and then tested on patients in developing countries will be more meaningful for those populations in developing countries in whom they were tested. Conversely, the results of clinical trials carried out specifically in minority new populations, such as the trial for BiDil tested on African Americans in the United States, will be more meaningful for patients in those developing countries from which the minorities originated.

The cost efficiency associated with the drug development strategy of prospective efficacy pharmacogenetics[29] will result in less expensive drugs for patients in developing countries. When drugs are prescribed to groups who are unlikely to enjoy any benefit (and may also suffer adverse effects), the national cost of healthcare is significantly higher than it need be otherwise. In Mexico, the doses of many drugs have to be altered significantly because they are either ineffective or too toxic at the levels recommended for the 'general' North American population. For example, L-asparaginase, an anti-cancer drug is given at lower doses in Mexico than in the United States to minimize toxicity (pancreatitis and/or hyperglycaemia). By contrast, doses of the anti-cancer drug 6-mercaptopurine that are toxic in the United States population produce less intense adverse effects in Mexican populations. So far, this is largely anecdotal, but the study of Mexican genomic diversity and its implications for public health is one of the priorities of the Mexican Institute of Genomic Medicine.[23]

Pharmacogenetics may also feature in post-marketing surveillance. For example, some sub-Saharan African populations have a polymorphism in the ABCB1 (ATP binding cassette, sub-family B [MDR/TAP], member 1) gene, which encodes the multidrug transporter P-glycoprotein, such that the carriers of this polymorphism might not benefit from antiretroviral therapy.[34] This finding might translate into closer scrutiny and early withdrawal of drugs that are found to be ineffective, saving many lives and millions of dollars. This will also stimulate the search for drugs that can bypass the effects of the polymorphism.

In terms of disease susceptibility, HIV demonstrates the importance of understanding genomic variation in human patients. A subpopulation of people with a 32-base pair deletion in the chemokine (C-C motif) receptor 5 (CCR5) gene (the CCR5-32 mutant allele) are sero-negative and healthy, despite repeated exposure to HIV1 infection, as the mutation prevents expression of the CCR5 receptor on cell surfaces, which HIV uses to gain entry through mucosal surfaces. Strategies are being pursued to reduce susceptibility to HIV infection by blocking the CCR5 receptor.[35] Recently, United States and Swiss researchers reported that coating the vaginal surfaces of macaque monkeys with an experimental drug that binds to CCR5 protects the monkeys against SIV (simian immunodeficiency virus) infection.[36]

Large-scale genotyping studies will give us greater insight into the distribution and frequency of genetic variation that has important public health implications.

Conclusion

Our increasing understanding of human genomic variation, and specifically its application in pharmacogenetics, might shift our focus away from interindividual differences towards interpopulation differences. In this article we have made three main points. First, that pharmacogenetics can be made relevant to developing countries, where it might reduce national healthcare bills. Essential drug lists in the future might have to take into account possible genomic variations between populations in developing countries. As often happens, for example with biotechnology,[37] it is the people in developing countries (who make up about 85% of the world's population) who could benefit the most in the long term from cutting-edge science and technology (vaccines are a good example).[38]

Our second point is that a deeper understanding of the genotypes of local populations with little admixture may make it possible, perhaps through the short-cuts and cost-efficiencies promised by haplotype mapping, to predict drug responses without the need to test each individual. This application will require caution and validation, but it could make an important contribution to improving drug use in economically deprived populations before the advent of personalized medicine.

Finally, there are potential opportunities for pharmaceutical companies and contract research organizations in developing countries to capitalize on emerging trends in genotyping and their application to understanding variable drug responses and disease susceptibility. Such opportunities, if applied properly, will benefit the health of people in developing countries.

Future outlook

We have some way to go before the vision of real benefits of pharmacogenetics to developing countries materializes. Substantial knowledge gaps will need to be addressed by well-designed studies in multiple populations.[39] There are also conceptual and technical problems that need to be resolved, and the use of population groups – at least as currently conceived in terms of race and other unsatisfactory descriptors that conflate with social constructions – is fraught with ethical and social problems that will need to be addressed with interdisciplinary research. The most satisfactory term for population groups at present is emerging as 'geographical ancestry', but as data accumulate we may discover other terms for communities of common ancestry that are more scientifically accurate and that avoid social constructions completely, making it possible to move forward with less likelihood of controversy. We need to change the paradigm from 'race' to human genome variation.[40]

If we are to help reduce global health inequities we must continue to support efforts to define the nature of human variation across the world, focused primarily on medical goals.[39] We need to formulate clear, scientifically accurate messages to educate researchers, healthcare professionals and the general public on the connections between race, ethnicity, genetics and health. For developing countries not to be left behind, to harness useful knowledge for their populations, and to avoid pitfalls, their researchers and policy-makers must participate in this important discourse as early as possible. We need an innovative global approach, such as the proposed Global Genomics Initiative,[41] to bring together industry, academia, nongovernmental organizations and international organizations, such as the World Health Organization, to examine how pharmacogenetics and pharmacogenomics can best be harnessed to improve the health of people in developing countries. Pharmaceutical and biotechnology companies from both developed and developing countries should plan for the long term and consider the realities of the developing world, because that is where there will be the largest population growth, disease burden, drug demand and future markets. If markets won't work, public-private partnerships will probably be created to address the important needs of developing countries. Academics should begin empirical case studies of genotyping projects in developing countries and of early applications of pharmacogenetics in both developed and developing countries to identify good practices and avoid pitfalls. ❑

Acknowledgments

We thank Stephen W. Scherer of the Hospital for Sick Children, Toronto; Charles Scriver of McGill University, Montreal; and Adrian Ivinson of the Harvard Center for Neurodegeneration and Repair, for reading the manuscript and making suggestions for improvement; and Nadia A. Daar for her help in preparing the manuscript.

The Canadian Program on Genomics and Global Health is supported by Genome Canada through the Ontario Genomics Institute, and by the Ontario Research and Development Challenge Fund, and other funders listed at the Canadian Program on Genomics and Global Health. Competing interests statement: The authors declare no competing financial interests.

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Further information

Canadian Program on Genetics and Global Health: www.utoronto.ca/jcb/genomics/index.html
Drugs for Neglected Diseases Initiation: www.dndi.org
Food and Drug Administration: www.fda.gov
Genome Institute of Singapore: www.gis.a-star.edu.sg
Grand Challenges in Global Health: www.grandchallengesgh.org
Human Genome Organization (HUGO) Pacific: www.hugopacific.com
Institute of Genomic Medicine (Mexico): www.inmegen.org.mx
Institute for OneWorld Health: www.oneworldhealth.org

Health research institutions and global health challenges

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Moving beyond disciplines and geography: the NIH experience



Article by Elias A Zerhouni (pictured) and Sharon H Hrynkow

Health research has always been an inherently international enterprise. Many of the major public health advances of our time have depended entirely on teams of scientists working effectively across international borders: vaccines against childhood diseases; the discovery of the structure of DNA and the subsequent mapping of the human genome; and oral rehydration therapy, were all developed and supported by international teams. This trend will surely continue.

At the same time, multidisciplinary and interdisciplinary approaches to health research are increasing. This is imperative as we work to link knowledge about genes, behaviour, nutrition, infectious agents, environment and social and cultural factors to better understand and treat disease. New actors, including social scientists, mathematicians, physicists and others will play increasingly important roles in the health research enterprise of the 21st century.

As scientists and science funding agencies work to develop the most effective mechanisms to conduct and support research, we should take stock of best practices and share expertise broadly. In this article, we describe paradigms used by the United States National Institutes of Health (NIH [part of the Department of Health and Human Services]) to overcome both geographic and disciplinary boundaries to advance biomedical and behavioural research.

Addressing the geographic barriers: the NIH as a permeable membrane

As the NIH works to support the best science to improve health, one thing is clear: international scientists will play a critical role in moving forward specific research areas, as the global burden of disease statistics demand this. As we consider the growing challenges of HIV/AIDS and tuberculosis (TB), scientists in countries most affected, namely those in the developing world, have a significant role in devising effective interventions that will be accepted by local groups. Only when effective interventions are shared across borders will we as a global community adequately prevent and treat these scourges.

The rationale for supporting science across borders goes beyond the global burden of disease. International teams of scientists always find ways to work together on problems of common interest, and this will surely continue. By 2001, 23% of all United States scientific articles had at least one non-US coauthor, compared to 10% in 1988 (Science and Engineering Indicators, 2004, National Science Foundation). The scientific enterprise is built on the collective and cumulative imagination and creativity of scientists, each of whom seeks others interested in unravelling specific research problems. With modern communication and travel, political borders no longer stand in the way of creative scientists finding and collaborating with like-minded partners. As scientific leaders and managers, our challenge is to support these teams through all available mechanisms.

Based on the premise that the best science should be supported regardless of the investigator's country of origin, the NIH system accepts applications from anywhere in the world. Scientists are invited to apply either as partners with United States colleagues or as independent investigators. While foreign scientists must meet specific criteria (Box 1) in order to justify expenditure of United States taxpayer dollars abroad, a significant increase in foreign funding occurs every year (Figure 1). Among foreign scientists, those in Canada and Europe have competed most successfully for NIH support. Yet, scientists in every region of the world receive significant support through the NIH competitive process (Figure 2).

Among the advances made by these teams are some of the most exciting and promising in medical research in recent years. New knowledge about diabetes, depression and AIDS are among the advances made in the past 2 years through the dedicated partnerships of international teams (Box 2).

Training the next generation of researchers is a critical mission for the NIH. In addition to supporting the training of United States pre-doctoral candidates and post-doctoral fellows, the NIH supports programmes to train foreign nationals. The NIH Visiting Program is an important element in our strategy to train the next generation of health researchers. Each year, the Visiting Program hosts about 2700 foreign scientists on the NIH campus in Bethesda, Maryland or at other NIH intramural laboratories within the

Box 1 | Criteria for foreign grants to receive NIH award

Applications must meet all of the following criteria:

- Project presents special opportunities for furthering research programmes through the use of unusual talents (such as teams of researchers), resources, populations, or environmental conditions in other countries which are not readily available in the United States or which augment existing United States resources.
- Project has specific relevance to the mission and objectives of the awarding institute or centre and has the potential for significantly advancing the health sciences in the United States.
- Application must be approved by the awarding institute or centre council/board.
- Grant may be awarded only after assurance that the foreign institution is in compliance with human subject, animal welfare, gender and minority requirements.

NIH Office of Extramural Research, Grants Policy Statement December 2003. Available from: http://grants2.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part12.htm#_Toc54600260

United States. Participation in the Visiting Program is based on scientific match and interest between the prospective participants – primarily post-doctoral fellows – and the laboratory chiefs. Other junior scientists from abroad, mostly post-doctoral fellows, receive training as part of specific NIH training and research grants at United States universities. Furthermore, through special programs of the Fogarty International Center, the NIH works to ensure that promising young scientists wishing to return to their home countries after training is complete have the skills and research support to do so. Importantly, we wish to maintain ties with these scientists, many of whom continue their collaborative work with United States mentors and scientists. This long-term approach creates value for the United States and the global community.

The special case of the Fogarty International Center

The Fogarty International Center is unique both within the NIH infrastructure, and in the world. Envisioned by Congressman John Fogarty of Rhode Island as a centre dedicated to a 'healthy America in a healthier world,' Fogarty plays two important roles. First, as the 'state department' or diplomatic focus for the NIH, Fogarty works with and on behalf of the NIH Director with NIH counterparts abroad, other United States agencies, including USAID, and colleagues within the Department of Health and Human Services on bilateral and multilateral policy and program issues. Second, Fogarty supports a robust portfolio of research training programmes aimed at building partnerships and scientific capacity in low- and middle-income nations. Working through over 60 United States and 100 foreign institutions, Fogarty programmes have contributed to the

Box 2 | Selected NIH-supported advances made by international teams

A research team composed of scientists from the NIH and around the world identified variants in a gene that may predispose people to type 2 diabetes, which affects roughly 17 million people nationwide. This form of diabetes, which disproportionately affects African Americans, Hispanic/Latino Americans, and American Indians, is characterized by a failure of the pancreas to produce enough insulin.

The NIH is spearheading an ambitious effort to create the next-generation map of the human genome – the HapMap. To create the HapMap, researchers have sampled 270 people from selected populations around the globe, and have already identified 9 million genetic variants that will be used to create the map of DNA neighbourhoods. When completed, the HapMap will serve as a powerful tool that researchers can use to find the gene variants that affect health and disease.

NIH-funded researchers recently discovered that avian influenza has become endemic in waterfowl in East Asia. The NIH is supporting research to develop vaccines against these newly emerging viral strains.

Accelerated efforts to develop malaria vaccines reached a milestone with the first launch of a clinical trial in Mali, a country where malaria is endemic.

Scientists found that men infected with both HIV and an apparently harmless virus called GBV-C were three times less likely to die than HIV-positive men not infected with GBV-C. This research provides clues as to why the course of HIV-1 infection is so variable among individuals.

A long-sought research goal has been to understand why stressful life experiences can lead to depression in some people but not in others. A recent epidemiological study by NIH-funded researchers revealed that people with the 'short' version of the serotonin transporter gene (5-HTT) have a much higher risk of depression than those with the 'long' version of the same gene.

The identification of the coronavirus that causes SARS demonstrates that the NIH is prepared to respond quickly to emerging disease threats and will help scientists worldwide to develop effective vaccines, drugs, and improved diagnostic tests to counter the further spread of SARS.

Box 3 | Fogarty International Center efforts in Haiti: a story of discovery

When HIV/AIDS began to ravage Haiti in the early 1980s, the research infrastructure developed with NIH funding became the foundation of a major NIH-supported HIV/AIDS and TB research effort in Haiti, which included the development of GHESKIO, a Haitian NGO. GHESKIO staff were the first to document cases of AIDS in a developing country. Numerous research grants supported by NIH's National Institute of Allergy and Infectious Diseases and training grants from the Fogarty International Center (FIC) were essential in delineating the epidemiology of HIV in Haiti, the importance of heterosexual transmission, mother-to-child transmission and the critical interactions between the TB and HIV epidemics. Personnel trained through the FIC AIDS International Training and Research Program formed the 'pillar' of the Haiti AIDS program, according to Dr Jean Pape, one of the leading AIDS scientists in Haiti and a long-standing FIC collaborator. After 15 years of Fogarty support, the AIDS human resource/research infrastructure in Haiti is stronger than ever. Haitian scientists have received NIAID grants to prepare for vaccine testing and prevention trials. Haiti was named a recipient of an award from the new Global Fund to Fight AIDS, TB and malaria. Haiti received one of four new Fogarty awards to train scientists from developing countries in clinical sciences. These awards have contributed over time to helping Haiti turn the corner on HIV/AIDS such that prevalence in prenatal clinics in Port-au-prince has decreased from 14% to 4% and HIV transmission in discordant couples has dropped from 6% to 0%.

strengthening of scientific infrastructure in Africa, Asia, Latin America, Russia and parts of Europe. Targeting human capacity, Fogarty programmes provide the critical underpinning that allows significant advances to take place in health research in poor countries (Box 3). Fogarty's guiding principle, 'Science for Global Health', reflects the broad NIH commitment to improving the health of Americans in a healthier world.

Addressing disciplinary barriers: the NIH as a semi-permeable membrane

Advances in technology have dramatically changed the way we view medicine and health research. Non-invasive imaging, rapid gene sequencing, computer-assisted rehabilitation strategies and molecular tools that allow diagnosis of disease before symptoms appear have all contributed. To foster a culture in which technologies are brought to bear or developed most effectively to improve human health, new ways of thinking are required and cultures of institutions must be adaptable to change.

The NIH Roadmap for Medical Research in the 21st Century is one way in which NIH is working to lower traditional disciplinary barriers. Launched in October 2003, the Roadmap is built on three pillars: new pathways to discovery; research teams of the future; and re-engineering the clinical research enterprise (http://nihroadmap.nih.gov/). Supported by each of the 27 institutes and centres of the NIH as well as the Director's Office, the Roadmap has identified major opportunities and gaps in biomedical research that no single NIH Institute could tackle alone, but that the agency as a whole must address in order to propel research forward. The following four projects are illustrative of the scope of the Roadmap work now underway.

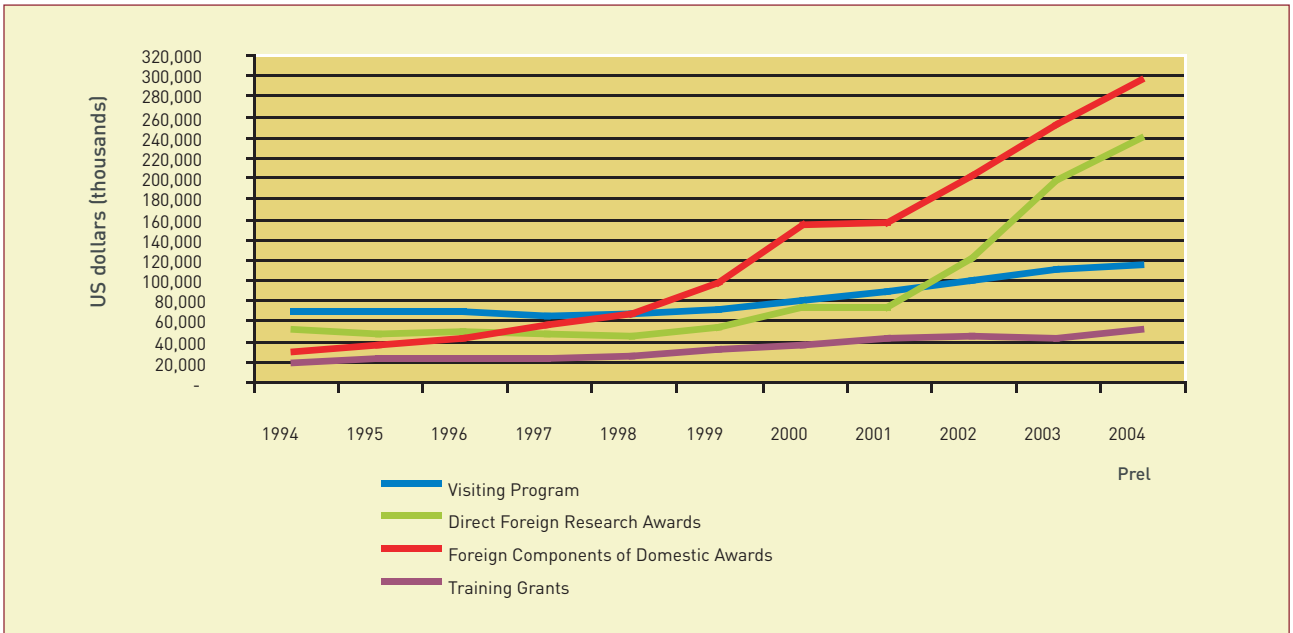


Figure 1: NIH- international research expenditures fiscal years 1994 to 2004

New pathways to discovery

Scientists at Harvard University Medical School are using molecular libraries – collections of drug-like small molecules – to develop high-throughput, whole organism, green fluorescent screens of the blood-stage form of *Plasmodium falciparum*, a malaria causing parasite. This project will analyse the diversity of potential biological targets that can produce leads for the discovery of chemotherapeutic agents to tackle malaria and to find ways of reversing drug resistance to previously effective chemotherapeutic agents.

Interdisciplinary research

Faculty from the schools of medicine, veterinary medicine, nutrition, engineering, and law at Tufts University have teamed up to create an interdisciplinary doctoral programme to train students to work with a global view toward assuring water security for the protection of health, environment and human livelihoods. The vision is to educate professionals who can use multidisciplinary perspectives and tools to solve water-related problems that impact health.

Re-engineering the clinical research enterprise

To advance the translation of scientific advances from the bench to the practitioner, health systems and communities, the University of Washington has established a multidisciplinary clinical research career development programme to provide investigators with in-depth knowledge of the full spectrum of clinical investigation, develop practical skills for conducting integrative clinical research, create an environment that infuses students with a sense of excitement about clinical research and, nurture early career development.

Pioneer awards – taking risks

To stimulate high-risk, high impact medical research, the Roadmap supports 'pioneer awards' that support ideas rather than projects and that encourage investigation in unexplored fields of research. One of the first pioneers is Dr Joseph McCune, University of California, San Francisco, who will build on his existing work in HIV/AIDS to develop interventions that will slow or prevent the development of AIDS in HIV-infected people.

NIH is now evaluating the applications submitted in response to the Roadmap in order to gain a broad sense of how the Roadmap played out at the level of individual scientists. Even as we take stock of our initial experience, we see that physicists, chemists, mathematicians and engineers (among others) have joined forces with life scientists in new ways. The success of the Roadmap will be measured not in numbers of grants, but in whether the change is sustainable that we now see in the applications and types of teams requesting support from NIH.

Another strategy to lower traditional disciplinary barriers is through the Fogarty International Center's Framework Programs for Global Health (www.fic.nih.gov/ programs/ framework.html). This innovative programme seeks to accomplish two critical objectives. First, it will bring new insights into the global health research arena by 'gluing' together multiple schools within universities in new ways. Schools of engineering, communications, dentistry, divinity, law and agriculture are encouraged to join forces with counterparts in schools of medicine and public health to advance the global health agenda in new ways. These new entities will foster novel thinking and approaches to global health on campuses in the United States and in the developing world. Second, to engage young people on global health issues as early as possible in their careers, the Framework will support curriculum development on global health studies for undergraduate and graduate students.

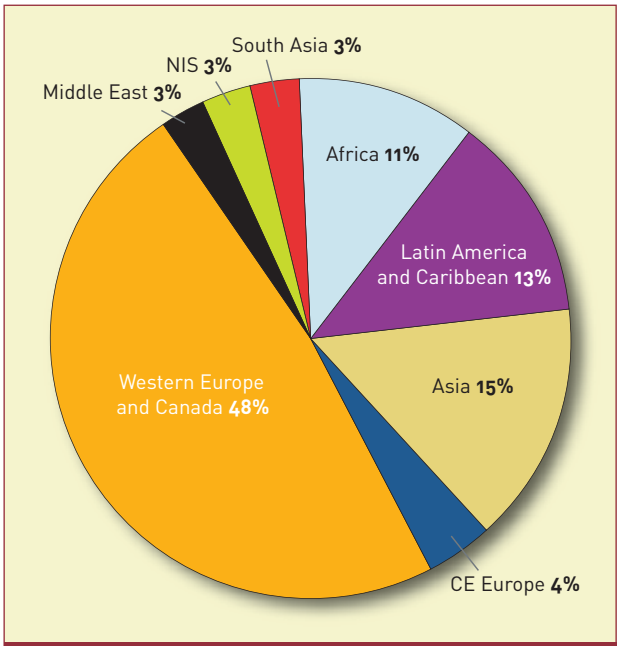


Figure 2: NIH-supported international partnerships 2004

Final note

President John F Kennedy once said, 'A rising tide lifts all boats. And a partnership, by definition, serves both partners, without domination or unfair advantage.' The NIH is committed to working in partnership with colleagues around the world to improve health. This article describes only some of the strategies adopted by NIH to enhance these international scientific partnerships. If this article has sparked new thinking on approaches on cross-border or cross-disciplinary programmes, we will have succeeded in meeting our overall objective. As NIH continues forward to identify the most effective strategies and partnerships to improve health, we will always welcome the opportunity to share our experience and learn from others. ❑

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Translating medical research into benefits for African people



Article by Colin Blakemore

At a time when African countries are improving infrastructure and living conditions for millions, many people across the continent nevertheless remain in poverty. The UN's Millennium Development Goals (MDGs) aim to halve world poverty by 2015, and as highlighted by the WHO's *Commission on Macroeconomics and Health*, health improvement is widely accepted as key to making economic progress. Fulfilment of the health-related MDGs will rely on the application of funds to assess needs and drive innovation through medical research as well as through the implementation of already proven technology and practice.

Against a backdrop of emerging diseases, infectious disease in particular, contributes the bulk of the disease burden in sub-Saharan Africa. According to the Global Health Council, 62% of all deaths in Africa in 2001 were caused by infectious disease, compared to 31% in South-East Asia and just 5% in Europe.

The figures are stark, and well known. Malaria remains a significant problem in Africa, causing perhaps as many as 2 million deaths per annum. But the biggest impact in recent years on economic and social progress has been due to the explosion in HIV and AIDS: 45 million people are now living with HIV infection.

In addition to affecting the general population, the impact has been felt acutely by the health profession trying to care for those infected. In 2000, the World Bank reported that 20% of student nurses in Mozambique died from AIDS and those who did graduate now work in hospitals where latex gloves and disinfectant are a luxury and where substandard equipment leads to a significant degree of injury.

The MDGs have added impetus to the international effort. The UK Medical Research Council (MRC), along with other leading research organizations, recognizes that the issues are multifaceted. The solutions are also likely to be complex. Acknowledging that success in the fight for a better life in the developing world will require a concerted international effort, the MRC plays a role in reducing poverty and contributing to sustainable development through delivering the products of high-quality health research. This can be achieved only through working in partnership with organizations such as the UK's Department for International Development (DFID), NGOs, drug companies and governments of both developed and developing countries.

Since its foundation in 1913, specifically to tackle the problem of tuberculosis (TB), much of the MRC's early work was dedicated to the investigation of tropical medicine. At that time tropical diseases were seen as sharply distinct from the medical problems of developed countries. However, today disease is increasingly global, with regional and local variations. Infections travel with their hosts and invertebrate vectors. Diseases such as AIDS and TB, formerly attributed to developing countries, are mirrored here in the UK. Equally,

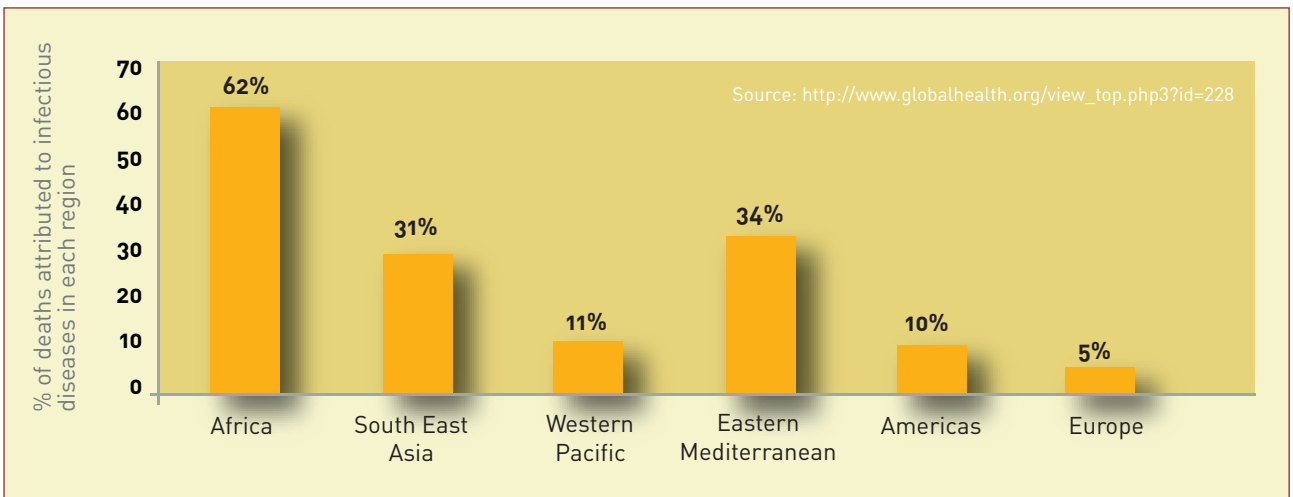


Figure 1: Infectious disease deaths as a proportion of all deaths 2001

noncommunicable and 'lifestyle' disorders traditionally associated with the northern hemisphere, such as allergy, depression and obesity, now pose major challenges across the world. In this sense, the MRC's research programme reflects the global nature of health problems. Our investment in research relevant to developing country health needs is an estimated £23 million per year, of which a total of £8.5 million is invested through the two Africa units.

An important challenge for research is to make the outcomes of our efforts relevant and easily implemented in diverse settings, translating research from the research settings into solutions for local communities. A model that supports this process, and that is adaptable to changing research needs and opportunities, is that of the MRC unit. Our units typically provide the infrastructure for concentrated, long-term multidisciplinary research in an area of research of strategic importance. MRC has two units outside the UK, one in The Gambia and another in Uganda, delivering science of international quality and local and regional relevance. Their programmes are now largely staffed – and increasingly led – by Africans.

Health in a resource-starved environment

Solutions effective in the north often fail to work equally well in low-income countries, either due to the poor infrastructure and healthcare systems that prevent implementation, or because of differences in the genetics or biology in the target population. MRC research in Africa aims to develop effective treatment strategies that are appropriate for such resource-poor settings.

For example, research in Uganda and Tanzania is investigating the social factors that contribute to the transmission of HIV. All over sub-Saharan Africa, AIDS has robbed society of many of the productive 15–45 year old working population, although in Uganda the government and its partners have had particular success in reducing the incidence of new infections. The MRC has contributed by supporting research on effective sexual health education amongst adolescents.

Recently, researchers investigated whether teaching young people in schools about HIV and sexual transmission would reduce the incidence of sexually transmitted disease. They found that, despite pupils being better informed, there was little immediate impact on the incidence of disease. However, further research aims to find out whether the benefits emerge when adolescent boys grow into young men choosing to establish sexual relationships with adolescent women. They might prove to be better informed, responsible partners, taking the necessary precautions against HIV. Such findings highlight the fact that: (i) the translational process, from early scientific research through to effective intervention policy, can often take many years; (ii) and with HIV, the epidemic will be defeated only through a combination of interventions. Behavioural change and the use of existing technologies such as condoms have as much a place in meeting the needs of Africans as has innovation in treatments or preventive vaccines.

In developed countries the picture is very different. Antiretroviral therapy (ART) has returned quality of life to many patients with HIV. This approach is now being introduced to parts of Africa. In the north, ART is usually provided with the support of well-trained medical staff and sophisticated laboratories to aid monitoring of safety and efficacy. Conversely, in Africa, especially rural Africa where many of the people live, the lack of such support is a major obstacle for rolling out ART. Understanding how ART could be better delivered in the absence of laboratory support is now the focus of a major ongoing international trial known as Developing Antiretroviral Therapy in Africa (DART), funded by the MRC, DFID and the Rockefeller Foundation.

Dr Heiner Grosskurth is Director of the MRC Research Unit in Uganda that works in partnership with the Uganda Virus Research Institute (UVRI) as well as other NGOs such as The AIDS Support Organisation (TASO), which was set up by Ugandans with HIV in the late 1980s to provide care and support for those affected by HIV.

The DART trial is investigating whether ART can be delivered in rural populations without the kind of sophisticated laboratory support that is found in the north.

'We are also investigating whether structured treatment interruptions can reduce pill burden, side effects and costs. So far, ART has shown a 10-fold reduction in AIDS-related mortality, a very encouraging result that we hope will be sustained,' said Heiner Grosskurth.

These results are promising, but there is some concern that the introduction of ART may, to a certain degree, reduce the use of existing prevention measures such as condom use. Also, erratic drug supply and suboptimal clinical and laboratory monitoring might accelerate the development of drug-resistant strains of HIV. Together with its partners, the MRC Unit in Uganda is trying to find answers to these important questions.

In fact, with or without ART, condom use presents huge cultural difficulties. In certain societies, women may have little power to force the use of protection on their husbands. An international initiative called the Microbicide Development Program (MDP) is one of a group of organizations that are developing and trialling a variety of intravaginal microbicide gels and devices, designed to protect against the transmission of HIV and other sexually transmitted infections, which will be used and controlled by women. DFID, together with the MRC, is funding the MDP's first large-scale microbicide clinical trial in local African communities, which is coordinated by the MRC's Clinical Trials Unit and scientists at Imperial College.

To a large extent, the success of microbicides will depend on their correct and consistent use and their integration into cultural patterns and religious beliefs in societies where high rates of infant mortality encourage couples to have many children. Each research site for the microbicide trial has a

community liaison officer to facilitate implementation of the technology. Julie Bakobaki is one of the clinical trial managers coordinating the trial across Uganda, Tanzania, Zambia and South Africa, where the intention is to recruit nearly 10,000 women and to follow them over the next 2 years.

'Widespread adoption of microbicides is dependent on a number of factors, not least of which is their level of acceptance by both partners in a relationship. The trials will not only look at the long-term safety and efficacy of the intervention, but also at social and behavioural factors,' said Julie Bakobaki.

Interventions such as microbicides are designed to slow down infection rates, but levels are still so high that the time between research and application needs to be minimized. Ideally, questions of a scientific, governmental, social and practical nature should be addressed in parallel rather than successively, and built into a national strategy as soon as possible. In The Gambia, insights from MRC researchers into HIV/AIDS have facilitated the establishment of a new National AIDS Secretariat supported by the President of The Gambia, and those insights have been incorporated into the National AIDS Control Programme.

Malaria: discovery science to behavioural change

Poverty and ill-health go hand in hand. Sick patients on low incomes are unable to afford the medication needed to improve their health enough to return to work. As with other infectious diseases, malaria is on the increase in poor countries with four times as many people contracting the disease at the end of the 20th century as in the 1970s. Each year well over one million people – mainly under 5 years old – die from malaria.

The MRC's work on malaria has ranged from implementing an insecticide-treated bednet programme in The Gambia to the discovery-level science involved in the development of new anti-malarial vaccines. Unlike expensive drugs that often fail to work against the increasingly resistant malaria parasite, insecticide-treated bednets not only protect the person using the net, but also reduce the mosquito population in each village, benefiting the whole community. The MRC is currently supporting a trial that will look at more radical use of nets to screen houses and living areas, in addition to beds.

Bednets, when used as intended, can substantially reduce the spread of malaria, but people need to maintain and replace nets on a regular basis. In rural communities, it is not uncommon to find nets with large holes or not properly wrapped around bedding. There have also been difficulties in ensuring the regular re-treatment of nets with insecticides. Furthermore, sometimes nets are used for other purposes, such as fishing. So, a radical and sustainable solution to malaria is still very much in demand. Hope lies in the development of a vaccine. As for most infectious diseases, an effective, inexpensive vaccine is the most practical and reliable solution.

The MRC Gambia Research Unit is at the forefront of malaria vaccine trials research in partnership with researchers at Oxford University. Two trials conducted in The Gambia showed that the RTS,S vaccine, developed by GlaxoSmithKline, is safe and induces immunity in children paving the way for efficacy trials currently underway in Mozambique. This vaccine is quite effective in preventing cerebral malaria in babies, but protection is incomplete and is not sustained for more than a couple of months.

Back in Oxford, the MRC is funding Professor Dominic Kwiatkowski and his team to use the latest genomic tools to discover precise molecular mechanisms by which the human immune system is able to resist malaria, a question that is fundamental to the next phase of vaccine discovery. Working with research partners in The Gambia and other malaria stricken regions of Africa, Kwiatkowski is analysing the DNA of thousands of individuals who contract the disease. The human genome contains millions of small person-to-person variations – these polymorphisms are what make each of us unique. Detailed comparisons of the genetic code of people who survive malaria and those who die may provide vital clues about the parts of the immune system that are critical for resisting the disease. Of particular interest currently are those genetic variants that stop parasites from invading and multiplying inside red blood cells, because this is the critical stage of infection that causes the illness. Understanding which genetic variants protect people who are constantly exposed to malaria might eventually enable researchers to translate this discovery-level science into an effective strategy for vaccine development.

Respiratory diseases – Africa's forgotten killer

It is often thought that control of the 'big three' – HIV, malaria and TB – is the solution to resolving the burden of infectious disease in Africa. But death rates from the less publicized acute lower respiratory diseases actually exceed those from HIV, killing 3.9 million people annually. Wide disparity exists between infant mortality in Europe/the United States and Africa, highlighting how unreliable and unaffordable vaccine supplies hinder the application of successful interventions used in the north to disease control in developing countries.

Haemophilus influenzae type b disease (Hib) has been all but wiped out in developed countries, but the bacterium still causes as many childhood deaths as does malaria in sub-Saharan Africa, mainly from meningitis and pneumonia. In these countries, many children die because they cannot reach a hospital in time or because medical staff are in short supply.

Now, a 5-year trial, conducted by the MRC Gambian unit and recently published in *The Lancet*, has shown that routine Hib vaccination in babies at 2, 3 and 4 months has reduced the annual incidence of meningitis over 5 years

from 200 per 100,000 to zero. This remarkable success is largely due to the implementation of a partnership with the government of The Gambia and its willingness to incorporate Hib vaccination into the Gambian Expanded Programme for Immunisation.

'Our study shows that despite an erratic vaccine supply, elimination of Hib disease is possible. We hope other countries will now be encouraged to also adopt routine Hib vaccination programmes,' said Dr Richard Adegbola from the MRC, who led this project.

Childhood mortality: quality not quantity

For over half a century, the MRC has maintained a field station among the people in and around the rural setting of Keneba, The Gambia. The station, working closely with the Gambian Government Divisional Health Team, concentrates on maternal and child health and on training local staff in clinical and scientific research. As well as running a feeding centre for malnourished children, and an out-of-hours emergency service, the centre has made significant advances in nutritional research.

Where the chance of surviving to adulthood is much reduced, families often resort to producing large numbers of children in the hope that some, at least, will live up to a working age to provide support. Unfortunately, quantity outweighs quality in terms of child-rearing in many developing countries.

In three villages in The Gambia, the issue of infant and child mortality has engaged MRC research for over 50 years. Mortality rates have been monitored over this period of time and have shown a dramatic 8-fold reduction from 162 to 36 deaths per 1,000 infants and from 367 to 66 per 1,000 in children aged under 5 years old.

Professor Andrew Prentice, Director of Science at the Keneba MRC unit, said: 'These improvements have been achieved through the efficient implementation of vaccination, simple medical care and nutritional interventions. The reduced mortality has led to a greater uptake of contraception, better birth spacing and reduced family size.'

Pivotal to success in reaching the goals in the battle against poverty is the continuation of strong mutually-supportive collaboration – involving international donors, governments and research organizations. The MRC and other international medical research organizations convene informally twice a year as the Heads of International (Biomedical) Research Organizations (HIROs) to discuss research progress and exchange ideas and experience. At their June meeting this year, HIROs focused on global health and especially research partnership with Africa, and decided to work towards a declaration to establish a new Global Health 'Cooperative' to strengthen capacity in global health research.

From descriptions in the media, people could be forgiven for believing that Africa is still the forgotten continent where living standards continue to spiral downwards. But this belies the significant gains that are being made in Africa by research teams, largely staffed by Africans themselves, in partnership with UK-based researchers, whose work reaches far into the villages and homes of the rural communities. Research aimed at medical problems in the UK can have an important impact in developing countries, but equally, findings from research in Africa provide valuable insight into disease mechanisms and management here in Britain. With its partners, the MRC is bridging the 3,000 mile gap between the UK and sub-Saharan Africa and closing the health gaps between rich and poor. ❑

***Colin Blakemore**, FMedSci, FRS, became Chief Executive of the MRC on 1 October 2003. He studied Medical Sciences at Cambridge and completed a PhD at the University of California in Berkeley. After 11 years in the Department of Physiology at Cambridge, he became Waynflete Professor of Physiology at Oxford in 1979 and was Director of the MRC IRC for Cognitive Neuroscience for 8 years. His research is concerned with vision and the early development of the brain. He has been President of the British Neuroscience Association, the Physiological Society and the new Biosciences Federation. He has also been President and Chairman of the British Association for the Advancement of Science and he is strongly committed to the public communication of science.*

Bringing modern health technology to the people



Article by Nirmal K Ganguly (pictured) and Kiran Katoch

It is well known that due to differences in disease profiles, access and implementation, there could be major differences in the effectiveness of a tool or technique when comparing the results of hospital-based analysis and field-based trials. Central JALMA Institute for Leprosy & Other Mycobacterial Diseases (ICMR) has attempted to conduct various studies in the field of leprosy, tuberculosis (TB) and filariasis in remote high-endemic settings. The institute had an old association with the Ghatampur area that is located about 300 km from the main Institute at Agra. During the Japanese period (1966–1976), this was a field centre for JALMA. The doctors and paramedical staff used to visit Ghatampur periodically from Agra, camping there for a number of days to examine and treat leprosy patients. After JALMA was taken over by the Indian Council of Medical Research in 1976, the focus shifted to research-cum-hospital activities at Agra. The link with Ghatampur was entirely lost for nearly 33 years until 1999 when the Institute's scientists were assigned the job of independent validation of the third survey of Mw vaccine trials. After assessing the initial logistics, the local field office of the project was shifted from Kanpur to Ghatampur. This opportunity re-established links with the public of Ghatampur. The programmes have expanded as the area is highly endemic for leprosy, TB and also filariasis whose co-endemicity has been linked with leprosy prevalence in Africa. In the first study – the third resurvey of the Mw vaccine trial, the prophylactic effect was assessed against leprosy and was followed by assessment of its effect against TB as well. These were multi-institutional programmes involving the National Institute of Immunology (NII), the Institute for Research in Medical Statistics (IRMS, ICMR), TB Division, the Government of India and JALMA.

Another collaborative study on the genetics of leprosy is being undertaken by JALMA and the All India Institute of Medical Sciences (AIIMS). Currently, there are focused programmes on various aspects of the epidemiology of leprosy, TB and filariasis. While two DBT-funded projects have been completed, one extramural ICMR task force project, one multicentric WHO funded project, one multicentric DBT funded project, one Government of India funded drug resistance surveillance project and an intramural project on co-endemicity of leprosy and filariasis are in progress. Three extramural projects, one each on leprosy, TB and filariasis are being submitted for funding. It is expected that these studies will provide scientifically important information that will help in translating the technological advances into active plans and strategies for effective management of these diseases at public health level. A special task force has been created by ICMR Headquarters to review the progress and draw a long-term strategy for these field programmes. This has helped to consolidate the gains and an integrated model project is being envisaged as a future vision for the unit.

The institute has a clear scientific agenda to determine the profile of diseases

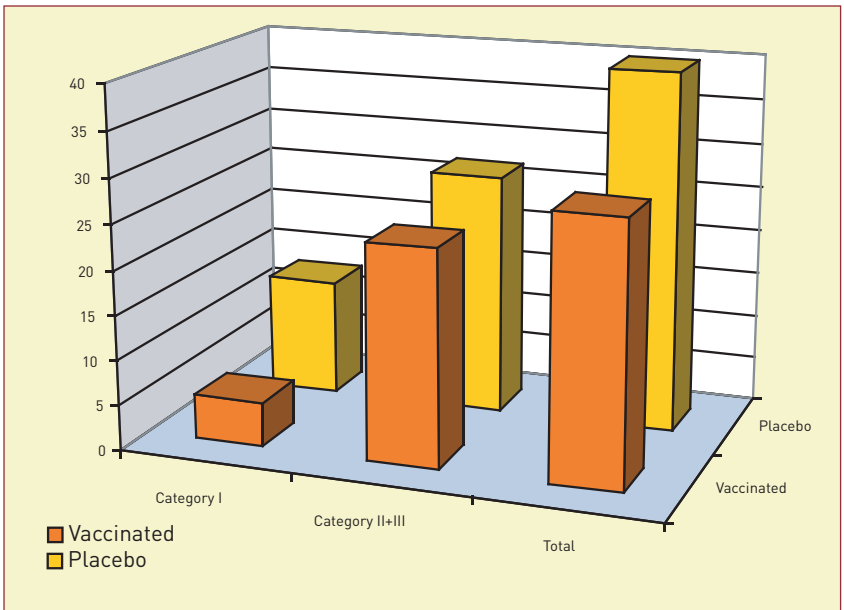


Figure 1: Prevalence of pulmonary TB during the survey in the Mw vaccinated and placebo groups

like leprosy and TB in high-endemic settings of Ghatampur. It also envisages the improvisation and/or evaluation of already established regimens developed by the institute in the field conditions. The broader goal includes generating newer information about various operational aspects such as how health systems function – people's access to health services, their attitudes and perceptions, effect of factors like financial ability, gender, ethnicity and the links with other parameters associated with the economy and health of the population. Overall, the institute and the ICMR have a committed mandate to bring health technologies from the laboratory to the field. This unit, which began as an assortment of independent research projects, has now interwoven and mutually supportive goals as well as strategies. It has a cohesive agenda for improving the management of leprosy, TB, filariasis, etc.

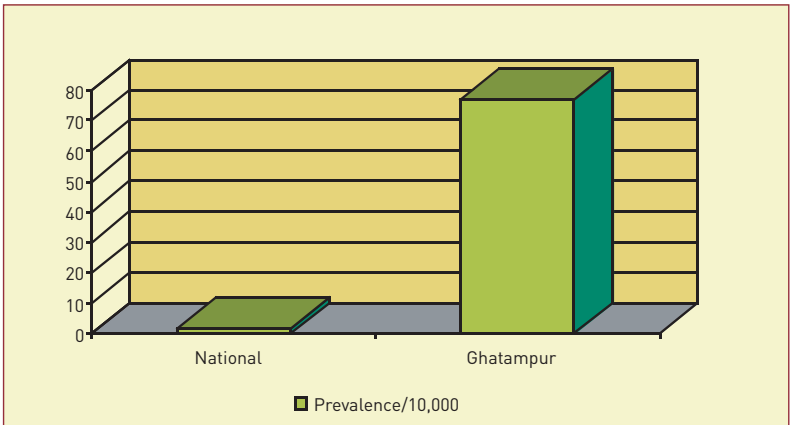


Figure 2: Prevalence of leprosy in Ghatampur field area of Cjilond (March 2005)

While the intervention studies are being carried out in the Ghatampur Tehsil, another drug resistance surveillance study in TB covers the whole of Kanpur District. Kanpur is an important industrial city and the district is surrounded by two major rivers – the Ganga, Jamuna and their tributaries. The rural belt has small towns like Ghatampur, Patara, Bidhnu, Sirsol, Jehanabad, etc. The land is fertile and there is a network of canals and tube wells (government as well as private). In addition to income from agriculture, there are small transport businesses of truck and tractor operators. Even though there are limitations of inadequate power supply the government has made considerable efforts to develop the infrastructure of this area which includes roads (cement, tarred and brick- lined to the remotest villages). Primary and middle schools exist in most of the villages belonging to all the communities. High schools are available within a radius of 10km. Many degree colleges and polytechnics have also sprouted up in the adjoining towns. There are effective telecommunication links with the rest of the country and the world. The state government has created a chain of sub-centres, Primary Health Centres and an upgraded, newly built community health centre at Ghatampur. The city of Kanpur has several ESI hospitals, a good district hospital and a reputed old medical college. Since its inception in 1999, the unit has made significant progress in achieving its scientific goals and also in reaching out to people so that it could serve as an integrated model for transferring the technology to the most needy segments of society.

The institute has conducted and is carrying out studies to address various scientific questions and assess the effect of intervention through improved regimens on the treatment, profile and spread of these diseases. Besides the achievements in terms of seeking answers to medical and therapeutic questions relevant to these important diseases, the programmes have led to several other major gains for the community:

(i) Bringing advanced health care and related technology to the people. By establishing these programmes and a field unit with headquarters in rural settings, the institute and ICMR have succeeded in providing modern facilities to diagnose and treat diseases like TB, leprosy and filariasis comparable to any advanced treatment centre in an urban area. Most of the staff for these field studies were recruited from educated people among the local population in an open competitive way, and many purchases were/are being made locally, which made the community stakeholders in the process. This has contributed to the success of these programmes in a very short time frame.

With the active participation of local people, the institute could finish two major studies: (a) the Third Resurvey of Mw vaccine trial in the Ghatampur area (1999–2001, DBT funded); and (b) Determining the point prevalence of TB in Mw vaccinated population of Ghatampur, Kanpur area (2002–2004, DBT funded) with 87.6% and 74.3% coverage of target groups, respectively.

Mw, a closely related mycobacterium with antigenic similarities to *M.leprae*, has been used as an immunoprophylactic and immunomodulating agent in leprosy, in a field trial in Ghatampur area. This trial was initiated by NII and the third survey was independently and jointly done by JALMA and IRMS. The pre-vaccination survey of the area recorded a prevalence rate of approximately 18/1000 at the time of vaccination. In this third resurvey, 87.6% of the trial population consisting of 24,060 contacts could be covered and examined 7 to 10 years after the vaccination. The result of this study shows the protective efficacy of the vaccine when given to both multibacillary (MB) patients and their household contacts. The protection against leprosy was up to 59–60% at the end of the second survey (5–6 years), which came down to 30–36% by the end of the third survey.

While Mw has shown good immunomodulatory action against leprosy in humans it has also been reported to be active against *M.tuberculosis* infection in experimental animals. This study was carried out to examine the

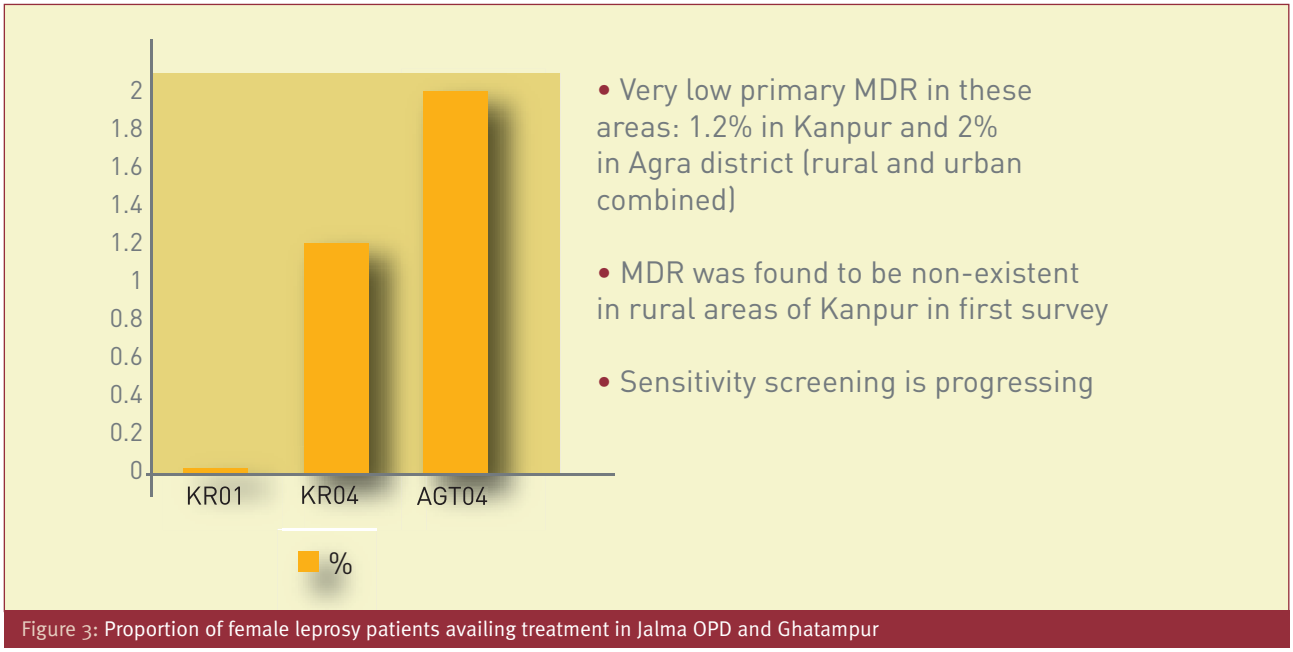


Figure 3: Proportion of female leprosy patients availing treatment in Jalma OPD and Ghatampur

immunoprophylactic role against TB by ascertaining the point of prevalence of TB in household contacts of leprosy patients, in whom Mw was given. About 74% of these contacts were examined during the survey.

When total prevalence during the approximately 10-year period was estimated by taking the history of TB and identifying cases that had documented evidence of receiving treatment during these years, the incidence of pulmonary TB was found to be significantly lower in the Mw vaccinated group as compared to the placebo administered group. The p value was 0.03 for new sputum smear positive cases and 0.002 for total cases of pulmonary TB occurring in the population. All patients were administered DOTS and responded to it, and no case of drug resistant TB was found in the area. It was also observed that contacts who suffered from leprosy did not suffer from pulmonary TB and vice-versa. Thus the results of the study show that two doses of killed Mw vaccine administered at an interval of 6 months appeared to have a prophylactic role in the prevention of pulmonary TB in the area. Apparently there was a limited influence of the BCG (TB) vaccination as less than 2% of the total contacts in the area had BCG scars.

(ii) Reaching out to deprived segments of the community. By doing active surveys and providing free treatment and care to all, deprived segments of the community have also been reached. The benefits were very clear in the case of leprosy in which deformities could be prevented and consequences of complications like reactions could be handled at home. This information emerged from a study entitled, 'Field programme for epidemiological studies at Ghatampur (ICMR Task Force Project, 2002–2005)'. This study is being carried out against the backdrop of the knowledge that the world is moving towards leprosy elimination as a public health problem (prevalence below 1/10,000). However, leprosy continues to be endemic in certain areas/pockets in the country (Figure 1) and special emphasis on these populations is needed.[1] The area of Ghatampur has been chosen for studying the dynamics of leprosy transmission, factors responsible for such high endemicity and to find out the effect of intervention measures. The main objectives of the project are: (i) to study the disease profile in the community; (ii) to study the difference in incidence of disease in relation to age, sex, relation and type of contacts, effect of hygiene, socioeconomic status, etc, on the prevalence and incidence of leprosy; (iii) to study the effect of treatment regimens in the field; and (iv) to study the transmission of the disease.

More than 75% of the population has been surveyed so far and about 84% of the estimated population could be covered as some of the inhabitants have migrated to other areas in search of work and for other reasons. A total of 2881 cases have been identified and are being treated. The prevalence of the disease in the examined population varies from 0 to 260/10,000 (average 77/10,000) of which about 70% are new cases. While there has been nearly a 50% reduction in the last 15 years, this endemicity is very high compared to overall national prevalence of 1.8/10,000 at the end of March 2005. These patients have been allotted standard and other user-friendly regimens, one of which one has been adopted by WHO as a uniform multi-drug therapy (UMDT).

A UMDT regimen for all leprosy patients (a WHO funded multi-centric study, 2003–2008) has been recommended by WHO for trials in India and other countries. In this strategy the same regimen is given to all types of leprosy patients making it operationally much easier to treat them. The majority of cases which are currently detected under field conditions are early cases, i.e. paucibacillary (PB) and smear negative multibacillary (MB) cases. The use of Clofazimine in

the PB regimen for 6 months was tried by us earlier and was observed to substantially decrease the incidence of persisting activity, reactions and with no relapses in the post treatment follow-up of 5 years. Therefore, all the PB cases receiving this treatment will be gainfully treated. For smear negative MB cases the bacterial load is low and theoretically, for most of these cases the duration of the present day MDT regimen can be reduced to 6 months. This study is field-based in which the patients will be followed up for 5 years after stoppage of therapy and failures if any detected during the follow-up will be put on standard MDT.

Of the total cases screened, only 1.9% had grade II deformities like claw hand, drop foot and depression of the nose. Because of this low prevalence of deformities the patients were not inclined to seek medical treatment. As only one case did not improve on treatment and one had late silent neuritis, it is apparent that other deformities also could have been prevented if these cases were detected earlier. Fifty-six patients (1.8%) had reactions before and during treatment. All these reactions could be controlled by concurrent administration of corticosteroids.

The institute is assessing the role of immunological tests like serological assays to identify individuals at higher risk of developing complications. Furthermore, in these investigations, molecular methods like PCR-RFLP (Polymerase Chain Reaction-Restriction Fragment Length Polymorphism), PCR-sequencing and DNA chips are being used to identify strain diversity among *M.leprae* for understanding the transmission of disease.

(iii) Bridging the gender gap. In the work done so far 2881 leprosy cases could be detected and successfully treated thus preventing dreaded morbidity due to deformities. Furthermore, the proportion of females treated was nearly 40% which is higher (by 10%) than found in self-reporting treatment centres (Figure 2). This is important as usually women have lesser access to health care than men.

(iv) Establishment of diagnostic services and implementation of DOTS in the area. During the earlier survey for prevalence of TB in the Mw vaccinated population the laboratory facilities were created, mechanisms of transport were worked for tests like culture sensitivity and PCR. The cases of pulmonary TB detected during the survey were successfully treated with DOTS when the system was not yet introduced in the district. We are currently partnered with the Revised National Tuberculosis Control Programme (RNTCP) for treatment and drug resistance surveillance studies. The institution provides culture sensitivity services wherever required by the district programme people.

In addition to the studies on possible protection of Mw against TB, another study, 'A survey of the prevalence of anti-TB drug resistance in Agra and Kanpur (Ghatampur) districts (Funded by Government of India, TB division, 2003–2006)' proved to be a major catalyst for this purpose. The study is being undertaken as a part of an operational research programme of the RNTCP of the Government of India. The aims of this study are to determine the changes, if any, in the prevalence of initial drug resistance in TB in Agra district and Ghatampur (Kanpur district) in order to use the levels of drug resistance as a performance indicator for the TB programme of the state and indirectly to assess whether recommended regimens are appropriate. The study also aims to establish the foundation for routine surveillance of drug resistance in order to observe future trends. It covers all the microscopy centres of both of these districts which include 24 centres (13 rural and 11 urban) of Kanpur Nagar district and 29 microscopy centres (16 rural and 13 urban) of Agra district. Samples from the field are transported to the institute and processed for culture and sensitivity. For all the cultures identified as *M.tuberculosis*, drug susceptibility tests are being performed for isoniazid (H), rifampicin (R), streptomycin (S) and ethambutol (E) using standard proportion methods. An intensive survey covering the entire Kanpur Nagar district has been completed and from available sensitivity results a 1.8% MDR rate has been observed in the earlier phase. Trends of pilot survey are also available from a limited number of centres of the Agra district and MDR was found to be present in 2.6% of *M.tuberculosis* isolates from fresh sputum smear positive cases (Figure 3).

iv) Filariasis. Presence of different concurrent infections could be altering the immunological balance. Such relationships have been noticed in HIV and TB, filariasis and malaria, onchocerciasis and TB and also between onchocerciasis and leprosy. The chronicity of infection with immune perturbation may tip the balance. The aim of the study is to analyse the relationship, if any, between the presence of lymphatic filariasis and leprosy in a selected population. An initial pilot survey in this area has revealed that the microfilaraemia rate varies from 4% to 10 % and the disease rate from 0.2% to 7% while leprosy prevalence is high in most of these villages. Available data suggest the presence of co-infection (both filariasis and leprosy) in some of the cases. The effect of intervention by mass drug administration with diethylcarbamazine (DEC) and DEC plus albendazole will be assessed on the endemicity of these infections. Filarial cases and individuals with microfilaraemia are being treated by standard DEC. In addition, mass drug administration (MDA) and new strategies for reducing the morbidity of disease are being contemplated which will bring down morbidity due to filariasis.

(v) Reaching out to young children through school surveys. While carrying out the surveys for leprosy and TB in school children, health education about common diseases, especially about personal hygiene is imparted.

(vi) Gaining insight into attitudes and beliefs of people. Working with this population (children), their teachers and peers has provided important insight into their beliefs, customs and social norms. Although the facilities of primary and middle education exist in far flung areas, their utilization varies because of their perception of the utility of education in terms of achieving a better life. Similarly only a small

fraction of the population utilized the state services for these important diseases. This information will serve as a basis to impart appropriate counselling and education for better utilization of services.

(vii) Improving knowledge and attitudes by interacting with local community leaders. Links with local community leaders are being made stronger for future interventions: counselling; methods to improve their economic and social well-being; better utilization of education and health services; hygiene; and early treatment of chronic diseases.

(viii) Developing linkages with state public health services and sharing expertise by providing training. By working in this area the institute has developed linkages with state health services which are being strengthened further by interactions such as providing training to different types of health professionals.

The success achieved in reaching out to the community has made it possible to plan several studies which will enable the delivery of products of scientific progress to the community:

- **Leprosy:** transmission dynamics (strain variation, viability outside human body using molecular techniques, etc), patient load and effect of different interventions, disease pathogenesis – using genomics and genetic tools, assessing the effect of new regimens, etc.
- **TB:** drug resistance, molecular epidemiology, especially to assess the effects of DOTS and DOTS plus immunotherapy.
- **Filariasis**: effect of interventions on co-endemicity of leprosy and filariasis, treatment of lymphoedema, etc.
- **Effect of other factors** like geo-helminths, HIV infection, malaria, nutrition, other socioeconomic factors, etc.

All of the above activities are to be integrated into a compact programme of providing a model to manage these important chronic health problems in high endemic settings.

It is hoped that this unit will not only serve as a model of understanding and management of these important diseases in difficult areas, but will also provide many insights into how to bring modern health technology into people's homes. ❑

Acknowledgements

The authors acknowledge the support of collaborators and participants from NII, IRMS, AIIMS and JALMA. Special thanks to the staff of the field unit, who have made this achievement possible. Financial support from ICMR, DBT, the Government of India and WHO is gratefully acknowledged.

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Support for research in and by low income countries: a proposal



Article by Berit Olsson

'If we are earnest in our ambitions of supporting developing countries, and in regarding them as equal partners, support for the development of their research community is an important ingredient of the Swedish development cooperation.'

This quote from the 1985 assessment of Swedish support for research cooperation with developing countries appears very timely these days when members of the international donor community have signed the Paris declaration on aid effectiveness. The declaration points to the destructive impact of many well intended but fragmenting cooperation projects and underlines the need for external assistance to be aligned with national development strategies. An implicit understanding is that national analysis is essential for the formulation of such strategies, as well as for the monitoring and evaluation of national and external efforts.

In relation to health, the failures in adopting and promoting the use of available knowledge and technologies are ascribed weak systems. It concerns weak health systems as well as insufficient capacity for research needed to follow, evaluate, adopt and promote knowledge. The report of the Commission on Health Research in 1990 pointed to two gaps in health research. One was the lack of capacity for research in poor developing countries, as alluded to above. The other was the omission of international research to address problems primarily affecting people in developing countries.

The Global Forum meetings have witnessed increasing attention to research on and for developing countries, not least demonstrated at the Mexico meeting last year held in conjunction with the WHO Summit on Health Research. Much less attention has been given to the strengthening of research in and by developing countries. Most efforts in capacity strengthening are made as elements of research projects designed by Northern researchers inviting developing country researchers to cooperate. Few are directed in support for institutional development within a national system for research.

Thirty years of Swedish research cooperation with low income countries has taught us several lessons. We feel it is high time to engage with colleague donor agencies in concerted efforts to support research systems rather than projects. Following a brief account of our learning process and some elements of success, I will propose how we could jointly enhance the effectiveness of support for research capacity.

The Swedish experience

A multitude of approaches flourish on how to build research capacity. The Swedish development cooperation has, since the start of research cooperation in 1975, tried different models. The modalities for support to sustainable research capacity building have gradually evolved, always in an open dialogue respecting the needs and priorities set by the cooperating partners.

Already in the early years, attempts were made to assist countries in their efforts to build research systems. For instance, attempts were made to set up research council-like bodies to offer possibilities for competitive research funding. However, these attempts turned out as somewhat premature as the numbers of advanced research groups were too scarce to provide a basis for peer review of competing application. Instead, projects were designed with the objective of contributing to creative research groups active in national institutions. Research training was designed as sandwich-programmes for staff development, with external supervisors visiting and short visits abroad by the PhD candidate. Equipment and library support was part of the comprehensive support programmes. As the research groups gradually developed, the support shifted from a patchy support to a more systematic approach of support for institutional capacity development.

Since the early 1990s, Sida support has been designed as comprehensive support for institutional development for research focusing on national universities. The underlying assumption is that each country needs at least one qualified research university to serve as the hub for research. In addition to research training of academic staff, equipment and infrastructure such as ICT and libraries, emphasis has been directed to university reform processes and research management, including mechanisms for evaluating and selecting research proposals. In these situations, capacity to formulate researchable questions, design and implement research is steadily growing along with enhanced quality of the academic teaching. Eventually, we hope to see that increased credibility and applicability of research results will stimulate the motivation for national spending on universities and research.

Parallel with country level support, Sida supports thematic regional and international research programmes within areas of particular concern for combating ill-health and poverty in

low-income countries. Efforts are made to facilitate links between national level research and these thematic research programmes. As obvious from the Tanzanian case described below, such links may be mutually beneficial. Increasing capacity for research at the national level enhances the capacity to draw upon international research for local use. Inversely, situated research may bring important findings to the international level.

The Tanzanian example

Inequalities prevail in research cooperation, with the stronger partner often taking the leading role, but we see encouraging examples of change. One example is the support to HIV/AIDS research in Tanzania. Attention to HIV/AIDS was called by researchers in Tanzania in the mid 1980s. In 1986, Sida responded to their request for funding, and has since then been supporting HIV/AIDS research in Tanzania through the bilateral TANSWED programme. Since its inception, the programme has brought together Swedish and Tanzanian researchers in over ten projects in clinical medicine, microbiology and immunology, epidemiology, reproductive health, as well as in social science. Support for research projects has been embedded in a framework agreement for institutional development including support for laboratories, libraries, ICT connectivity as well as open funds which faculties can allocate for minor research.

Support for research projects has been embedded in a framework agreement for institutional development including support for laboratories, libraries, ICT connectivity as well as open funds which faculties can allocate for minor research

Research areas and results of the TANSWED programme include epidemiological studies that made it possible to monitor changing infection rates, e.g. the decreasing incidence in Kagera region in Tanzania, one of the areas where HIV was first detected. Another important field of research has been the evaluation of laboratory tests and testing strategies tailored to conditions in Tanzania. Today, these tests are used throughout the country. In 2002 the prestigious medical journal *The Lancet* published the results of the Petra study, one of the first large intervention trials in Africa of mother-to-child transmission of HIV. The study was a WHO/UNAIDS-coordinated multicentre study in South Africa, Tanzania and Uganda, where Sida financed the Tanzanian study. One important result is that short-term treatment of mothers and children with a combination of two antiviral drugs reduced the rate of infection transmission up to 6 weeks of age by more than 60%. After 18 months, however, transmission was comparable with the rate in a group that received no treatment. The discouraging results are still important because they show the significance of infection transmission via breast milk. This study was followed by the MITRA study that investigated a strategy for preventing the spread of infection via breast milk. In this study, children born to HIV-infected mothers in Tanzania received continued prophylactic treatment for 6 months. This is followed with an ongoing follow-up study.

Since the late 1980s Sweden has supported several projects focusing on developing HIV vaccines. An EU and Sida supported vaccine trial to see whether the vaccine is safe and free of unacceptable side effects started in 2005 in Stockholm, Sweden. If the results show promise, it will pave the way for larger vaccine trials in Tanzania in 2006. The vaccine was developed to target the viral types prevalent in East Africa. According to international regulations the vaccine, which was first manufactured in Sweden, has to be tested on healthy volunteers in Sweden. However, the capacity built in Tanzania will allow for the next phase there.

Fred Mhalu, professor at Muhimbili University College of Health Sciences and coordinator of the TANSWED programme has summarizes the outcome as follows: 'The programme has had a big impact on the building of research capacity in Tanzania and on training of Tanzanian researchers. Another impact is the creation of knowledge and experience that has been utilized by the national AIDS control programme in Tanzania, but also in global AIDS strategies. The programme's greatest strength is that Tanzanians have been in the driver's seat. Swedish support has been essential and catalytic. But the decision-making has been on our side. I would say this has been exceptional north-south collaboration. Not many collaborative research projects have been able to do it this way.'

It is clear that Sida support for national level research has contributed to building research capacity, which adds the perspective of low-income countries to the international health research scene

It is clear that Sida support for national level research has contributed to building research capacity, which adds the perspective of low-income countries to the international health research scene. As for the lasting impact on national research capacity, a number of problems need to be overcome at individual, institutional and national levels. At the level of the individual, there are many challenges. Often clinical activities may be demanding and professionally more rewarding than research when resources are scarce. Institutional awards and promotions do not always favour research efforts. Most importantly, however, is the lack of a national strategy for optimising resources for research and the subsequent fragmenting impact of external cooperation opportunities. Even when addressing similar issues, such projects rarely cooperate. In contrast, they often compete for the few qualified national counterparts.

Conclusion

The Tanzania case illustrates the benefits of supporting institutional capacity for research, as compared to individual projects. However, important challenges remain unsolved in relation to sustainability of the capacity gains. Institutional reform based on strategic plans, for the institution at large as well as for research, brought about decided improvements in the capacity of the university to promote and support research and make better use of external support. Similar coherent plans are needed at the national level. When Tanzania implements its joint assistance strategy, a coherent plan for research development should supplement the various sector strategies. Forging support from the multitude of donors who have pledged to align themselves could mean a breakthrough for the development of Tanzanian research.

Proposal for joint action

We now invite our donor colleagues to join in the country level dialogue for a coherent research strategy – not merely for health research but for research at large. Strategic use of scarce resources is not the least important in low income countries which need a research system to 'think themselves out of their predicaments'. A possible test case would be Tanzania where plans for alignment to national strategies and harmonization of donors are advanced. A national system for research should develop based on analysis of current policies, organization and resources flows for research, and an overall analysis leading to a strategy for how to make the best use of available resources. It involves strategies for institutional arrangements, for creating and stimulating individual researchers, for allocating national funds and for utilizing cooperation opportunities. We should all make sure that our support for research in and research cooperation with developing countries is in line with national strategies. We should also encourage the efforts of the WHO to underline the need for national funding of health research as part of a research system.

A second proposal is to combine the work of the Global Forum on Health Research and the Council on Health Research for Development (COHRED) in joint efforts of understanding options for systems conducive to health research. Such systems would be able to promote capacity for biomedical, behavioural and social health research capable of interacting with international research as well as capacity to study health systems.

The success of the Global Forum should be better exploited for the benefit of low-income countries. The COHRED concern for country-level approaches should be given equal weight in this combined organization. Sida would be willing in the future to provide continued support for such a new alliance. ❑

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A new school of public health in Bangladesh



Article by A Mushtaque R Chowdhury

The world has made spectacular progress in the past century, which has brought prosperity and better health to many. However, the benefit of this has been much less striking for the greater part of the developing world. The poor-world rich-world divide is well known, as is the divide between dominant and marginalized groups within countries. While the inter-country inequities in health were known previously, the past decade has seen the unearthing of intra-country inequities in almost every corner of the world.[1,2] Unfortunately, the gap between the rich and the poor in many societies has either remained the same or has shamelessly widened.

The Millennium Development Goals (MDGs) have raised new hopes for a world free of poverty and other 'deprivations', including ill health. A recent report published by the Task Force on Child Health and Maternal Health under the UN Millennium Project has called for a new vision and strategies to address the health problems that people in developing countries face. The report concluded that the world has enough knowledge and necessary technologies available to solve many of the health problems, but the real challenge lies in how these would be made available to the world's poor.[3] In other words, the potential to prevent the vast majority of the estimated 10 million annual child deaths and annual half million maternal deaths is within the world's reach, but there is a lack of relevant experience, resources, and probably, the will and political commitment, to make it happen.

Good public health is critical to making further progress, particularly in preventing deaths and suffering. Public health, as defined nearly a century ago by CEA Winslow, is 'the science and art of preventing disease, prolonging life and promoting health and efficiency through organized community effort.'[4] The Alma Ata Conference of 1978 reaffirmed the critical role of public health in attaining Health for All with particular emphasis placed on the centrality of equity, community participation and intersectoral collaboration. The recently formed WHO Commission on Social Determinants of Health recognizes the ever-important role that 'beyond health' measures play in ensuring and sustaining good health.

The extent of emphasis given to 'science' and 'art' that compose public health has recently been under scrutiny in the context of Schools of Public Health in the United States. It has been suggested that the schools in the United States have systematically ignored the art (application) in favour of the science (discovery and the medical model of diagnosis and treatment), has resulted in the imbalance and mismatch in the progress of the two arms of public health.[4] However, the failure to make many life-saving discoveries available to the vast majority of the world's population in the South cannot be fully attributable to this imbalance in the North. The history of developing countries investing in public health schools is not one of great pride, and their contribution to the improvement of the public's health is unclear at best. While the debate rages in the North, there is not much discourse in the developing countries, mainly due to the near absence of public health education (or public health schools) as a whole.

One of the first public health educational institutions in South Asia was the School of Tropical Medicine set up in Kolkata in 1922. However, such schools or their 'microcosm' in the Department of Preventive and Social Medicine in medical colleges in India and other South Asian countries failed to create much impact, as mentioned in a recent critique, due to: 'neglect, assignment of lowest priority, low prestige, poor quality of staff, and inadequate facilities such as transport, field practice areas'.[5]

Most public health schools set up in developing countries followed the path laid out by their counterpart schools in the North. To integrate community experiences in public health education, the Rockefeller Foundation helped set up a few 'Schools of Public Health without Walls' in Uganda, Kenya, Ghana, Zimbabwe and Vietnam. However, the number of such and other public health schools is too small to cater to the need. Then there are questions about their relevance and effectiveness. The Joint Learning Initiative on Human Resources for Health (JLI) identified a shortage of human resources in health as a major impediment towards attaining health goals in most developing countries. It was estimated that Africa alone would need a million new health workers if it is to achieve the MDGs.[6] To address the many problems that public health faces now and to test new teaching-learning methodologies, BRAC, a non-governmental organization (NGO) has set up a school of public health in Bangladesh. Named after the late Executive Director of UNICEF, the James P Grant School of Public Health is breaking new ground in innovative teaching and in creating

leaders for public health in developing countries.

The James P Grant School of Public Health

From its long involvement in the health field,[7] BRAC felt the need for a new breed of public health graduates who would simply be different in order to serve the poorest. FH Abed, the founder and chair of BRAC first conceived the idea of the School in the late 1990s. Afterwards, he consulted with a few public health leaders in the world: Jon Rohde, Patrick Vaughan, Richard Cash, Lincoln Chen, Cole Dodge and David Sack, who enthusiastically welcomed it. In 2001, Jack Bryant and Richard Cash undertook a feasibility study. It was preceded by a detailed survey of existing public health education in Bangladesh and the region, their relevance, quality and method of instruction and the job prospects of public health graduates.[8] The Bryant-Cash study found great potential for a new school of public health that could cater to the needs of not only Bangladesh but the region.[9] A meeting of the JLI in June 2003, hosted by BRAC and attended by HR experts from all over the world, wholeheartedly backed the idea of the School. BRAC thus went ahead and set up the School in collaboration with ICDDR,B: the Centre for Health and Population Research, also based in Bangladesh.

Why a school of public health and why at BRAC?

The shortage. As mentioned earlier, there is an acute shortage of human resources for health in developing countries, and the institutions that provide training are inadequate to meet the need. The United States, with a population of about 280 million, for example, has over 30 accredited schools of public health. South Asia with a population of 1.5 billion, on the other hand, has 12 institutions dedicated to public health training.[10] Bangladesh with a population of 140 million has only one institution that offers a Master in Public Health degree (MPH).

Clearly there is a need for many more such schools

Curriculum and teaching methods. For many of the existing schools, the curriculum followed is not always relevant to society's needs. In the absence of a modern and latest curriculum, the students are not well prepared to take on effective leadership roles and responsibilities in an ever-changing world. The teaching methods used are often less effective as they use didactic and rote learning without much emphasis on interactive learning. There is hardly any practice of field-based experiential learning.

Public health and Bangladesh. Despite widespread poverty, Bangladesh has done quite well in social development, particularly in education and health. The infant mortality and fertility rates have more than halved since independence, life expectancy has risen to over 60 years, with the disappearance of female disadvantage, various intervention programmes such as oral rehydration therapy (ORT) for diarrhoea, immunization and family planning have been successful and health equity has registered improvements.[11] Bangladesh is the home of many of the world's most successful NGOs such as Grameen, BRAC, etc. Yet challenges galore remain: maternal mortality is still unacceptably high; nutritional status has not improved to an expected level; and people remain poor. The management of the health system is a major challenge.

Presence of ICDDR,B. ICDDR,B is one of the most reputable health research institutions in the developing world. With its world-class researchers (potential faculty for the school), state-of-the-art laboratories, and libraries it is a great resource for any school of public health. It has one of the world's most sophisticated demographic databases.

BRAC as the host. BRAC is one of the world's largest and most successful NGOs. Its innovative programmes have earned wide reputation: ORT, TB/DOTS, nutrition, non-formal primary education and micro-finance. BRAC is present in over 70% of Bangladesh's 84,000 villages and has a wide network of residential training centres. Its research department is large and carries out relevant interdisciplinary research. BRAC's dependence on donor support has diminished significantly as it generates nearly 80% of the budget from its own domestic resources. The school builds on and demonstrates the experience of BRAC in the provision of affordable health services to the poor. Access to such a resource is a privilege which no other school can imagine.

Combat brain drain. It is expected that graduates trained in the South will stay in the South.

Goals and mission of the BRAC school

The long-term goal of the school is to improve health outcomes in Bangladesh and other developing countries, applying the best public health science. The school aims to produce graduates who are:

- Life-long, problem-based learners and critical inter-disciplinary thinkers.
- Contributing to the expansion of knowledge through research.
- Leading public health practitioners, researchers, managers, academicians and policy makers.
- Advocates/stewards of public health and policy at the community, district, national and international levels.
- Promoters and practitioners of both the science and art of public health.
- Committed to the health needs of the global South.

The training provided at the school will:

- Be community-oriented providing experiential problem-based teaching centred around the public health problems of Bangladeshi communities.
- Emphasize critical, innovative thinking that is rooted in best practice and rigorous research methods.
- Use a multidisciplinary intersectoral approach to teaching and problem-solving.

- Inculcate the values, vision and experiences of its founding and partner institutions into the daily work of its students and graduates.

Core values

- Equity – improving the health of the poorest, ethnic minorities, women and children, and other disadvantaged and marginalized groups.
- Scaling up – bringing the fruits of development and new innovations to as large a population as possible.
- Responsiveness to, respect for, and learning from communities.
- Learning from own mistakes and building on successes.
- Intersectoral and interdisciplinary approach to development.
- Diversity and heterogeneity among student body.
- Partnership and collaboration.
- Creating new knowledge and translating it to improving the health of the population (the science and art of public health).

Partnerships and collaborations

BRAC is working with many institutions in implementing the school's goals. These include ICDDR,B (Bangladesh), Columbia University (the United States), London School of Hygiene and Tropical Medicine (UK), Uppsala University (Sweden), University of Amsterdam (The Netherlands), Carleton University (Canada), George Washington University (the United States), Harvard University (the United States), Johns Hopkins University (the United States), Karolinska Institute (Sweden) and Umea University (Sweden).

An International Advisory Board (IAB), chaired by Professor Allan Rosenfield of Columbia University, provides guidance in implementing the school ideals.

The Master of Public Health Programme

The School's first major undertaking is a Master of Public Health (MPH) Programme which opened its doors to students in February 2005. It is a 12-month programme divided into three blocks. The first 6 months, which are completed at a rural campus, teach public health concepts, competencies and approaches (anthropology, biostatistics, epidemiology, health economics and management). For the next block the students move to Dhaka where they attend[11] short courses on various aspects of public health practice. In the final 10-week block, students carry out independent field studies of intervention programmes of their own choice.

Curriculum development

The school followed a rigorous process of consultation and learning in designing the curriculum for the MPH programme. The feasibility study provided some initial suggestions on the list of potential courses that were further revised by the JLI meeting. The IAB in its various meetings also provided inputs into the process. But the major inputs came from the two meetings of course coordinators that were held in August 2004 and April 2005. The first meeting, attended by all course coordinators and curriculum experts, discussed the various courses and came out with the curriculum, with a day-by-day lesson plan. The second meeting reviewed the experiences thus far and discussed the curriculum for the Dhaka-based courses. An important discussion point in both the meetings was how to operationalize the community-based experiential learning approach.

Community-based experiential learning

The village exposure is the 'foundation' of the programme. Each class gets its 'own' village (the social laboratory) raising a sense of uniqueness by students and the real work of their community exercises. The village is chosen in collaboration with local leaders who are well briefed in advance. The village leaders are informed about students' work (interviewing, making maps/sketches and observing village life), but the students provide no intervention in terms of health care or other inputs. However, they do advise villagers to go to existing facilities in case of any perceived or discovered needs, and after the conclusion of their work in the village BRAC would start discussing new interventions in the village based on the identified needs. Students provide feedback to villagers that may include recommendations for further action. During the Dhaka semester, students visit urban communities for specific purposes such as gaining an understanding of the life of the elderly, assessment of water and sanitation and waste disposal.

The first course (Introduction to public health) started with an immersion of the students into the life of the villagers (and urban slums). On the second day, the students walked through the village (transect) and then investigated a pre-selected issue such as food security, nutrition, major illnesses, sanitation, housing, or government health services by informal interview, observation, and participatory methods. This was repeated in an urban slum on the fourth day. The second course, anthropological approaches, took the students further into the village situation exposing them to different aspects of health such as menopause, ageing, sanitation, traditional practice of medicine, essential drug use, etc. They spent an extended amount of time with villagers visiting them three to four times in a week.

Such close interactions create close bonds between students and villagers. For the third course (epidemiology, biostatistics and research design) the students surveyed the village for a specific health problem such as hypertension (blood pressure measurement) and used the data to add meaning to various concepts, competencies and skills they learned in biostatistics. In epidemiology they do outbreak investigation, and in research design, they carry out a quantitative health needs assessment. For the health management course, the students visit and study different primary and tertiary health facilities run by government,

NGOs and the private sector for hands-on learning of management concepts. They also visit organizations that are known for better management practices, such as BRAC.

The student body and faculty

The first MPH programme has 25 students. They all have at least 16 years of schooling and were selected through a rigorous process of a written test, group meeting and individual interview. The group is diverse:

- Female: 13, male: 12.
- Bangladeshi: 15, international: 10 (Afghanistan, India, Kenya, Nepal, Pakistan, Philippines, Uganda, the United States).
- Medical doctors: 15, non-doctors: 10 (dentistry, nursing, demography, philosophy, economics, statistics, sociology, business).

The core faculty is small with just four members. The others, numbering nearly 40, come from BRAC, ICDDR,B and foreign partner institutions. For each course there is a foreign faculty member and one or more local counterpart(s). The plan is to gradually reduce dependence on foreign faculty through induction of more core faculty.

To facilitate all-round learning, the school also organizes seminar programmes and other events. For example, in a seminar series on 'successful public health programmes', the students present case studies selected from a recent volume.[12]

With generous grants received from donors, BRAC provided full scholarships to all students in the first group. The one million dollar Global Health Award that BRAC received from the Gates Foundation in 2004 is being used as an endowment for the school.

A built-in evaluation is in place to understand progress and to measure success. A doctoral student from the Teachers College of Columbia University is documenting progress as a participant observer.

Research

Research is a core function of any vibrant academic institution. Although it is not emphasized in Bangladeshi universities, research is an important component of the BRAC school. Current research projects comprise:

- Monitoring equity in the Bangladesh health system (with ICDDR,B and MoH).
- Study on sexual and reproductive health and rights (with IDS/Sussex, Indepth Network, Engender Health, etc).
- Global Health Equity Project (The World Bank).

Concluding remarks

The BRAC School of Public Health is new, with the promise of becoming a centre of excellence in research, practice and education in Bangladesh. BRAC is promoting a new paradigm in public health education that is problem-based, community-centred, experiential and yet academically rigorous. As we gain new experiences through the first MPH group and research programmes, it will be scaled up to train a larger number of future public health leaders. It is hoped that with the core values inculcated, BRAC School graduates will simply be different, breaking new grounds in both public health practice and research. ❑

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Establishing schools of public health in India



Article by K Srinath Reddy

India is experiencing a rapid health transition, with multiple contributors to early death and disability threatening the strength and stability of her developmental efforts. While several regions in India still suffer the burdens of infectious diseases, nutritional deficiencies and pregnancy related problems, many other regions are experiencing rapidly accelerating epidemics of noncommunicable diseases such as cardiovascular diseases, diabetes, cancers, mental illness and chronic lung diseases. New infections like HIV/AIDS and a rising toll of accidental and non-accidental injuries also contribute to this triple burden of disease which assails health and limits the productivity of persons in early and mid-life years.

Not withstanding the substantial progress in health indicators since independence (e.g. doubling of life expectancy to 63 years, halving of infant mortality to 67 deaths below 1 year for every 1,000 child births), India faces two serious health challenges:

- Rising disease burden – resurgence of communicable diseases, rise in lifestyle driven noncommunicable diseases (e.g. cardiovascular, cancer, diabetes), and emergence of other health burdens (e.g. accidental injuries).
- Inadequate response to the growing health challenge – inadequate government spending on health (only 0.9% of GDP compared to 1.8% by China), poor allocation of the amount that is spent (wide urban/rural disparity, most needy states spend less) and inefficient, ineffective utilization of the allocated resources (e.g. 10–25% of funds allocated are actually spent on programme delivery).

This composite threat to the nation's health and development needs a concerted public health response, which can ensure efficient delivery of cost-effective interventions for health promotion, disease prevention and affordable diagnostic and therapeutic health care. Since the determinants of health are multisectoral, it is essential to develop a supportive policy framework that addresses and influences all of those determinants. Health care too needs to be addressed not only from the scientific perspective of what works, but also from the social perspective of who needs it the most. Equity issues and a human rights perspective, therefore, become important considerations in exercising choices in health care.

Research, which informs policy and empowers programmes, is a critical ingredient of the desired public health response. Diverse disciplines such as epidemiology, health economics, social and behavioural sciences and medical ethics need to establish synergistic links in designing and delivering health care in prioritized sectors. The interventions proposed need to be evidence-based, context-specific and resource-sensitive.

Public health should emphasize prevention through collective actions to address the underlying causes of disease and foster conditions in which communities or population groups may lead healthy lives. In this way, it extends the ambit of health care to areas beyond medical care. At the same time the broad domain of public health also embraces essential medical care and seeks to define its optimal utilization levels

This multipronged effort requires capacity building for health research, policy development and analysis, programme development and evaluation, health systems organization and for developing sustainable models of health care financing. Scientific research too has to span the spectrum of basic, clinical, social, economic, policy and programme research to be fully informative.

Public health practitioners include a wide range of professionals. Among them are health professionals policy analysts, epidemiologists, demographers, social and behavioural scientists, health promoters, social workers and community health workers. The development of their ability to meaningfully involve communities in public health, work in multidisciplinary teams and communicate with government and community leaders is as important as training them in technical skills. Public health practitioners need to have a sound understanding of the social, economic and environmental determinants of health to be able to have a useful role in their health impact. Public health administration is a specialized function to be discharged by trained pubic health professionals, rather than generalists who may be simply assigned such tasks as a matter of routine.

For decision-making in public health, reliable data and information tend to be unavailable. Even if data and information were to be available, to use these effectively would require analytical skills which may not be readily

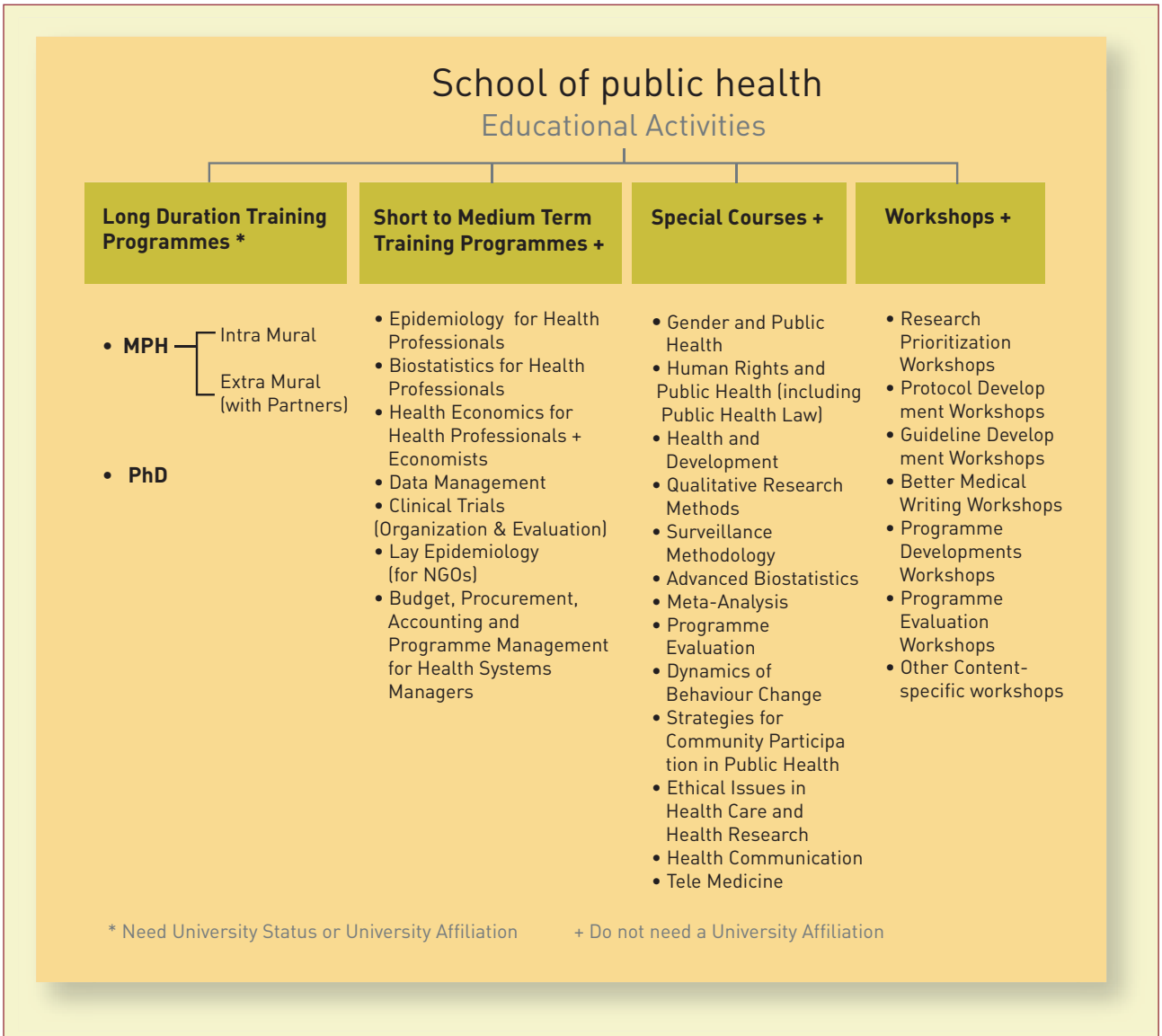


Figure 1: School of public health educational activities

available within the health system. To meet this gap, specific skills for designing, assessing and financing interventions would be required. Health policy analysts and health managers are two professional groups whose contributions could be vital to public health.

There is presently very limited institutional capacity in India for strengthening such research and policy development in the area of public health. It is essential to put in place staff who are well trained in the precept and practice of public health, through structured MPH and PhD programmes. At the same time, it must be recognized that training in public health need not and should not be confined only to long-term post graduate courses for a few students, but should also address the need to upscale the public health knowledge and skills of diverse groups of health professionals, health system managers and health NGOs who play a vital role as public health functionaries. This can be done through suitably structured short-term and medium-term training programmes.

Communities and civil society organizations are key allies for public health. Communities are a rich resource of skills and knowledge, playing a key role in serving the health and health-related needs of the community. Building their capacity for public health requires more attention than has been given in recent years. There is scope to build on their initiatives to expand the resource base for public health. The participation of communities and civil society organizations brings new institutional, technical, political and financial resources to public health. For this to occur, capacity needs to be created for evolving policies and programmes, which are informed by evidence and experience derived from good practice.

Health impact assessment is an evolving approach that could be used to consider the potential, or actual health impact of a proposed policy, programme or project. Health impact assessment is helpful for understanding and dealing with risks to health before they become unmanageable. There is scope to enhance the health impact assessment capacity

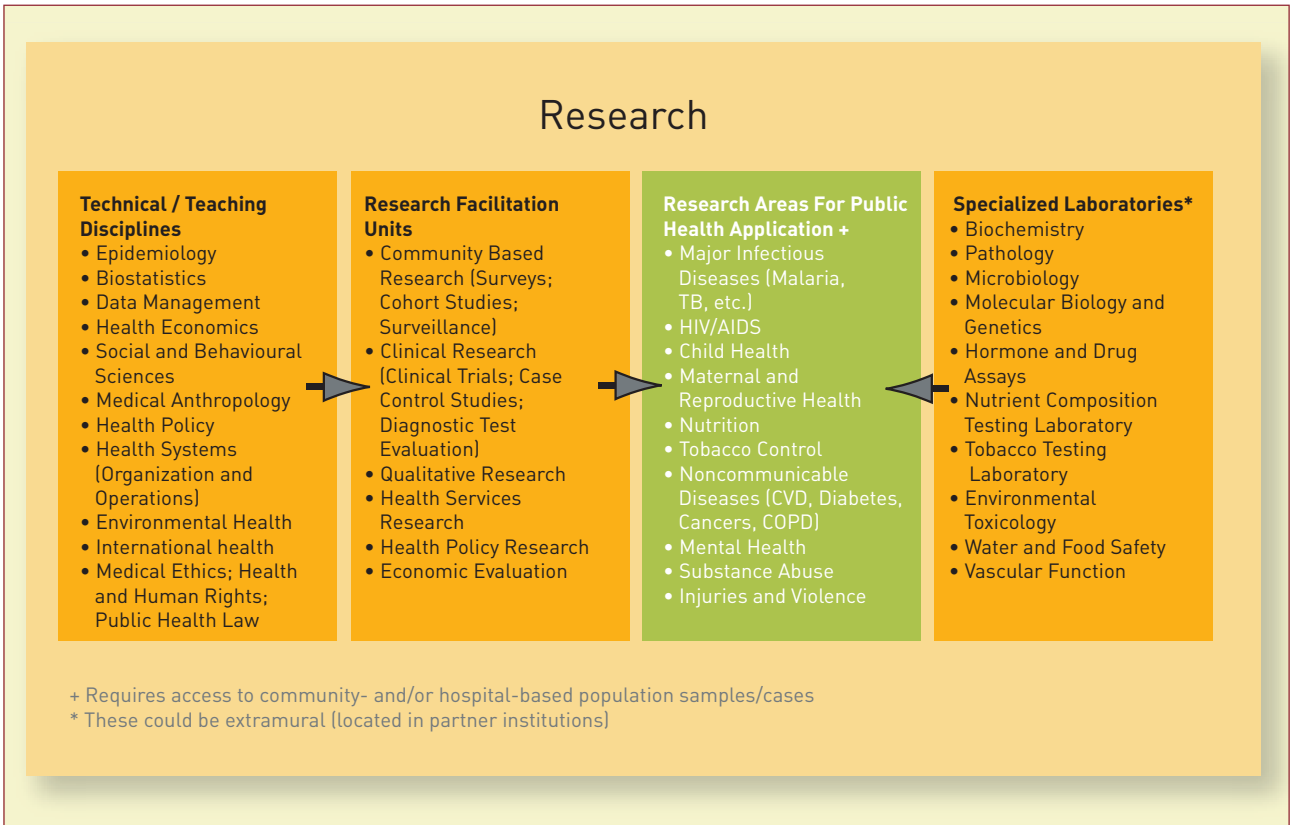


Figure 2: Research

not only of health ministries, but also of other ministries whose decisions and actions impact on health. Trained public health professionals would be valuable resources for conducting such an appraisal across several sectors.

There are two key deficiencies that explain the state of public health response in India:

- Insufficient human resource capacity.
- Inadequate support structures.

On the human resource side, there is a dearth of public health professionals in the government health machinery – more than 10,000 public health professionals would be required on an annual basis at different levels (from Primary Health Care Officer to the central level public health functionaries) to equip the government machinery with a qualified public health workforce. The supply of public health professionals falls far short of the need, with 95 institutes producing just 375 public health professionals. Even the best institutions are small in scale, suffer from a serious faculty crunch and run programmes of suboptimal quality. Moreover, there is a wide difference in the quality of existing public health professionals due to lack of academic standards. Finally, there is an absence of demand in the government machinery as there is neither a mandate for public health qualifications (push) nor a meaningful career track for those who qualify themselves in public health (pull).

With regard to support structures, there are three key deficiencies: absence of a surveillance system to collect and disseminate timely and accurate data; limited applied research that can utilize available data to shape policy; and absence of a credible entity that utilizes even the scarce available research to help shape policy.

Therefore there is a need to address the problem in an integrated manner that simultaneously works on the supply and demand sides of the problem. So far, no single entity has adopted this holistic approach to the problem.

School of Public Health: the concept

The School of Public Health (SPH) would focus on:

- ***Educational programmes*** (at masters and doctoral level) in public health, with standards of excellence comparable to the best institutions in the world and a course content which is especially relevant to India's needs.
- ***Training of health and allied professionals*** in the principles and practice of public health, through structured, multidisciplinary and target-specific educational programmes.
- ***Research on the prioritized health problems of India*** as relevant to strengthening public health interventions. SPH would initiate, conduct and evaluate such research which would include both knowledge generation and knowledge translation components.

Figures 1 and 2 profile the proposed activities and linkages related to education, training and research. The SPH would:

- Offer MPHs and PhDs. Subsequently, masters degrees in epidemiology, statistics, demography, health economics, health administration and health care financing could be

offered, based on the faculty strength which will accrue as SPH grows.
- Include trainees for the MPH programme from the following – doctors, dentists, nurses, nutritionists, social scientists as well as basic scientists allied to health. PhD students would be drawn from diverse disciplines relevant to public health. In addition, short- and medium-term courses would cater to specific target groups (Figure 1).
- Need to evolve a model best suited to India's needs and capable of addressing the agenda proposed in Figures 1 and 2. Given the large size of India and paucity of institutions which are actively engaged in training and research related to public health, SPH would adopt a 'Hub and Spokes' model in which it links with multiple institutions and agencies with convergent interests. Training as well as research would be conducted at several sites, with SPH playing the role of catalyst and coordinator.
- Be treated as part of the university system. It would seek and obtain a deemed university status, and would establish and build upon close connectivity with reputed medical colleges.
- Initially have to be drawn from existing Indian academic and research institutions, through advertised selection, and be supplemented by visiting faculty from affiliated international Schools of Public Health.
- Need strong linkages with academic medical institutions of excellence located in its vicinity. This would provide a broad platform for public health training and research, extending from the community to the clinic.
- Interface with the National Law Schools located at Bangalore, Kolkota, Hyderabad and Bhopal as well as with other leading law schools interested in developing the disciplines such as public health law and health and human rights. It would also seek collaboration with schools of business, management and administration for developing disciplines such as health care financing, health administration, health economics and health policy. It would link with schools of social sciences to develop training and research programmes in areas such as social determinants of health and disease, behaviour change and community interventions.
- Need to link with a community/population field unit that will serve as a demonstration site (for research and training).
- Need strong laboratory support for conducting multidisciplinary research relevant to public health interventions in the prioritized areas of communicable diseases, nutritional disorders, maternal and reproductive health and noncommunicable diseases. The nature of laboratory support required is indicated in Figure 2. Ideally, all or most of these laboratories should be located in the institutional complex of SPH. Some of these laboratories may be identified in partner institutions and linkages established.
- Draw trainees from two categories: (a) people already employed in government, academic institutions or NGOs who are engaged in occupations relevant to public health; and (b) people who are not currently employed, but are desirous of pursuing a career in public health.

The former category would return to their agency of employment, with enhanced knowledge and skills and would probably be provided opportunities to utilize them for the benefit of public health. The SPH graduates who are not so employed are likely to find employment in academic institutions, health research organizations, NGOs, international organizations working in the health sector in India and possibly with the government. If mechanisms are initiated by the government to create a cadre of public health professionals in health services, the employment opportunities would greatly increase. The government would also be well served by such a move.

Public Health Foundation: catalyst and coordinator

The efforts to establish a SPH in India would be facilitated by setting up a Public Health Foundation of India. Its role would be to:
- Establish new SPH, enhance existing institutions and network them to form a closely integrated group which will pursue the mission of strengthening public health related research, training, policy development, programme development and evaluation.
- Stimulate, support and strengthen research in prioritized areas of public health (knowledge generation research and knowledge translation research) by catalysing research initiatives by institutions/groups capable of undertaking such research and improving their capacity to conduct high quality research (through technical support as well as providing links to donors).
- Evaluate evidence required for policy and programmes (through analytic work involving critical appraisal of research results).
- Ensure better utilization of knowledge created through research, in formulation of policies and development of programmes (packaging, presentation and advocacy of research results, to develop evidence-based, context-specific and resource sensitive interventions).
- Facilitate implementation of prioritized health programmes by enhancing capacity among health system functionaries, across all levels of health care, to design and deliver the various strategic programme components.
- Promote transdisciplinary collaboration in the creation of knowledge that is relevant to public health and facilitate multisectoral coordination of implementation pathways.
- Facilitate the development of standards for training in public health and help to establish a credible and independent accreditation process.

The first steps: a multi-stakeholder consultation

To advance the agenda of establishing new SPH, and to strengthen existing institutions performing such a role on a limited scale, a multi-stakeholder consultation was conducted in September 2003, by the Ministry of Health and Family Welfare, Government of India.

The consultation had wide participation from critical stakeholder groups: public health officials from central and state governments; academic experts from leading public health or medical institutions in India; representatives of civil society groups; experts from public health institutions in the United States and Europe; and several multilateral and bilateral agencies.

The day workshop addressed four major areas relevant to the establishment and growth of public health institutions in India: governance of the public health foundation; curriculum design; research agenda; and pathways to catalyse demand for public health professionals in the government system.

There was strong support from the participants for strengthening capacity for public health related research and training in India. Some state governments were willing to make the required structural changes to create a public health cadre. Several bilateral and multilateral agencies expressed their support through commitments of technical and/or financial contributions.

The path ahead

Based on the recommendations of this consultation, the Ministry of Health, with some key partners from academia and the private sector assisting it, is moving ahead with plans for establishing the Public Health Foundation of India as a public-private partnership. This process is expected to be completed by September 2005.

The foundation, when formed, would mobilize resources for establishing two SPH initially (at Chennai in southern India and New Delhi in northern India). Later, it is proposed to establish three more schools at Hyderabad, Ahmedabad and Kolkata.

Conclusion

Investment in health is an imperative because health is a cornerstone of human capital and a critical component of economic growth. The once widely accepted notion that health goals would be taken care of as an automatic consequence of economic development has been strongly challenged. It is now well accepted that health and development are bi-directionally linked and investment in one reaps rich rewards for the other. It is essential that countries both invest in public health and ensure optimal performance of their health systems to realize the full potential of their developmental efforts.

The challenges that many developing countries are experiencing in improving their health systems are, to a large extent, the result of long-term neglect in the planning and management of capacity building in public health. This need is now being urgently addressed in many developing countries. India has begun this task in earnest. ❑

Acknowledgement

The author wishes to thank Mr Prashanth Vasu and his colleagues at McKinsey & Company, whose analytic work contributed to the identification of the needs and opportunities for establishing SPH in India and is reflected in this article. McKinsey & Company, through its pro bono work, is assisting the Government of India in creating public-private partnerships for establishing the Public Health Foundation of India and new SPH.

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Professor Reddy is also Chair of the World Heart Federation's Scientific Council on Epidemiology and Prevention. He is currently assisting the Government of India in the initiative to establish SPH.

Health research in Central Asia



Article by Sylvia de Haan (pictured), Kaspar Wyss and Maksut Kulzhanov

Health research is essential to obtain up-to-date information of relevance to the local situation to inform policy and decision-making.[1,2,3] Health research can also contribute to identifying, analysing and addressing inequities, for example in resource mobilization, allocation and utilization resulting in unequal health status. Essential inputs for health research are human resources and institutions. Recently, a number of publications have highlighted serious health workforce shortages[4,5,6,7] that are further aggravated by poor human resource management practices,[8,9] and it is becoming increasingly clear that human resources largely determine whether and how health services are offered to those in need[10,11,12] as well as whether national health research contributes to addressing the health needs of countries.

This general concern with human resource development and management is particularly valid for the situation in the Central Asian countries. These countries in transition face many challenges in improving population health, health care delivery and access to health facilities thereby addressing equity concerns and poverty alleviation. While Central Asia has progressively become a priority area for development assistance and health sector development, investments in health research have largely remained a neglected area. Using the example of Kazakhstan and Tajikistan, this article argues that health sector development and ongoing health sector reforms in the Central Asian Republics would benefit from strategies and policies to strengthen institutions and their research capacity to address priority health needs and contribute evidence to inform decision-making.

These countries in transition face many challenges in improving population health, health care delivery and access to health facilities thereby addressing equity concerns and poverty alleviation

Central Asia – a region with countries in transition

At the crossroads between Asia and Europe, the countries of Central Asia (Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan and Uzbekistan) have faced many challenges in establishing and stabilizing their states since gaining independence in 1991 upon the dissolution of the Soviet Union. The countries have gone through a health and health system transition. Health status indices, as well as human development indicators, have deteriorated since the 1980s. The first years of Kazakhstan's independence were characterized by economic decline. Economic recession in the early and mid 1990s led to a dramatic rise in poverty, rising unemployment rates, growing income disparities, uneven regional development and declines in health and educational services.

The country's transition problems have been reflected in its decline in development rankings. In 1990 Kazakhstan was among the countries with high human development, ranking 54th out of 173 countries in UNDP's Global Human Development Report.[13] In 1995 it had dropped to rank 93, and in the most recent Global Human Development Report Kazakhstan occupies the 78th position.[14] Although GDP increased on average 8% annually over the last 5 years, this has not led to an increase in the proportion of GDP spent on health, which remained at 2%. The transition period in Tajikistan has been more difficult, as it was worsened by civil war. Its economy collapsed, and between 1991–1997, GDP contracted by almost 70%. With a per capita GDP of US$180, Tajikistan remains one of the poorest countries in the world.[15] It ranks 116 in the 2004 Human Development Index.[14]

Health systems and health sector reform in Central Asia

Along with social and economic disparities, inequality has emerged in the population's health and in access to health care.[16,17] For example, in Tajikistan the better off income groups are reported to have higher health service use rates than poor groups.[17] Central Asian countries inherited a Soviet health system, which offered in theory universal access to a basic level of health care. This system was found to be no longer affordable and years of under-investment left their mark. Public expenditure on health in Tajikistan is estimated to be a mere US$1.5 per capita.[15] Health sector reforms are being implemented across the region. In Tajikistan the focus is on strengthening primary health care, distributing resources according to need, developing human resources, rationalization of services, improving quality of care, strengthening management capacity, ensuring necessary information for management and creating personal responsibility for individual health among the population.[18] It

is clear that, in spite of available knowledge, these priority areas require additional evidence, information and research to support rational decision-making and policy development in key areas like family medicine strengthening, financing reforms (including social health insurance) or human resource development.

Health research in Central Asia

The health and health research workforce have faced special challenges during these last two decades, being exposed to a new market economy setting, changing institutions and decreasing funding levels. Health research systems, inherited from the Soviet era, largely focus on clinical and biomedical disciplines, and include a network of scientific centres and a health research workforce focusing on these disciplines. Historically, less emphasis is given to public health, primary health care research priorities and needs[19] and social science. In addition, the financial resources for health research are used primarily to cover salaries and infrastructure, and thus few resources are available for the actual carrying out of research.[20] This makes the health research system sensitive to the influence of external donors and international research institutions and may lead to these actors determining the research agenda,[21] rather than national needs and priorities guiding national research activity.

Recognition of the need to reform the health research system, along with the health system, is shown in the recently approved national health programme in Kazakhstan for 2005–2010.[22] The broad public health oriented focus of the national health plan is supplemented by a chapter referring to the need for a reform of the medical sciences. The fundamental as well as applied research disciplines should focus on public and population health priorities. For this approach to succeed major emphasis on strengthening the human resources for health research is required.

Human resources for health research

A wide range of skills (both at individual and institutional levels) are needed to generate, analyse and utilize knowledge that can be used to inform decision and policy-making and thus contribute to better health and a more equitable distribution of health gains.[23,24] Besides training sufficient numbers of people in all relevant disciplines, an enabling environment for producing research, including career opportunities, research inputs, and access to networks, are generally crucial for strengthening human and institutional capacity for health research. The absence of these preconditions has been highlighted as contributing to the migration of health professionals.[25] Komarov and Tcherniavskii[26] describe the health research situation for the Russian Federation, in which they point to the decreasing number of institutions as well as number of researchers. A recent study in Georgia, a country with a similar system and experiences, illustrates the negative impact of the decrease in human and institutional research capacity, and worked on rebuilding this capacity to ensure that health research contributes to a responsive health care system.[27]

The fundamental as well as applied research disciplines should focus on public and population health priorities

An additional concern is that many of the international, vertical, disease-oriented initiatives attract well-qualified national professionals

Besides the migration of health and health research professionals to other countries, an internal brain drain is taking place. Well qualified people are increasingly attracted to favourable employment conditions in the private sector, as well as to international institutions operating within the country. An additional concern is that many of the international, vertical, disease-oriented initiatives attract well-qualified national professionals. This leaves more integrated approaches to health systems strengthening understaffed and under-researched. Evidence from other parts of the world shows exactly this: published peer-reviewed research from low-income countries is directed towards health priorities addressed by the major international vertical programmes, leaving other national health issues under-researched.[28]

Supporting health research development in Central Asia

The transition from the Soviet era and the drastic changes which characterize at present health systems in Central Asian countries, underline the need for data, information and knowledge, which could provide the basis for informed decision-making in health sector reform. It also underlines the need for a critical mass of individuals skilled in the production, management and utilization of such knowledge. Developing human capacity has to be complemented by building-up institutions that enable health researchers to work in a conducive environment.

No detailed and up-to-date assessments of health research and human resources for health research are available for Central Asia. Although it is clear that there is a discrepancy between the need for information and routinely collected health data and the information resulting from health research currently conducted, additional information on the health and health research situation in these countries is urgently needed. The Council on Health Research for Development (COHRED), jointly with local partners, is initiating projects in the region to map health research

systems. This process is, for Tajikistan, supported by the Swiss Development Cooperation (SDC), one of the few bilateral agencies actively supporting the health sector in the region. The information that will be gathered through these projects will provide a base for discussion with national and international partners on how to reform health research systems and ensure a better linkage between health research and health systems strengthening. In Tajikistan, project Sino, also funded by SDC and implemented by the Swiss Tropical Institute, strengthens capacity for planning, monitoring and evaluating health interventions. Using a participatory approach, systematic inquiries and research are undertaken by individual and institutional actors at various levels of the Tajik health system. The aim is to improve practices in the area of health sector reform, as well as to deepen the understanding of these practices and of the situations in which they are carried out. These experiences (e.g. in the area of financing reforms) are fed into national policy-making, and subsequently disseminated at oblast and rayon level.

Conclusion

A reorientation of health research in Central Asia towards a more public and population health oriented approach to address the most urgent health problems is needed. Existing institutions will need to review their mandates and discuss what their roles are in contributing to finding solutions for the national health needs of their country, and what capacity is required to fulfil this role. National and institutional policies for human resource and institutional development need to be developed that also take into account the enabling environment needed to offer appropriate working conditions. In addition, international research projects and programmes will have to contribute to the goals and strategies laid out in institutional and national plans. Their capacity building efforts should contribute to the overall national capacity to address public and population health priorities, thus strengthening national health systems. ❑

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Addressing neglected health issues

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Progress on the MDGs and the importance of an AIDS vaccine



Article by Robert Hecht (pictured), Sarah Post and Anita Alban

The movement to achieve sustainable reductions in poverty in developing countries has become a top global priority, as exemplified by the widespread and highly visible commitment to strive to reach the Millennium Development Goals (MDG) by 2015.

With increased investments and political support today and in the coming years, AIDS vaccines could be a pivotal element of this long-term effort to achieve the MDGs and reduce poverty. Because HIV and AIDS have a significant negative impact on many of the MDG indicators, lowering the number of new HIV infections through improved prevention could improve the chances of making progress on these social goals. And an HIV vaccine will almost certainly be needed in order to implement successful HIV prevention and stop the current AIDS pandemic.

Because a licensed and widely used AIDS vaccine is still some years away, it would not be realistic to expect such a vaccine to have a major impact over the next 10 years, up to the 2015 target date for the MDGs. But over the longer run, a vaccine could have a tremendous effect on the health and well-being of the developing world and its billions of citizens – in that sense, an AIDS vaccine should be seen as an essential tool in the quest to sustain and deepen progress on the MDGs for the entire 21st century.

This paper describes the results of recent policy research from the International AIDS Vaccine Initiative (IAVI) and others, illustrating the relationship between AIDS and several of the other MDG targets and highlighting the need and potential impact of a vaccine as an HIV prevention tool. Increasing worldwide investment in AIDS vaccine research and development must become a significant component of the world's long-term poverty reduction goals.

Interactions between AIDS and other development indicators

There are significant and complex interactions between conditions of poverty and AIDS. The causal relationships between conditions of underdevelopment and AIDS epidemics go in both directions (see Figure 1). Poverty creates conditions for the more rapid spread of HIV, and AIDS has a substantial negative impact on a wide range of social and economic development indicators.

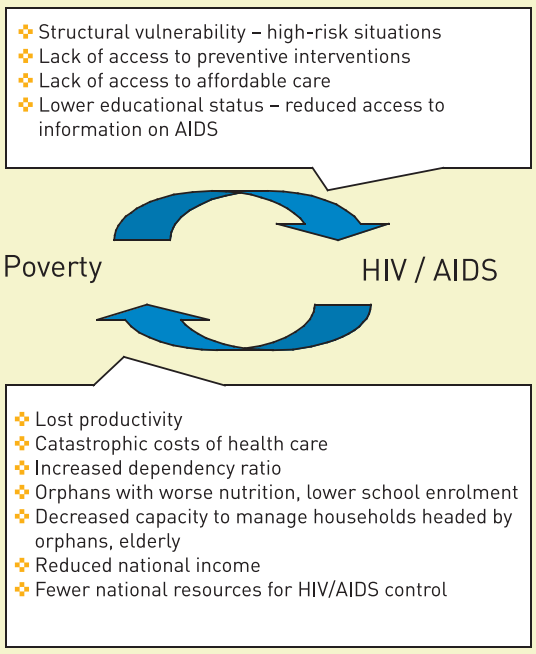
Underdevelopment can exacerbate both the transmission of HIV and the health effects of AIDS. People living in poverty generally have less education and are therefore less aware of the HIV threat and the methods by which they can protect themselves. Lower health status contributes to disease susceptibility. Many people living in economically precarious conditions end up in high-risk situations (engaging in commercial sex, injecting drugs, etc). Those who are poor and have limited access to medical care receive less antiretroviral treatment and therapy for opportunistic infections.

There is also a large and growing body of evidence suggesting that AIDS itself is a large contributor to poverty and other conditions of underdevelopment. In the sections below, we summarize evidence on the effects of HIV and AIDS on national and household poverty, food security and child nutrition, basic education, child health and the global tuberculosis (TB) epidemic.

National and household poverty

The first MDG target is halving the proportion of people whose income is less than $1 per day. Because the illness and death associated with AIDS increase household poverty, the AIDS epidemic is substantially undermining attempts to reduce extreme poverty in many countries, especially in Africa. Adults who fall ill lose income, and households must spend savings, sell assets, or take out loans to cover expenses and pay for medical treatment. In high-prevalence areas, widespread sickness and absenteeism can impair productivity and drag down GDP growth by as much as 2.5% per year.[1] A recent analysis that used household data from Botswana, predicted that the share of households below the poverty line would increase by 6 percentage points due to HIV/AIDS, and that the income loss among the poorest households would be, on average, almost double that of the population as a whole.[2]

The increasing number of orphans, especially in sub-Saharan Africa, is likely to further increase the impact of AIDS on poverty. At the end of 2003, there were more than 15 million children who had been orphaned by AIDS worldwide; this number is expected to grow to more than 18 million by 2010.[3] One projection estimated that in South Africa, 71% of children in 2010 will grow up in families missing one or both parents, as compared to just 15% living



Source: UNAIDS. AIDS, **Poverty Reduction, and Debt Relief.** Geneva, UNAIDS, 2001

Figure 1: **The causal relationships between conditions of underdevelopment and AIDS epidemics go in both directions**

in orphaned situations in 1990.[4] Orphaned children receive few of the advantages of parental investment, and a high proportion of orphans strains resources at a community level.

Furthermore, widespread disease can cause a vicious-cycle effect on parents' behaviour. As a recent paper outlines, scarce household resources (especially in households afflicted by AIDS) force parents to make investment trade-offs. In conditions of high HIV prevalence, parents assign a lower value to their children's human capital in adulthood, so they neglect long-term investments in the next generation's human capital (e.g. education). The result is that children (particularly those whose parents have died of AIDS) possess less human capital, and this effect will spill over through succeeding generations, reducing productivity and earnings, causing a gradual economic slowdown and potential collapse of the economy.[5]

Nutrition and prevalence of underweight children

The financial difficulties associated with HIV and AIDS can have a direct negative impact on progress toward another MDG target, that of halving the prevalence of underweight children by 2015. Illness and poverty can cause or aggravate food insecurity, as afflicted families reduce outside expenditures on food items, spend less time growing crops, or plant less nutritionally valuable crops to save time. For instance, a cross-sectional study in Rwanda found that 60–80% of rural households suffering illness or death reduced farm labour.[6] Adult mortality negatively impacts children's nutritional status as well: a study in Tanzania showed that maternal death was associated with a decline of one standard deviation in child height for age (known as 'stunting') while paternal death was associated with a decline of one-third of a standard deviation.[7]

HIV prevalence is strongly correlated with falling calorie and protein consumption and increasing income inequality in sub-Saharan Africa.[8] And because the energy requirements of children living with HIV/AIDS may be raised by 50% or more, the effects of inadequate nutrition are further exacerbated for infected children.[9]

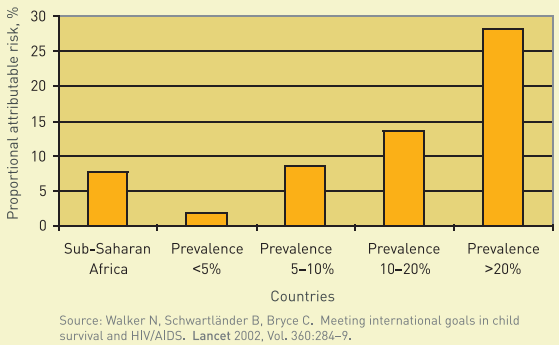
Primary school completion

AIDS affects student enrolment and teacher availability, both of which could have detrimental effects for the MDG of achieving universal primary education. Children in AIDS-affected areas leave school because they can no longer afford fees and school supplies and because their families increasingly rely on them to contribute economically to the household. This effect is most noticeable when a parent dies. For instance, one study in a high-prevalence area of Tanzania found that young children (7–10 years) who lost their mothers had their schooling delayed; another showed that maternal death in Mexico caused a significant increase in dropout rates.[10,11]

The increase in teacher mortality due to AIDS is a growing problem in sub-Saharan Africa. A comprehensive study of the South African public school system found that the proportion of mortality-related teacher attrition increased from 7.0% in 1997–1998 to 17.7% in 2003–2004, with contract terminations attributed to illness rising from 4.5–8.7% over the same period.[12] In many poor countries, administrators may face substantial challenges in finding qualified teachers to replace those who die of AIDS, so schooling suffers as a result. Even when replacement teachers may be readily available, the death of a teacher exacts costs (for temporary and permanent replacement as well as for training) on education systems that are already seriously short of funds.

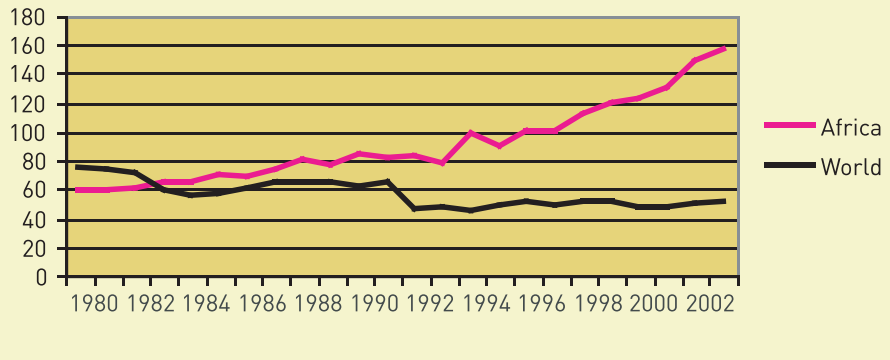
Child mortality rates

The AIDS epidemic has direct and indirect effects on the goal of reducing under-5 years mortality by two-thirds by 2015.



Source: Walker N, Schwartländer B, Bryce C. Meeting international goals in child survival and HIV/AIDS. **Lancet** 2002, Vol. 360:284–9.

Figure 2: **HIV-related population proportional attributable risk of dying before age 5 years, sub-Saharan Africa, 1999**



Source: WHO, Global tuberculosis control: surveillance, planning, financing. **WHO Report 2005.** Geneva: WHO, 2005.

Figure 3: Tuberculosis case notification rates, 1980–2003

In the absence of antiretroviral therapy for infected pregnant women, about 35% of children born to HIV infected mothers will acquire the infection. More than 60% of these children will die before their fifth birthday.[13,14] Beyond the direct mortality from HIV and AIDS, even uninfected children face risks from the economic and social consequences of parents' illness and death. Several studies have shown that children born to HIV-infected mothers are approximately three times more likely to die during childhood than those born to uninfected mothers, regardless of the child's HIV status.[15–17]

Incidence and treatment of TB

In many areas of the world, campaigns to reduce the prevalence and death rates associated with TB, and thus achieving the MDG of halting and reversing the global TB epidemic by 2015, are succeeding. However, the higher incidence of TB among HIV-infected individuals means that rates are actually increasing rapidly in high-HIV-prevalence areas, particularly in sub-Saharan Africa (Figure 3), Russia and some other countries of the former Soviet Union. One analysis found that if sub-Saharan Africa and the region of the former Soviet Union were excluded from global statistics, the 2015 TB prevalence rate would be half what it was in 1990.[18]

The risk of acquiring TB doubles soon after infection with HIV and continues to increase during subsequent years.[19] One study estimated that 9% of the estimated 8.3 million new adult TB cases in 2000 were directly attributable to HIV infection; the proportion reached 31% in the WHO African region.[20] Latent TB infection is much more likely to progress to active disease among people who are co-infected with HIV. HIV co-infection can also complicate the treatment of TB, making such treatment less effective and worsening the disease burden of both TB and AIDS.[21] In this way, the HIV pandemic stands as a significant barrier to achieving the MDG targets for TB prevalence and cure rates.

Existing responses to AIDS – better but insufficient

Because of the relationship between AIDS and other markers of development, scaling up and improving current prevention, treatment, and impact mitigation interventions can make an important contribution to broader development efforts. Antiretroviral drugs can reduce AIDS morbidity and mortality, improve household productivity and income and thereby food consumption and nutritional status. Orphan care programmes can help children stay in school, maintain better nutrition and grow up with better social skills and a positive outlook on life.

Existing HIV prevention methods, such as voluntary counselling and testing, condom provision and blood screening, are also part of the continuing effort to diminish the epidemic's effects and thereby reduce the negative effects of AIDS on the other MDGs. These interventions, however, have only been partly successful in stopping HIV transmission. New infections continue at a high rate – in 2004 more than 5 million people became infected with HIV. Existing prevention methods are also costly and may prove difficult to sustain over time. Without more effective prevention technologies, including the development and widespread use of vaccines and microbicides, it will be nearly impossible to curb the AIDS pandemic and attain the MDG of halting and reversing AIDS, and the other MDGs described will be difficult to maintain.

The United Nations Programme on HIV/AIDS (UNAIDS) estimates the cost of an effective global response to HIV/AIDS will grow to US$20 billion a year by 2007, of which US$10 billion will be needed for prevention services and US$7 billion for treatment, including antiretroviral drugs for just over 6 million people.[22] In 2003, by contrast, total official development assistance of OECD member countries was US$69 billion, including US$10 billion for all health services in the developing world.[23] Without a vaccine, these expected financial needs to fight the pandemic could swamp health spending and absorb a large fraction of all donor aid, crowding out funds for other vital development needs.

Treatment provision can facilitate HIV prevention, by fostering an environment of greater hope and openness and encouraging people to seek voluntary testing and counselling. Antiretroviral therapy alone, however, has little impact on HIV transmission or incidence, as empirical research and modelling has shown.[24–26] Without stronger prevention efforts, the number of people requiring AIDS care will continue to increase, further compounding costs.

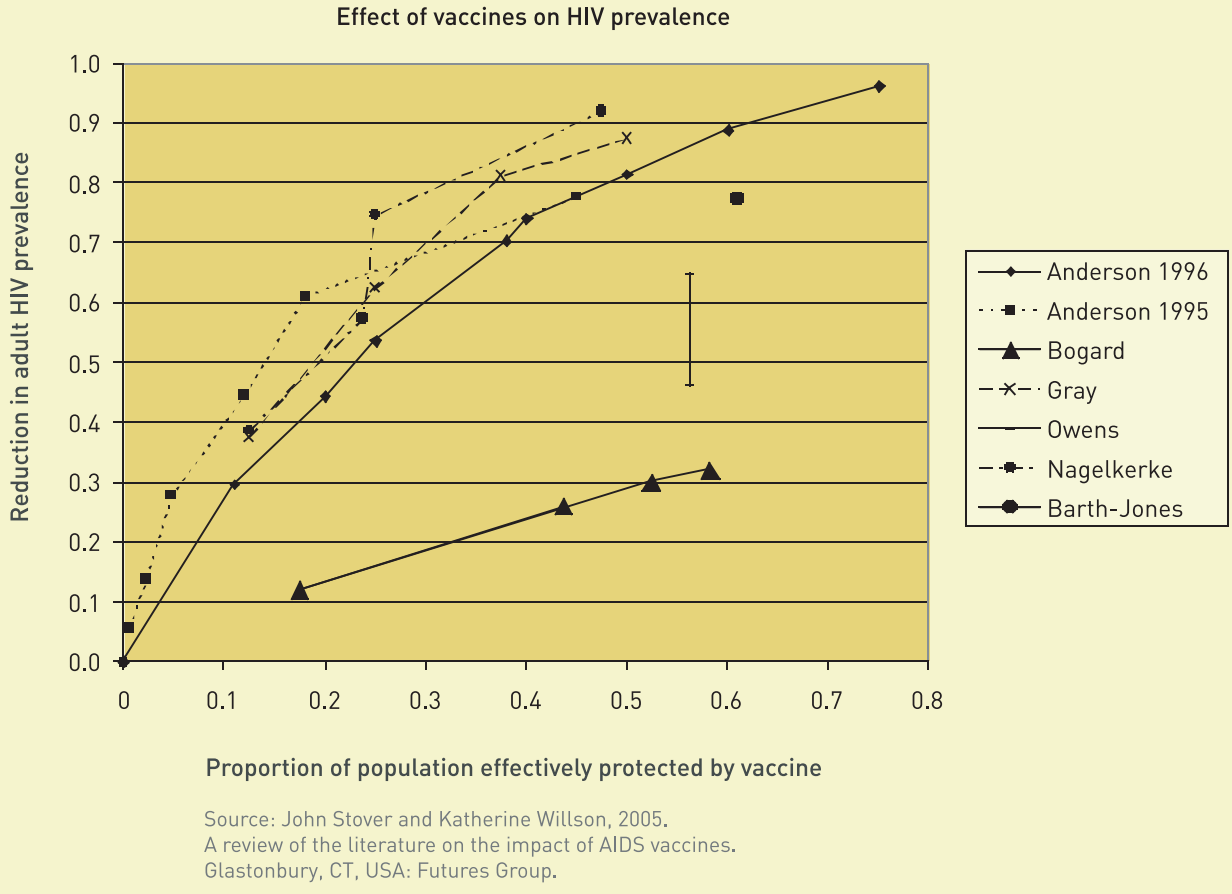
Current HIV prevention methods have achieved some noteworthy successes, but these have taken place mainly in countries showing high-level political leadership and effective management, as well as grass-roots implementation. But many of those infected with HIV or at greatest risk of infection live in countries where political commitment to fight AIDS or the capacity to manage prevention programmes is weak. In 2000 an estimated 17.1 million people with HIV infection were living in such 'fragile states' where intervention is most difficult.[27] To prevent the spread of HIV in countries with weak governance, easier and simpler prevention methods such as a vaccine are needed.

The first generation of AIDS vaccines may be only partially effective and will take time to deliver to at-risk communities. Hence they will need to be deployed in tandem with existing prevention methods, including condoms, as part of a comprehensive prevention strategy; antiretroviral coverage will remain an essential component of addressing the epidemic as well. Still, a vaccine would play a tremendously important role as part of an improved strategy to fight HIV/AIDS.

Why an AIDS vaccine would make a difference

Compared to other interventions, an AIDS vaccine would be less expensive and easier to deliver than existing prevention methods. It would provide durable protection via a few courses per person with occasional re-vaccination, or even via a 'one-time' inoculation. Vaccines can be delivered even when health systems are fractured and ineffective: they may have simpler technological requirements than current interventions and involve relatively low levels of staff training. Unlike AIDS treatment, interruptions in vaccine provision, though undesirable, would not undermine previous gains.

Vaccination programmes for other diseases have proven to be relatively good at reaching the poor and women, so an AIDS vaccine could help reverse some of the income and gender disparities that have fuelled the epidemic. The success of vaccine-mediated ceasefires in countries affected by armed conflict, including Sudan, Sierra Leone, Afghanistan and El Salvador, indicates the ease of vaccine delivery compared to other health interventions.[28] Because vaccine provision is not directly linked to sexual or other high-risk activities, it could



Source: John Stover and Katherine Willson, 2005.
A review of the literature on the impact of AIDS vaccines.
Glastonbury, CT, USA: Futures Group.

Figure 4: Impact of an AIDS vaccine on adult HIV prevalence after 20–25 years as a function of effective coverage

help reach marginalized or vulnerable populations and could also reduce stigma associated with HIV prevention.

Analysis of the potential impact of an AIDS vaccine suggests that even low-efficacy vaccines would provide significant benefits in terms of infections averted and healthy life-years saved. A review of the literature on AIDS vaccine impact modelling suggests that at moderate levels of effective coverage (a combination of vaccine efficacy and population reached), a vaccine could reduce the prevalence that would have been reached without a vaccine by as much as 70–80% in high-prevalence settings (Figure 4). One study found that in a high-prevalence population, a vaccine of just 20% efficacy could reduce prevalence by 44% over the course of 25 years if given to 60% of sexually active adults.[29] Another study, based on data from a long-term cohort study in Rakai, Uganda, found that a very low-efficacy vaccine could have a substantial impact on prevalence and incidence when combined with widespread use of antiretroviral therapy.[30] If an AIDS vaccine turns out to be highly effective and is used by larger numbers of adults and adolescents, its impact would be even greater.

Conclusion

The results from the work cited here indicates that a vaccine would be a vital new HIV prevention method, one that is needed to end the AIDS pandemic and help the global community succeed in reducing poverty and achieve the MDGs. They also show how a well-structured programme of policy research and analysis can help support such an argument. Such policy research can show how a disease like AIDS undermines progress toward other social and economic goals, how existing prevention tools are unlikely to stop the epidemic, and why a vaccine against HIV could make a significant impact.

From a policy research perspective, the next step is identifying the financing gaps and other public policy measures that would speed the AIDS vaccine research and development (R&D) process and hasten introduction and uptake. The International AIDS Vaccine Initiative and its partners are currently examining policy options to accelerate the development of a vaccine, including increases in targeted R&D spending, market guarantees to stimulate greater industry investments in AIDS vaccines and removal of legal and regulatory barriers that currently blunt vaccine research efforts.

Existing proposals to reduce poverty by increasing aid, tackling debt and reforming trade will help break the cycle of poverty and disease that grips many parts of the developing world. These efforts, along with expansion of existing HIV prevention methods and wider access to AIDS treatment, will help fight the epidemic and achieve gains in other areas such as education, child health and nutrition, and control of TB. But without new methods to prevent HIV infections, existing AIDS programmes will only have a limited impact in slowing the epidemic and AIDS will continue to threaten and undermine other social and economic goals. Redoubling current efforts to develop and deliver an AIDS vaccine will be essential for securing long-term development and prosperity for hundreds of millions of families in the world's poorest countries. ❑

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Opportunities for overcoming tuberculosis: new treatment regimens



Article by Maria C Freire

For centuries, tuberculosis (TB) has targeted the most vulnerable populations during their most productive working years, threatening economic and social well-being as well as health. TB is overwhelmingly concentrated in developing countries and its resurgence has been driven, in large measure, by the HIV/AIDS pandemic. Global control efforts, while making important strides, have been hampered by the shortcomings of existing diagnostic, prophylactic and therapeutic tools.

Breaking the links between TB and poverty and winning the battle against this killer depends upon modernizing today's cumbersome TB therapy that induces noncompliance, burdens healthcare systems and drains economies. A major goal and public health priority today has to be to make TB therapy as straightforward as curing other common infections by using the best, most modern and effective antibiotics possible. Although developing and delivering more effective medicines is the norm for diseases in industrialized countries, this does not hold true for diseases that disproportionately affect the poor. Fulfilling the Millennium Development Goals (MDGs) requires the international community to make an equal commitment to providing better treatments for TB and other diseases of poverty.

For the first time in almost half a century, a TB treatment breakthrough is possible due to concerted international efforts by members of the Working Group on New TB Drugs of the Stop TB Partnership. With contributions from public-private partnerships (PPPs), industry, academic and public researchers, multiple compounds are in or are advancing toward clinical trials, providing the foundation for a revolutionary drug regimen that can help achieve the MDG target to halt and begin to reverse the incidence of TB. The task is not simple, and success will depend on the sustained commitment and drive of scientists, policy-makers, donors and the public health community worldwide.

The need for new TB therapies

Modernizing TB therapy is a medical and moral imperative with direct public health benefits and significant socioeconomic returns. Improved TB treatment will save millions of lives by increasing compliance, speeding time to cure, overcoming resistance and being compatible with HIV/AIDS anti-retroviral (ARV) therapy.

Despite several important recent regional successes with the current method of drug delivery that helps ensure patient compliance – directly observed treatment short-course (DOTS) – overall disease trends reflect the inadequacy of the TB drugs themselves. It is estimated that between 2000 and 2020 nearly 1 billion people will be newly infected with TB, 200 million will become sick and 35 million will die.[1] TB's financial consequences for patients and their families as well as for healthcare systems and national economies are well understood. TB costs the world US$16 billion annually – $4 billion for the costs of diagnosis and treatment and $12 billion from lost income.[2]

These ongoing costs as well as the epidemic's trends mobilized donors, endemic countries, patients, as well as advocacy and treatment organizations to create the global movement known as the Stop TB Partnership in 2000, with the goal of eliminating TB as a public health problem. The Partnership's operative arm is composed of seven distinct Working Groups, three which work collaboratively to ensure that patients today are protected, diagnosed and treated as soon as possible while working diligently to develop the next generation of interventions (drugs, diagnostics and vaccines) and new control strategies to finally defeat this centuries-old foe. (The seven Stop TB Working Groups are: DOTS Expansion, TB/HIV, DOTS-Plus for MDR-TB, New TB Drugs, New Diagnostics, TB Vaccine Development and Advocacy/Communications/Social Mobilization.)

When it comes to treatment, the current arsenal of drugs is no match for TB. Standard TB treatment now relies on a 6–9 month regimen of four drugs, each of which has significant disadvantages. While the current regimen successfully treats TB under appropriately implemented DOTS, the combination has failed to substantially reduce the overall levels of morbidity and mortality. Patient noncompliance has fuelled the emergence of multi-drug resistant strains (MDR-TB), and the symbiotic interaction between TB and HIV/AIDS and the incompatibility of their separate treatment requirements is increasing the incidence of both diseases.

The Working Group on New TB Drugs (Working Group) of the Stop TB Partnership coordinates international R&D efforts with the goal of developing new, affordable TB drugs that: 1) simplify or reduce the necessary duration of treatment to 2 months or less; 2) effectively treat MDR-TB; 3) enable the simultaneous treatment of TB and HIV/AIDS; and 4) provide treatment for patients with latent TB infection. Since its inception, the Working Group recognized that drug development in general

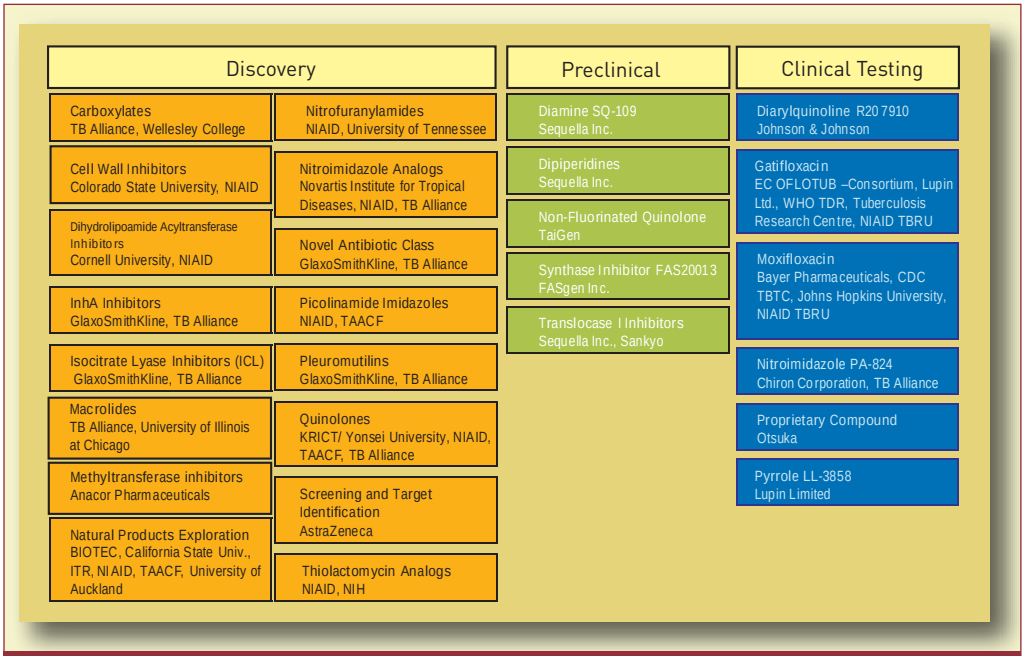


Table 1: Global TB drug pipeline, July 2005

was a slow process (8–12 years), and that TB drug development, in particular, could not rely on traditional market forces for sustainability.

With the Global Alliance for TB Drug Development as its lead agency, the Working Group is tapping and strategically advancing the scientific discoveries, capacity and know-how of all its members. It acknowledges the reality that no new therapies can be effective unless they reach those whose lives depend on them. Intelligent R&D partnerships, often between and among its members, and a pragmatic approach help ensure that resulting regimens are priced affordably, embraced by public health-care workers and accessible to patients through adequate infrastructure.

A remarkable transformation in the TB drug pipeline has occurred in the few short years since the creation of the Working Group. Today, we are able to envision an environment by 2015 that will allow for the sustained development of new TB drugs that can ultimately be combined into completely novel and revolutionary TB regimens. The global community recognizes that continued worldwide commitment, sustained cutting-edge research and expanding grassroots support are necessary to maintain and advance a consistent pipeline of new antimicrobials in order to eradicate TB within the 21st century.

A revolutionary concept for TB drug development

Due to the complex biology of the TB bacillus and the history of TB control, TB treatment requires drugs taken in combination. The current 6-month TB therapy relies upon four drugs that date back to the 1960s or earlier: isoniazid, rifampin, pyrazinamide and ethambutol. In the standard regimens, these drugs are given daily for the first 2 months, followed by an additional 4-month therapy using only rifampin and isoniazid.

Table 1 shows the global TB drug development pipeline, from discovery through clinical trials. It is noteworthy that this is the first pipeline for new potential TB drugs in decades. Just as in any drug development endeavour, several of these candidates will likely fail to meet all of their developmental hurdles. Nevertheless, the pipeline is deep enough that other candidates can succeed and become new TB drugs or serve as the basis for the successful development of analogues or derivatives. Three key factors provide optimism that the pipeline could yield a significantly shorter and better regimen that would also overcome MDR-TB and be used in conjunction with ARV treatment: 1) preclinical results that many of these drugs, when used strategically in the existing regimen, may help reduce treatment time by as much as 50%; 2) the chemical diversity of the pipeline candidates; and 3) the fact that all of these candidates are screened for cytochrome P450 enzyme interactions to ensure compatibility with ARV treatment.

In recent years, the operating strategy for new TB drug development has been to improve therapy by substituting new drugs, one at a time, into the current combination. This strategy is demonstrated and being successfully implemented in ongoing clinical trials in which quinolones such as moxifloxacin and gatifloxacin are substituted for ethambutol or isoniazid.

However, given the depth, scope and quality of the current drug pipeline, it is possible to envision a revolutionary new paradigm that allows the design of novel treatments by rationally combining totally new drugs into completely new therapeutic regimens. These new regimens will remove some of the most pressing public health hurdles for TB treatment today, such as the length of therapy, the severity of multi-drug resistance and the difficulty of simultaneous TB-HIV therapy. They will also expand the scope of current TB control by redefining public health targets – for example, by allowing the treatment of a larger pool of TB patients before they become contagious. When combined with other new interventions in development, such as improved diagnostics, new drugs will have an even greater impact.

Leveraging the drug pipeline's potential, it is possible to apply classic principles of drug development and testing in a novel and rapidly progressive way. Each drug candidate will advance in the traditional way through Phase I, establishing its preclinical efficacy, safety and pharmacokinetic profile. Successful candidates could then be tested in combination. By

examining individual drug profiles and looking for complementary targets, optimal combinations can be created and moved through preclinical and clinical evaluation, even as new molecular entities continue to be tested individually for inclusion in the pipeline. Early bactericidal activity (EBA) studies, used to predict drug potency, will be conducted on combinations that successfully pass Phase I human safety studies to solve a major problem in TB drug development. Combination therapy minimizes the threat of developing drug resistance, so EBA studies using combinations could safely be extended from the current 3–5 days to as long as 2 weeks, providing truly predictive data that assures that only the most effective and safe combinations will move into the larger and more costly Phase II and Phase III studies.

To implement this revolutionary paradigm, we must enlist the guidance and help of regulatory agencies worldwide, fortify and expand clinical trial capacity to provide good clinical practice (GCP) facilities in which to conduct the highest quality ethical clinical trials. In addition, it is imperative to establish valid surrogate and biomarkers to help shorten the duration of clinical trials substantially.

The successful introduction of new tools, such as new drugs and new regimens for TB, depends on acceptance by broad constituencies, including governments, international health organizations, health care providers and patients and their advocates. For this reason, new and harmonized guidelines are necessary to accelerate the approval and adoption of new TB therapies. Furthermore, any drug development partnership must result in affordable pricing and leverage the contributions of developing countries' expanding scientific and medical capacities.

On the agenda: lessons learned and the job ahead

Today we have a unique opportunity to successfully and rapidly develop new TB drugs and design breakthrough regimens. Success will depend on strong collaboration between and among all participants of this enterprise – from public-private partnerships to pharmaceutical and academic scientists to regulatory officials – as well as the public sector, particularly donor and endemic country governments. By sharing the responsibility and moving forward in a concerted way, we set a course to ensure resources are efficiently and effectively leveraged. Specifically, there are four areas where this broad collaboration can further advance the efforts made to date in modernizing TB treatment:

- Identifying new candidates – the TB pipeline needs to be nurtured and strengthened with additional promising compounds. Identifying and validating new targets, particularly those associated with the persistent state of *Mycobacterium tuberculosis*, is critical to screen and select new compounds for development. Such compounds may already exist in libraries or may come from basic research discovery.
- Expanding clinical trial capacity – there is an urgent need to expand and improve TB drug clinical trial capacity to evaluate new multi-drug regimens. The recent commitment by the European Union to fund clinical trial networks for AIDS, TB and malaria is an example of how donor countries can contribute, and endemic countries can work side-by-side with investigators to prepare and sustain the infrastructure necessary for ongoing clinical trials.
- Advancing new technologies – the successful use of surrogate markers in the evaluation of HIV/AIDS therapeutics has demonstrated that valid surrogate and biomarkers can significantly reduce the length of clinical drug trials. Such markers must be developed for TB.
- Ensuring regulatory harmonization – to avoid delays in the approval of new therapies and to accelerate the adoption of new TB drug regimens, TB-specific regulatory guidelines and their global harmonization are essential.

Without new medicines, TB will only grow as a global threat, driven by its deadly synergy with HIV/AIDS, complicated by multi-drug resistant strains, and amplified by the consequences of poverty. New, more effective and shorter treatment regimens will speed cure rates and save lives – they will increase productivity, enhance current TB control efforts, and alleviate much of the current burden on health care systems. When introduced alongside other advancements, such as diagnostics and vaccines, new drugs will expand the scope of current TB control and redefine public health targets. All of this requires adequate funding and a continuing commitment from public, private and governmental sources throughout the world every step of the way. We are in this effort together. ❑

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Microbicide research: empowering women with their own STI barrier



Article by Chander Puri (pictured), Sanjay Chauhan and KVR Reddy

The power in relationships between men and women is too often unequal, particularly in the lower socioeconomic classes, women generally on the receiving end particularly in Asia and Africa. As a result, many women learn that speaking up on the job, at home, or in a relationship, can have negative consequences. The inability to control the method of prophylaxis used during sex and the resulting risk of pregnancy and/or infection is a symptom of this lack of power.

Reproductive tract infections (RTIs) including sexually transmitted infections (STIs) cause suffering for men and women around the world. Once again, their consequences are far more devastating and widespread among women than among men. The high and gradually increasing incidence of RTIs including STIs and HIV/AIDS is a cause of concern.[1] Over 333 million curable RTIs occur globally in the 15–49 year age group each year, of which approximately 173 million occur in the Asian region.[2] The presence of RTIs facilitates the acquisition and transmission of HIV infection.[3] The risk of contracting HIV infection when associated with RTIs such as gonococcal, chlamydial infection and trichomoniasis, increases up to four-fold in women.

The number of people living with HIV/AIDS in the world by the end of 2003 was estimated to be 38 million, of which 17 million were women (Table 1). In India, the estimated HIV positive cases increased from 4.6 million in 2002 to 5.1 million in 2003, and the numbers are continuing to rise. The transmission of HIV from mother to the child is also increasing and is a matter of great concern. Therefore, in order to achieve the Millennium Development Goal (MDG) of reversing the trend of HIV spread by 2015 to 25% among the young, much will depend on how effectively RTIs/STIs are prevented in the community.[4]

Although very little is known about gender differentials in the epidemiology of STIs, the low status of women – social inequality, poor nutrition, and higher rate of transmission from male to female – makes them vulnerable to these infections. The concept of a female-controlled HIV prevention technology that could be applied vaginally to prevent the sexual transmission of infections began to take hold in the early 1990s. The idea of a 'topical microbicide' is particularly appealing because the majority of the currently used prevention strategies such as condoms and monogamy rely predominantly on the male partner. If he is unwilling to adopt these strategies, women throughout the world often have no choice but to remain at risk of contracting HIV infection.[5] Microbicide, as a user controlled method, could empower women, particularly vulnerable and poor women to prevent STIs including HIV infection and pregnancy (by use of spermicidal microbicide) and reduce the inequity in health (see Figure 1).

The availability of microbicide would immensely benefit women. Having additional protection against HIV and STIs would be a great breakthrough, but another important benefit would be that it could help women gain more control in their relationships and their lives. Consequently, the balance of power in their relationships might begin to change. The path of development of microbicides is currently ridden with many bottlenecks, some of which are highlighted in this article. The article also aims to appeal for a global advocacy in favour of microbicides research and development, which is essential for creating the political will to ensure sufficient investments by governments and private foundations.

Current status of microbicide development

The identification of novel microbicidal compounds is one of the most rapidly expanding areas of HIV prevention research. In 1994, only a dozen compounds were in the preclinical stages of development, with just eight ready for Phase I safety trials and none in the later stages of clinical testing. Today, according to the Alliance for Microbicide Development, 38 biotech companies, 28 not-for-profit groups and seven public-sector agencies are investigating the development of microbicides.[6,7] About 60 products are currently in the pipeline: 34 are in preclinical stages of development, 15 are in Phase I safety trials, four are in Phase II expanded safety and preliminary effectiveness trials (Savvy cream, Emmelle gel, Lactobacillus Crispatus suppository and Praneem Polyherbal suppository) and three are about to enter Phase II/III (BufferGel and Pro-2000 gel) or phase III (Carraguard gel) trials.[8,9] This is a reflection of the realization by various agencies of the urgency of preventing further spread of STIs. Nonetheless, there is a need for enhanced funding as well as redefining regulatory requirements to facilitate the development of a microbicide.

Topical candidate vaginal microbicides fall into four categories based on their mechanism of action:[5,8] (i) compounds that kill or inactivate infectious pathogens;

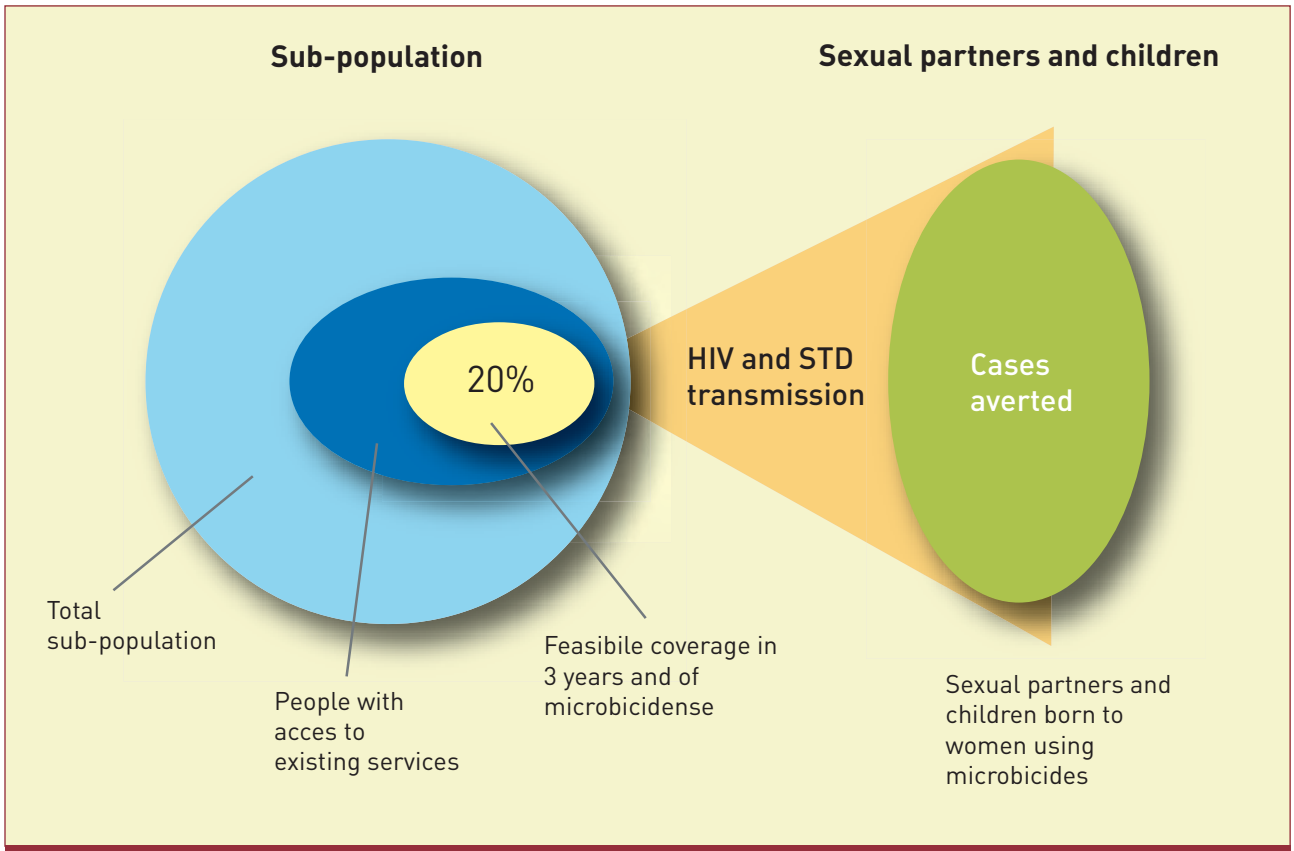


Figure 1: Potential public health impact of microbicides (Source: Global Campaign for Microbicides)

(ii) inhibitors that block attachment of pathogens to the mucosal surface of target cells; (iii) compounds that inhibit post-fusion activity; and (iv) enhancers of naturally occurring vaginal defence mechanisms. Currently, about 35 products in the pipeline have a contraceptive as well as microbicidal action and 21 have only microbicidal action.[8] The detailed list of microbicidal products in various stages of clinical development is given in Table 2.

The major organizations involved in microbicide research and development include: Contraceptive Research and Development, the United States; National Institutes of Health, the United States; Medical Research Council, UK; Centre for Disease Control, the United States, Population Council, and Indian Council of Medical Research, India. In India, institutes like: the National Institute for Research in Reproductive Health (NIRRH), Mumbai; National AIDS Research Institute, Pune; and National Institute for Pharmaceutical Education and Research in Chandigarh are the front runners. The research programmes at NIRRH include: studies on vaginal and cervical ecology; pathophysiology of RTIs/STIs; isolation of products having microbicidal activities from animals, plants or bacteria; preclinical evaluation of candidate microbicides;[10–12] clinical trials with promising microbicides; and behavioural interventions for acceptance and use of microbicides (Figure 2).

Potential public health and economic benefits of microbicides

Public health benefit of microbicides will be maximal among the high-risk community where the level of condom use is low. In such situations, even a microbicide of modest efficacy could have substantial benefits. It is quite likely that the first generation microbicides will be only partially protective. Epidemiological modelling of data from 73 low-income countries indicates that a microbicide of only 60% efficacy, used by 20% of individuals reachable by existing services and used in 50% of sex acts without condom use could avert 2.5 million infections in women, men and children over a 3-year period (see Figure 1).[13,14] This estimate is based on computer models that measure the impact of microbicide use on the chain of HIV transmission in four population groups namely: (i) sexually active youth; (ii) sex workers and their clients; (iii) women in regular partnerships; and (iv) intravenous drug users and their sex partners. In India, the findings from a district level modelling analysis, which estimates the impact of a partially effective microbicide, indicate that a 40% and 60% efficacious microbicide would avert 18% and 35% of the 5,150 expected HIV infections[15]. This indicates how the widespread use of even a relatively low efficacy microbicide could have an important impact on HIV transmission. The most dramatic expected change will be a reduction in the growing number of women who test positive each year for HIV and other sexually transmitted infections.

The potential benefit of microbicides in averting HIV infections should be examined against the annual incidence of HIV in the world. UNAIDS reports that globally 4.1 million adults were newly infected with HIV during 2003, i.e. about 12,000 infections per day. Of these infections, half were concentrated among women. The total number of adult deaths due to AIDS was 2.4 million during 2003. The

Number of People living with HIV		
Total	37.8 million	[34.6–42.3 million]
Adults	35.7 million	[32.7–39.8 million]
Women	17 million	[15.8–18.8 million]
Children <15 years	2.1 million	[1.9–2.5 million]
People newly infected with HIV in 2003		
Total	4.8 million	[4.2–6.3 million]
Adults	4.1 million	[3.6–5.6 million]
Children <15 years	630,000	[570,000-740,000]
AIDS deaths in 2003		
Total	2.9 million	[2.6–3.3 million]
Adults	2.4 million	[2.2–2.7 million]
Children <15 years	490,000	[440,000-580,000]

Source: UNAIDS, 2004 report on the global HIV/AIDS epidemic: 4th global report

Table 1: Total number of adults and children living with HIV: 38 million (35–42 million)

availability of microbicides could greatly reduce the morbidity and mortality figures. The economic benefits of introducing a microbicide include: savings in the costs of treating AIDS patients and caring for them and their families; a reduction in productivity losses due to AIDS as those affected are usually young people at the height of productive life; and averting potentially devastating economic and political instability in the worst-affected regions. Mathematical modelling, using data from 73 low-income countries, indicates that over 3 years, savings in health-system costs could amount to US$2.7 billion. There could be US$1 billion in productivity savings, gained from preventing absenteeism and reducing the need to retrain and replace workers.[13,14]

Phase I	Phase II	Phase III
A. Spermicidal and microbicide activities		
1. ACIDFORM 2. Avert and comfort spongies 3. BCT-100 4. Buffer-Gel 5. CSS 6. Gossypol acetic acid 7. Invisible condom/ thermo-reversible gel 8. LASR 9. PRO 2000 10. Polystyrene sulfate (PSS) 11. Q-2 12. Savvy/C31G	1. PC-503 2. Praneem suppository	1. Advantage-S 2. Pevent X/Geda-Plus
B. Spermicidal activity and possibly antimicrobial activity		
	1. Protectaid sponge (Axcab [Canada])	1. Vaginal contraceptive Film/VCF (Apothecus)
C. Antimicrobial with no documented spermicidal activity		
1. Beta-lactaglobulin /B195 IB-367 2. Lactivacillus/ LB suppository PMPA 1.	Dextran sulfate/D25	

* Source: Alliance for Microbicide Development, July 1999

Table 2: Microbicides under clinical development

Inadequate funding: the bottleneck in microbicide development

In 2002, Rockefeller-funded Pharmaco-economics Study concluded that if a single pharmaceutical company was managing all microbicide research leads, that company would have to invest US$775 million over 5 years to produce at least one safe and effective product. This analysis only considered the costs directly related to product development, omitting other necessities like basic research, discovery of new leads and work to assure that the products will be acceptable and accessible to users. The study also indicated that if current funding levels continue, the amount spent on microbicide research and development worldwide between 2001 and 2005 would total about US$230 million only. This leaves a shortfall of minimum US$545 million between current funding levels and the expected cost of getting one successful microbicide to the market. This could be one of the major reasons behind six candidate products of proven safety having not moved forward to large Phase III effectiveness trials in 2003.

The major pharmaceutical companies are not investing in microbicide development because in the short-term it is perceived to be not profitable as the potential returns on investment in a first generation microbicide may not be attractive. Secondly, the majority of potential users of microbicides are located in developing or poor countries with low paying capacity. In addition, the possibilities of litigation, as one microbicide may not be 100% effective against every known pathogen, also dampen the interests of companies. In the absence of major pharmaceutical interest, a number of medical councils, universities and non-profit organizations have taken the lead on microbicide research. Although some government and foundation funding is being made available it remains grossly inadequate resulting in a clogged research pipeline.

Accelerating support and funding for microbicide research

The most likely scenario suggests that a first-generation microbicide could have a global market of US$900 million by 2011 in industrialized and developing countries. A third-generation product might have sales in excess of US$1.8 billion by 2020.[16,17] As mentioned earlier, it is unlikely that major pharmaceutical companies will participate in the development of microbicides at this stage. Therefore, first-generation microbicide research and development cannot advance efficiently without a

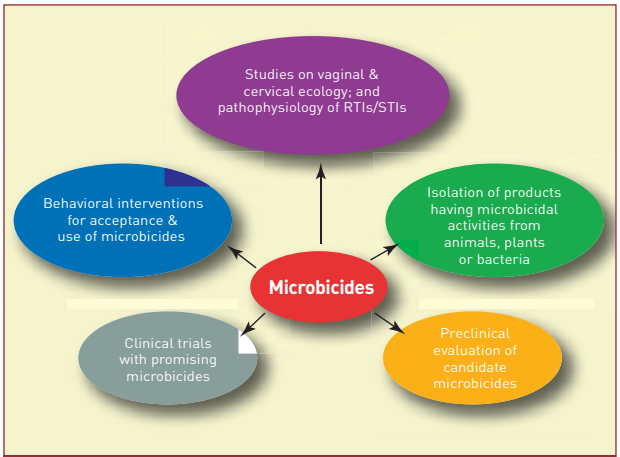


Figure 2: Microbicide research programme at the NIRRH, Mumbai, India

substantial increase in government and international foundation funding. Simultaneously, strategies must focus on the resource-intensive component of microbicide development. Strategies should also be focused on forging partnerships between like-minded organizations that have made a dent in the development of a safe and effective product. ❑

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Global research challenges for oral health



Article by Poul Erik Petersen

The World Health Organization (WHO) recently published a global overview of oral health, a statement that described the WHO Oral Health Programme's approach to promotion of further improvement in oral health during the 21st Century.[1] The report emphasized that despite great improvements in the oral health status of populations across the world, problems still persist. This is particularly so among underprivileged groups in both developed and developing communities. Oral diseases and conditions, including oral cancer, oral manifestations of HIV/AIDS, dental trauma, craniofacial anomalies, and noma (cancrum oris), all have broad impacts on health and well-being.

Dental caries and periodontal diseases have historically been considered the most important global oral disease burden. At present, the distribution and severity of dental caries vary in different parts of the world and within the same country or region (Figure 1 and Figure 2). The significant role of socio-behavioural and environmental factors in oral disease and health is demonstrated in a large number of epidemiological surveys.[2] Dental caries is still a major public health problem in most industrialized countries, affecting 60–90% of schoolchildren and the vast majority of adults. It is also a most prevalent oral disease in several Asian and Latin American countries, while it appears to be less common and less severe in most African countries. However, it is expected that the incidence of dental caries will increase in the near future in many developing countries of Africa, particularly as a result of growing consumption of sugars and inadequate exposure to fluorides (Figure 3). The current pattern of dental caries reflects primarily distinct risk profiles across countries (i.e. living conditions, lifestyles and environmental factors) and the outcome of implementation of preventive oral health systems.

While in some industrialized countries there has been a positive trend of reduction in tooth loss among adults in recent years, the proportion of edentulous persons amongst the elderly is still high in some countries (Figure 4).[3] In most developing countries, access to oral health services is limited and teeth are often left untreated or are extracted because of pain or discomfort. Tooth loss and impaired oral function are therefore expected to grow as a public health problem in many developing countries. Meanwhile, tooth loss in adult life may also be due to poor periodontal health. Severe periodontitis which may result in tooth loss is found in 5–15% of most populations.[1] In industrialized countries, studies show that tobacco use is a major risk factor for adult periodontal disease.[4] With the growing consumption of tobacco in many developing countries the risk of periodontal disease and tooth loss, therefore, may increase. Periodontal disease and tooth loss are also related to general chronic diseases such as diabetes mellitus.[5] The growing incidence of diabetes may further impact negatively on the oral health of people in several developing countries. Oral cancer is highly related to use of tobacco and excessive consumption of alcohol. The incidence of oral cancer is particularly high among men, the eighth most common cancer worldwide (Figure 5).[6] In south-central Asia, consumption of tobacco in various forms is particularly high and cancer of the oral cavity ranks amongst the three most common types of cancer. The variation in oral cancer incidence rate across the world primarily reflects different risk profiles and access and availability to health services.

In several industrialized Western countries, oral health care is made available to the population, comprises preventive and curative services and is based on either private or public systems. Meanwhile, people in deprived communities, certain ethnic minorities, homebound or disabled individuals and older people are not sufficiently covered by oral health care. Many developing countries have a shortage of oral health personnel, services are mostly offered from regional or central hospitals of urban centres and little importance is given to preventive or restorative dental care.

Research for oral health

Essentially, we have sufficient knowledge about the causes of most oral diseases for public health action, yet our knowledge about causal factors related to certain diseases such as cleft lip and palate and noma is incomplete. The major priority for new research is on prevention policy, translation of science and evaluation of programme effectiveness. Clinical and public health research has shown that a number of individual, professional and community preventive measures are effective in preventing most oral diseases.[7] However, optimal intervention in relation to oral disease is not universally available or affordable because of escalating costs and limited resources in many countries. This, together with insufficient emphasis on primary

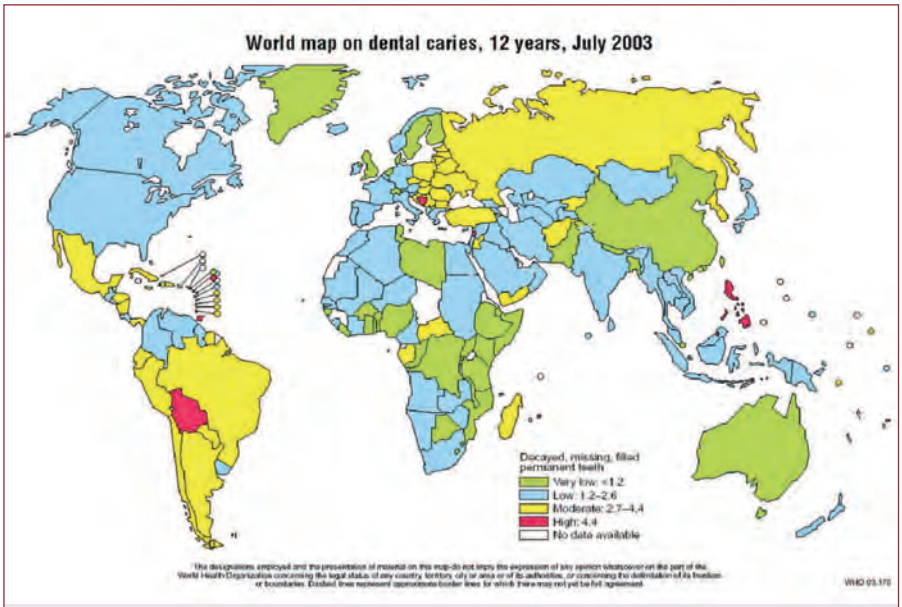


Figure 1: Levels of dental caries experience in 12-year-olds as measured by the Decayed, Missing due to Caries, Filled Teeth (DMFT) index [1]

prevention of oral diseases, poses a considerable challenge for several countries, particularly developing countries and countries with economies and health systems in transition.

The major challenges of the future will be to translate knowledge and experiences of disease prevention into action programmes. Advances in oral health science and knowledge have not yet benefited developing countries to the fullest extent possible. Clear disparities in economic strength, political will, scientific resources and capabilities, and the ability to access global information networks have, in fact, widened the knowledge gap between rich and poor countries.

Building an international research agenda for oral health

The need to re-examine an existing research agenda for international collaborative research has been stimulated by recent oral health sessions held at the annual Forums of the Global Forum for Health Research in 2002 in Tanzania, in Geneva in 2003 and most recently in Mexico City in 2004:

a) The 5th Forum session focused on developing international collaborative research that actively involves research centres in developing countries. Significant experiences have been gained by the WHO Collaborating Centre for Dental, Oral and Craniofacial Research at the National Institutes of Health, Bethesda, Maryland, the United States.

b) The 6th Forum session considered examples of international collaborative research that spans developing and developed countries and focuses on the measurement of socio-dental outcomes for the purpose of planning and evaluating oral health services.

c) The 7th Forum session discussed the development of an international collaborative research agenda that would be relevant to the Millennium Development Goals (MDGs) and included discussants from the WHO, the International Association for Dental Research (IADR) and some of the WHO collaborating centres sited in the Americas. The session focused on building research teams that address questions of global importance. Such research includes oral disease-systemic disease inter-relationships, HIV/AIDS related oral disease, cranio-facial anomalies, oral cancer, health outcomes measurement such as quality of life indicators, and health promotion. It is considered highly relevant to ensure integration of oral health research into other health research projects at a community level that should enable efficient linkages of oral health measures with biological, social and environmental health determinants.

WHO and oral health research

In the future, more emphasis should be devoted to certain areas of research:

- Modifiable common risk factors to oral health and chronic disease, particularly the role of diet, nutrition and tobacco.
- Oral health-general health interrelationships.
- Psychosocial implications of oral health/illness and quality of life

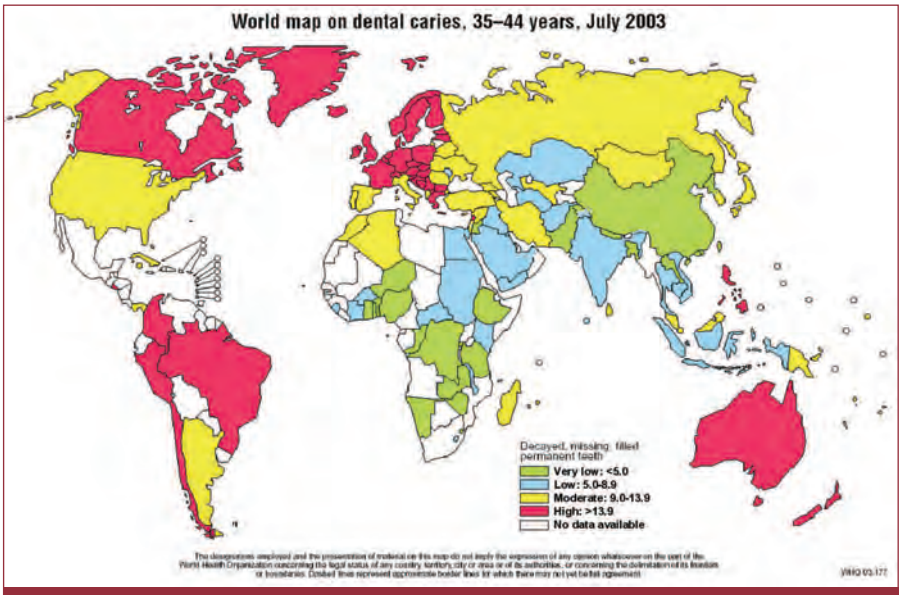


Figure 2: Levels of dental caries experience in 35–44-year-olds as measured by the DMFT index[1]

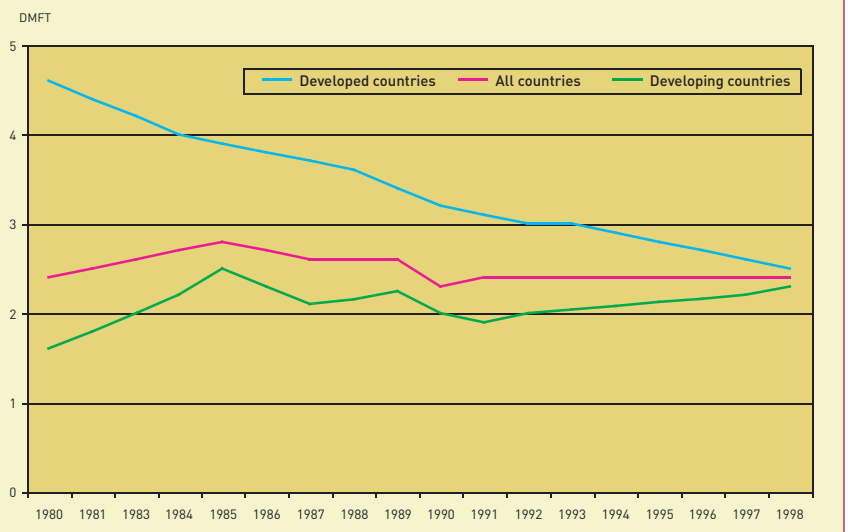


Figure 3: Changing dental caries experience index (mean number) of 12-year-olds in developing and developed countries as measured by the DMFT index[1]

- Inequity in oral health and disease.
- Diagnostics and cost-effective intervention strategies in relation to certain conditions such as noma and craniofacial birth defects.
- Identification of the most indicative oral manifestations of HIV/AIDS.
- Population studies of oral mucosal lesions, including epidemiological surveys of HIV/AIDS related oral disease in developing countries.[8]
- The burden of oro-dental trauma, particularly in developing countries, and related risk factors.
- Evidence in oral health care: clinical care and public health practice.[9]
- Operational research on effectiveness of alternative community oral health programmes, including research on optimal levels of fluoride from multiple sources.
- Health systems research on reorientation of oral health services towards prevention and health promotion.
- Time-series data for oral health surveillance in developing countries.

The WHO Oral Health Programme has prioritized oral health research as part of the global strategy for better health.[1] The Programme stimulates oral health research for, with and by developing countries in several ways:

- Supporting initiatives that will strengthen research capability in developing countries so that research is recognized as the foundation of oral health policy.
- Increased involvement of WHO Collaborating Centres on Oral Health in high-priority areas of research within national, regional or interregional centres.
- Encourage oral health research training programmes at local level or based on inter-university collaborative 'sandwich programmes'
- Provide universities and research institutes in developing countries with easy access to the scientific literature within oral health and online access to scientific articles and reports
- Facilitate the use of the Cochrane Library that provides systematic reviews about the evidence for public health action.

In addition to WHO Collaborating Centres on Oral Health, the WHO Oral Health Programme supports research in developing countries in joint projects with non-governmental organizations such as the IADR and the World Dental Federation. Reducing the '10/90' gap in oral health research cannot take place in an isolated way, but may effectively take place through work within the framework of the Global Forum for Health Research. This forum provides support to priority-setting methodologies, sound measurement, and dissemination of results in order to break the vicious circle of 'ill health and poverty'.

Most recently, the WHO published the *World Report on Knowledge for Better Health*.[10] The report provides a

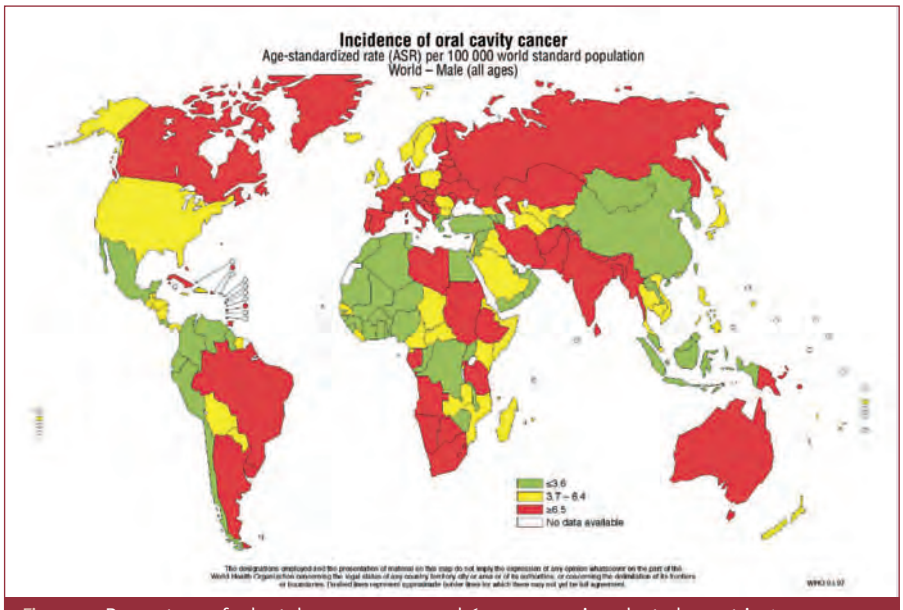


Figure 4: Percentage of edentulous persons aged 65–74 years in selected countries[1]

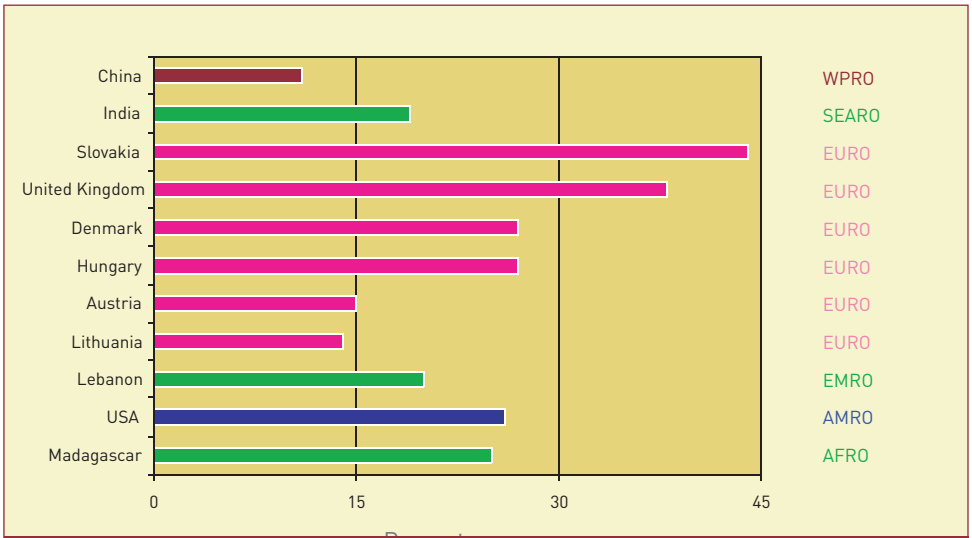


Figure 5: Age-standardized incidence rates of oral cavity cancer in males worldwide[6]

compass to reorient health research so that it may respond more effectively to public health challenges on a national and global level. This re-orientation requires a strengthening of the health research sector, an environment that is more conducive to research-informed policy and practice, and more focus on key priorities for research to improve health systems. The analysis and recommendations of the report apply to continuous oral health systems development and adjustment as well as to oral health research. ❑

Acknowledgement

The author is grateful for the valuable comments made to a previous version of the paper by Dr Lois K Cohen, PhD, Director of the WHO Collaborating Centre for International Collaboration in Dental and Craniofacial Research, NIH, Bethesda, Maryland, the United States. The WHO Collaborating Centre has provided significant support to the development of an agenda for global oral health research and Dr Cohen played an important role in leading Forum sessions on oral health research at the annual meetings of the Global Forum for Health Research, beginning in Tanzania, 2002.

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The MDGs, sexual and reproductive health and the research agenda



Article by Marianne Haslegrave

The development agenda between now and the year 2015 will be guided by the Millennium Development Goals (MDGs) that were developed following the Millennium Summit in 2000. They provide the world with time-bound and quantified targets for addressing extreme poverty in its many dimensions including hunger, disease, lack of income and adequate shelter and exclusion. They are also based on the human rights of each individual including those to health, education and security as included in the Universal Declaration of Human Rights and the Millennium Declaration, which was adopted at the Summit.

The MDGs include three health goals on reducing child mortality (Goal 4); improving maternal health (Goal 5); and combating HIV/AIDS, malaria and other diseases (Goal 6). Each goal has its own targets and indicators for monitoring its attainment by the target date of 2015. In looking at these three goals there is an issue that has an impact on these three areas, but is not included either in the goals or in the targets – sexual and reproductive health. Without attainment of the International Conference on Population and Development (ICPD) goal of universal access to reproductive health through the primary health care system by 2015, it is unlikely that maternal and child mortality will be reduced or that the spread of HIV/AIDS will have been halted, let alone reversed.

At the time of the 10th Global Forum for Health Research in 2006, Heads of Government meeting at the General Assembly High-Level Plenary, will review the progress that has been made over the past 5 years and will make recommendations for their future implementation and monitoring. It is hoped that sufficient emphasis will be placed on the importance of sexual and reproductive health that a target on universal access will be introduced by the Inter-Agency Expert Group (IAEG) of the UN Statistical Division, the body responsible for the technical soundness of the monitoring system when it meets following the High-Level Plenary. Given that many donor governments are increasingly basing their funding decisions on the implementation of the MDGs, funding for sexual and reproductive health may diminish, if it remains outside the framework, which will in turn affect its research agenda.

Millennium Project

The Millennium Project, which was established by the UN Secretary-General under the leadership of Professor Jeffrey Sachs, his Special Advisor on the MDGs, in its report *Investing in Development – A Practical Plan to Achieve the Millennium Development Goals* emphasized in recommendation 9 that, 'International donors should mobilize support for global scientific research and development to address special needs of the poor in the areas of health…'[1] The Task Force 10 on Science, Technology and Innovation in its report *Innovation: applying knowledge in development* did not make specific recommendations for addressing the reproductive health aspects of the MDGs on child mortality, maternal health or HIV/AIDS.

It is therefore important to examine what could be included in the research agenda for the next 10 years in this area. This should encompass biomedical and clinical research. Research, however, will also be necessary into the health systems and policies to strengthen the full integration of reproductive health into health systems, particularly primary health care, and to integrate fully both reproductive and sexual health services, so that, for example, a woman can also be treated for any sexually transmitted infections that are found when she attends for contraceptive services. Further operational research is a prerequisite to ensure that reproductive and sexual health is included at all levels of health care delivery particularly at community and district levels and that, for example, emergency obstetric care is accessible to women who suffer complications in childbirth. Social science and behavioural research should also be undertaken to ensure that the underlying problems, such as those of domestic violence, attitudes of adolescents towards asking for information and services, and the impact of unsafe abortion are properly addressed.

International Conference on Population and Development (ICPD) and ICPD+5

As a starting point the recommendations should be reviewed on research for sexual and reproductive health included in the *Programme of Action of the International Conference on Population and Development (ICPD)* held in Cairo in 1994[2] and the *Key Actions for the Further Implementation of the*

Programme of Action for the International Conference on Population and Development (Key Actions) of the 21st Session of the General Assembly held in New York in 1999.[3] Both these documents are the 'road maps' for sexual and reproductive health up to 2015 and have guided governments in their activities in this area since their adoption (see Box 1).

Box 1 | *ICPD Programme of Action*, paragraph 12.10

- 'Research, in particular biomedical research, has been instrumental in giving more and more people access to a greater range of safe and effective modern methods for regulation of fertility. [It] needs to be guided at all stages by gender perspectives, particularly women's, and the needs of users, and should be carried out in strict conformity with internationally accepted legal, ethical, medical and scientific standards of biomedical research.'

A whole chapter of the *ICPD Programme of Action* (Chapter XII) is devoted to 'technology, research and development' in which recommendations are made for: action on basic data collection, analysis and dissemination; reproductive health research; and social and economic research. While it includes many key issues that need to be addressed, regrettably it is not often used, or referred to, and as such is a resource-in-waiting that can provide the basis for the political will that is needed to ensure the implementation of the goal of universal access to reproductive health through the primary health care system by 2015.

As a basis for action the *ICPD Programme of Action* calls for 'valid, reliable, timely, culturally relevant and internationally comparable data' as the basis for policy and programme development, implementation, monitoring and evaluation. Among the gaps in baseline data that it identifies specifically are the lack of vital data on births and deaths, which has an impact on our knowledge of newborn deaths and stillborns, and the need for gender and ethnicity-specific information 'to enhance and monitor the sensitivity of development policies and programmes' (Box 2).[2]

Among the areas of biomedical research called for in the *ICPD Programme of Action* are: new methods for the regulation of fertility for men, which currently are limited to male condoms, vasectomy and withdrawal; technologies to meet the health needs of adolescents; research on sexually transmitted infections (STI) including HIV/AIDS; and infertility. In the light of the threat posed by unsafe abortion to women's lives, there is also a call to understand and better address the determinants and consequences of induced abortion, including its effects on subsequent fertility, reproductive and mental health and contraceptive practice. As one of the recommendations on operational research the *ICPD Programme of Action* calls on governments to look into ways of developing new forms of partnerships between the public and private sectors, including women's and consumer groups while involving national drug and device regulatory agencies at all stages of development to ensure that all ethical and legal requirements are observed.

Box 2 | Reproductive health within the context of primary health care

- Family-planning counselling, information, education, communication and services
- Education and services for pre-natal care, safe delivery and post-natal care, especially breast-feeding and infant and women's health care
- Prevention and treatment of infertility
- Abortion (where it is legal and where it is not used as a method of family planning), prevention of unsafe abortion and the management of the consequences of abortion
- Treatment of reproductive tract infections
- Sexually transmitted infections (STIs) and other reproductive health conditions
- Information, education and counselling, as appropriate, on human sexuality, reproductive health and responsible parenthood
- Referral for complications such as those of pregnancy and for STIs, including HIV/AIDS
- Active discouragement of harmful traditional practices such as female genital cutting[2]

Included in the recommendations for social and economic research are the linkages between women's roles and status and demographic and development processes. Research should also be undertaken into areas such as: changing family structure; the interaction between women's and men's diverse roles, including their access to power and decision-making and control over resources; and the causes of differentials, particularly gender differentials in mortality and morbidity, particularly at younger and older ages.[2]

The Key Actions reinforce the recommendations in the *ICPD Programme of Action*, but are less specific. There are two recommendations in the Key Actions for the clinical research necessary to implement the ICPD goals by the year 2015. The first is on the development of new, safe, low-cost and effective family-planning and contraceptive methods, for both men and women, including female-controlled methods that both protect against STIs, including HIV/AIDS, and prevent unwanted pregnancy. The second is on research on the development of microbicides and other female-controlled methods, simpler and less expensive diagnostic tests, single-dose treatments for sexually transmitted diseases and vaccines. Both microbicides and vaccines are critically important in preventing the sexual transmission of HIV/AIDS as currently the only available means are male and female condoms, education and behavioural change. There is also a recommendation for research on 'men's sexuality, their masculinity and their reproductive behaviour' in connection

with improving gender awareness, making boys more gender-aware and enabling men to support, promote and respect women's sexual and reproductive health and reproductive rights.[3]

Sexual and reproductive health research for achieving the MDGs

According to Stan Bernstein, Senior Adviser on Sexual and Reproductive Health, Millennium Project, research towards the implementation of the health-related MDGs requires research into the following areas of sexual and reproductive health:

- Measures of impact such as maternal mortality on infant mortality or on families.
- The need to go beyond disability adjusted life years (DALY) in measuring the impact of disability to look at 'functional disability' e.g. the impact of carrying firewood for women or having too many children is not considered in budgeting.
- New methods of contraception.
- Diversity among adolescents and ways of providing young married women with services.
- Involving men and social mobilization.
- Increasing support for sexual and reproductive health outside the health sector, e.g. economic arguments.

These build on, and go beyond, the recommendations emanating from ICPD and ICPD+5.

In her presentation at the session on sexual and reproductive health at the 8th Global Forum for Health Research, Adrienne Germain, President of the International Women's Health Coalition, stated that two imperatives should be observed in research in this area, namely, ensuring that the framework be woman-centred and rights-based in conformity with the *ICPD Programme of Action*, and that a more solid evidence base be developed to persuade policy-makers to prioritize investment in reproductive health and rights, particularly in situations of scarce resources. With respect to the latter she pointed out, for example, the lack of, or inadequate, vital registration systems and population-based surveys to ensure the correct measurement of maternal mortality, morbidity, and suffering, and its direct causes, especially unsafe abortion.

It is also necessary, according to Germain, to establish the extent of the problem and the impact of women's reproductive ill-health and death on families and societies. The only cited study on the impact of maternal death on infant death, in which 95% of the infants died in the first year, was carried out in 1974. Better data are also required on areas such as child nutrition and school attendance after the mother of a family dies, or is incapacitated, or on the negative effects of domestic violence, including not only the immediate, debilitating – and often deadly – physical injuries, but also the relationship of such violence to increased HIV/AIDS vulnerability. She also specified the importance of data on productivity losses due to unwanted or complicated pregnancy, unsafe abortion, complications in delivery and postpartum, and sexual coercion and violence and the 'cost effectiveness' of reproductive health, including access to safe abortion services and even emergency obstetric care. Finally, it is important to assess how reproductive health services help reduce and prevent HIV/AIDS infection in the vast majority of girls and women who are not so-called 'core group transmitters', but are nonetheless at significant risk.

The task ahead

As can be seen there is an enormous research agenda that needs to be addressed. Until now the agenda has been driven particularly by the needs of those living in more developed countries as much of the financing for research has come from the private sector, which relies on the sales of its products for the return on its investment. This means, in reality, that research into the sexual and reproductive health problems of developing countries and particularly the poor in these countries has not been adequately addressed. The research into the development of microbicides as a female-controlled method of protection against HIV infection has had very little emphasis until recently when developed countries and other donors have begun to fund research in this area. Likewise, research into areas like maternal mortality and unsafe abortion has not been fully promoted.

In addition to problems in getting private sector investment for research that is aimed at improving the lives of poor women living in developing countries, some governments have cut their financial budgets for research and research into sexual and reproductive health is not high on the agendas of many non-governmental organizations. Serious attention will therefore have to be paid to funding sexual and reproductive health to enable the health MDGs to be achieved during the next 10 years. ❑

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Oral and precancer screening: from research to policy and practice

Article by Saman Warnakulasuriya and Toru Nagao

Oral and pharyngeal cancer is the sixth most common malignancy reported worldwide and one with high mortality ratios among all malignancies.[1] The global number of new cases was estimated at 405,318 (age standardized incidence rate, 6.42 for male and 3.27 for female per 100,000), about two-thirds of them arising in developing countries. Highest rates are reported in south Asian countries such as India and Sri Lanka; almost 40% of all reported cancers may occur in the mouth or pharynx. Oral cancer is increasing among all European and high incidence countries particularly in the younger birth cohorts. Unfortunately 5-year survival rate has not improved (50% overall) for the last few decades except in specialized cancer centres. Although the oral cavity is one of the accessible sites and about half the population receives regular oral examination through routine dental care in industrialized countries, most of the patients arrive at a late stage of disease (mostly with T3 and T4 cancers) because of lack of knowledge of symptoms and unawareness of oral malignancies. It is not difficult to imagine a far worse situation in less developed countries where medical facilities and resources are limited.

Tobacco and alcohol misuse are major risk factors for oral cancer. Oral cancer is related to poverty in most countries. Betel nut (areca nut) chewing (Figure 1) containing alkaloids, is a major risk factor for oral cancer and precancer (oral leukoplakia in Figure 2) among Asians and Pacific Islanders.[2] In Asia this is a common social habit among the poor who are also undernourished. Many societies use indigenous plants containing stimulant alkaloids. Asians and South Pacific Islanders chew areca nut to obtain a mild narcotic stimulation, increased alertness, decreased fatigue, and a sense of well-being.[3] Betel/areca chewing can produce dependence, and there have been few educational efforts to control its use.[4]

It is obvious that if communities are knowledgeable about the symptoms of oral cancer and seek care earlier, associated morbidity could be reduced and the survival rate and their quality of life will be improve. The evidence confirming a reduction of mortality by screening through early detection is unclear. It is noted that early detection is facilitated by education and screening. Every high-risk country should have a national oral cancer control programme. The World Health Organization [WHO-IARC], maintains a database on global incidences of cancer,[5] to help understand the magnitude of the problem. National studies are needed on the stage of presentation of disease, mortality, medical facilities, human resources and other expected social impacts as a means of developing an oral cancer control programme. Published international research studies particularly from high incidence and high mortality countries could provide information on trends and what constitutes an efficacious screening programme through the outcomes of research findings worldwide.

Scientific basis for oral cancer screening

An efficacious screening programme has the capacity for oral cancer and precancer to be detected at an asymptomatic phase. The disease satisfies the majority of criteria needed to justify screening. The prevalence of the target disease would be high in most developing countries and in high-risk populations as the disease has a high mortality rate and serious morbidity if the treatment is delayed. The screening test available – visual examination – is low cost and does not require advanced technology, and has a high predictive value. Consequently, the early detection and subsequent intervention may achieve a significant reduction of mortality rate. A high compliance rate, particularly in the high-risk groups, is expected for screening to be cost-effective. On the other hand, with implementation of screening there could be several undesired effects such as false positive test results leading to anxiety and unnecessary further examination, and false negative test results leading to false reassurance and over-treatment of benign lesions. For most common cancers, particularly colo-rectum, breast and cervix, relatively reliable screening tests have been available for some time, and a population benefit recorded from many studies. There are, however, many difficulties that need to be overcome, especially in improving compliance and in the psychosocial area to make screening acceptable.[6] In order to improve outcomes from experimental studies, selection bias, lead-time bias, overdiagnosis,[7] and other biases should be eliminated.

Oral cancer is one of the accessible lesions for screening. Early detection of oral cancer using visual inspection of the mouth has been performed in few countries where

Country	Year	Target population	Examined	%	Screeners **	Referred (%)	Attended (%)	Correctly refered (%)	Sensitivity	Spacificity	Positive predictive value	No. of cancer	Detection rate per 100,000	No. of precancer	Detection rate per 100,000	Investigators
India	1983	117,281	39,331	34	PHCW	1	72	45	59	98	31	20	51	-	-	Mehta et al [17]
India	1996/98	114,601	49,179	43	HW	7	52	-	94 ***	98***	87***	36	73	1,310	2,664	Sankaranarayanan[8]
Sri Lanka	1981/82	87,277	29,295	34	PHCW	4	54	62	95	81	58	4	14	1,220	4,164	Warnakulasuriya et al[10]
Sri Lanka	1982/83	72,867	57,124	78	PHCW	6	62	80	97	75	80	20	35	2,193	3,839	Warnakulasuriya et al[9]
Japan	1996/98	52,058	19,056 (9,536*)	36.6 (18)	D	1	69	96	92	-	78	2	10	77	404	Nagao et al [11]

* Excluded repeaters
** PHCW: primary healthcare workers
HW: healthcare workers (university graduate)
D: dentists
*** Calculated by random sample of 2,069 subjects

Table 1: Oral cancer screening research

incidence is high, such as Bangladesh, India, Nepal, Pakistan, Sri Lanka and Taiwan.[8] Primary health care workers have been shown to be able to examine large numbers of people, and detect oral cancer and precancerous lesions with acceptable accuracy.[9] Lack of a sufficient number of the randomized controlled trials performed in different settings to assess the impact of screening on morbidity and mortality means that recommendations for mass screening are premature.[10] A major problem of mounting a screening programme is non-participation of at-risk subjects. Furthermore, subsequent treatment interventions for oral leukolakia after detection (including chemoprevention) have not been established and natural the history of oral squamous cell carcinoma still remains uncertain.

Oral leukoplakia as a main target disease for screening

A recent systematic review estimated that the crude annual oral cancer incidence rate attributed to leukoplakia would be between 6.2–29.1 per 100,000, thus suggesting that the global number of oral cancer cases is probably under-reported, particularly in developing countries.[11] It has been suggested that the fraction of oral cancer cases attributable to or arising from leukoplakia range between 17–35%.[12] These epidemiological findings show that we have to focus on the early detection of oral leukoplakia as a main target disease for secondary prevention, although some cancers may arise *de novo*. Optimal frequency for screening of oral cancer/precancer has not yet been determined, but annual screening allows detection of new lesions.[13] Table 1 shows the summary of large size oral cancer screening programmes in India, Sri Lanka and Japan, being both high and low prevalence countries for oral cancer and precancer. These studies have achieved accessible sensitivity and specificity, 59–97% and 75–98%, respectively. The method of detection using adjunctive aids has however, not received sufficient attention.

Improving screening abilities by medical and dental education

Most dentists and physicians are unlikely to spend much time on screening mouths in opportunistic settings, advising on primary prevention and taking part in comprehensive oral health promotion.[14] In Europe, most GDPs (General Dental Practitioners) undertake systemic inspection of intraoral soft tissues to role out oral cancer and precancer, but only 60–70% of them advise their patients of the benefits of cessation of tobacco and alcohol consumption.[15] In undergraduate medical and dental education, the curricula are insufficient on modules on primary and secondary prevention of tobacco and alcohol associated cancer in terms of clinical and community cares. Only half of European dental schools include in their curricula specific training in strategies for counselling patients about cessation of tobacco use.[16] The attitudes of dentists, physicians and other health related personnel to primary prevention could impact on the education of the community on lifestyle, diet and delay in seeking an initial consultation for suspected cancers.

Standardization of clinical screening abilities, availability of an appropriate standard health form with questions on lifestyle, a fail-safe referral system for screen positives could all improve the quality and outcome of screening. Protocols for the management of oral precancerous lesions should be revised/established and included in undergraduate and postgraduate education. Knowledge and skills should be evaluated during and upon completion of undergraduate education and during postgraduate clinical training programmes. Screening abilities by visual inspection should be improved by appropriate calibration and sensitivity and specificity of a standardized screening tool maintained at an optimal level. To educate screeners it is important to use standardized teaching materials, such as representative clinical photographs, electronic teaching tools and sometimes patients. The latter is most valuable as an education tool. Monitoring and evaluation of their abilities should be carried out in order to sustain their knowledge and skills for screening. The WHO Collaborating Centre for Oral Cancer and Precancer based in London, UK, could be consulted to improve skills and for calibration of trainers.

Education of the public

A satisfactory compliance of a population during mass screening or in opportunistic settings contributes to improved success. As shown in Table 1, the compliance to

attend screening varies, ranging from 34–78%. The compliance to attend for secondary examination has also been poor, ranging from 54–72%. This could depend on the accessibility of the referral centre,[18] social background and the degree of education of screen positives, which is the most influential factor for this health behaviour. Providing brief health education at the time of screen detection is known to increase compliance.[19] A demonstration programme in Japan has shown that it is feasible to integrate oral cancer screening into general health screening undertaken as a prevention programme aimed at improving citizens' health.[20] The National Cancer Institute[21] and the American Cancer Society[22] recommend that an oral examination should be included in periodic health examination. Educational opportunities for health related risk factors using leaflets and displaying clinical photographs or other visual media for self-examination could be given at the screening sites or prior to screening. It gives the public good motivation for health consciousness and regular health check ups. Opportunistic screening in a dental practice setting, particularly if high-risk groups can be targeted, might be a realistic alternative to population screening.[23]

Health workers could make smoking and chewing secession programmes available at minimum cost. Interventions for the improvement of poverty including welfare and social lives provide a new strategy for health promotion. It is, however, very hard to implement in terms of policy decision making. Education should include information about screening benefits as well as unexpected screening failures to inform of the realities of a screening programme.

Screening positives	oral cancer, leukoplakia, erythroplakia (oral submucous fibrosis)
Target population	> 40 years of age
High-risk population	regular smokers, betel chewers, heavy drinkers poor diet, poor hygiene, socially neglected
Compliance factor	personal risks, education, awareness
Risks	screening failure
Screening frequency	every year recommended
Researches	awareness education, progression of lesions high risk individuals,molecular markers, methodology Compliance, efficacy of early interventin Cost analysis

Table 2: Screening science for oral cancer and precancer

A demonstration programme in Japan has shown that it is feasible to integrate oral cancer screening into general health screening undertaken as a prevention programme aimed at improving citizens' health[20]

Further research

Numerous systematic reviews have been carried out to elucidate what treatments are effective. This methodology provides scientific evidence, however, the outcomes depend on the quality and availability of studies. The latest Cochrane Systematic Review[24] has concluded that there is no evidence to recommend inclusion or exclusion of screening programmes for oral cancer using visual examination in the general population, which confirms earlier views. Because randomized controlled studies using visual examination are so few, it is quite difficult to evaluate the efficacy and efficiency of oral cancer screening for both population screening and opportunistic screening in private sectors. Furthermore, most oral cancer and oral mucosal screening programmes initiated in the past 20 years have been limited to a single examination of the population under study, the only exemption being an annual screening programme undertaken in Aichi Prefecture in Japan from 1985–1988.[13] Table 2 shows the summary of screening outcomes for oral cancer and precancer. Based on these facts and our own experience having undertaken several screening programmes in both high and low risk countries, we propose research on the following: awareness education; natural history of oral cancer; compliance; efficacy of early intervention; high risk individuals; models of screening; value and place of molecular markers; and cost analysis. Oral cancer is likely to occur among those who are less educated, with poor hygiene and those under-utilizing health facilities for regular dental/oral health checks, those that are addicted to smoking, chew betel and misuse alcohol, are undernourished and socially deprived. There could also be other groups who have a rather healthy lifestyle without serious risk factors, particularly elderly females or young people. Greater understanding of the genetic basis of oral cancer is an essential prerequisite to the development of molecular markers for screening of subjects without environmental risk factors.[24]

The policy of oral cancer screening ought to differ between less developed and developed countries. It should be noted that mass screening requires continuous input of budgeting and well-motivated and trained human resources. However, it cannot succeed without a well-developed primary health care system. In those countries, a societal approach with support from community leaders may improve outcomes.

Conclusions

Oral cancer is a sociopublic health problem in countries where incidence is high and medical resources limited – primary prevention and early detection are neglected,

particularly in South-East Asian and African countries. To cope with these circumstances, various international organizations for cancer prevention, and overseas development agencies from developed countries should work with governments and national investigators to develop appropriate screening models and evaluate their effectiveness. Developing and improving adjunctive aids to accelerate taking a biopsy from a suspicious area of oral mucosa need further research. ❑

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Acknowledgements

The Publishers hereby acknowledge the assistance of all the contributors who have helped in the production of the publication and the advertisers and sponsors who have made the publication possible.

They would also like to thank the following:

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