Global Forum
for Health Research
HELPING CORRECT THE 10|90 GAP

Global Forum Update on Research for Health Volume 4

Equitable access: research challenges for health in developing countries

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Global Forum Update on Research for Health volume 4: Equitable access: research challenges for health in developing countries

Foreword by Pramilla Senanayake

Life expectancy and other indicators of health have, on average, increased markedly across the world during the last century. At the same time, however, health inequities within and between populations have persisted and in some cases worsened.

Recent efforts to reduce some of the large gaps in health status have been channelled through international initiatives such as the Millennium Development Goals and a variety of international health initiatives, including new public-private partnerships to develop products for neglected diseases and large pools of funds to assist disease-endemic countries to purchase drugs and vaccines. But ensuring that individuals everywhere can enjoy the right to health involves much more than creating medicines and supporting their purchase for the poorest countries. It requires enabling people to have equitable access to information, health services and products and to basic living and working conditions that give them real choices and opportunities to maintain good health and avoid diseases and injuries.

Research has a central role to play in addressing health inequities. It can identify the presence of major health disparities, help to create understanding of the underlying causes and provide potential solutions to be tested, verified and scaled up. The spectrum of research required to support equitable access to health is therefore very broad. It encompasses not only biomedical research to understand biological causes of ill-health and develop medical solutions, but also research into economic, environmental, political and social determinants of health; and it ranges from studies of how policies are developed and implemented at global and national levels to the examination of their effectiveness and impact on the health of those who have been marginalized.

This year's edition of the *Global Forum Update on Research for Health* and the annual Forum meeting of the Global Forum for Health Research take as their theme the issue of equitable access and the research challenges it poses in trying to improve health and reduce health disparities in developing countries. We are extremely grateful to the many distinguished authors who have contributed their time and expertise to the articles in the *Update*. These provide concise, expert summaries and opinions to complement the rich array of presentations and discussions of the many facets of equitable access that are on the agenda of Forum 11 in Beijing this year. ❑

Pramilla Senanayake *is Chair of the Foundation Council*
Global Forum for Health Research
August 2007

Research contributions to improving equitable access to health in developing countries

Article by Stephen A Matlin

Everywhere in the world, issues of equitable access are fundamental to improving the health of all the people[1]. Limitations of access to information, to services for prevention and treatment, or to good quality health-related products are among the many factors that create gradients in health status within and between societies.

High levels of malnutrition, maternal and child mortality and infections with HIV/AIDS, TB, malaria and a number of pathogenic tropical parasites in some developing countries have attracted much attention and led to the establishment of the Millennium Development Goals[2] to reduce some of the starkest health gradients between countries. But these do not address the broader health conditions that affect people throughout the world, including a host of noncommunicable diseases that are becoming increasingly prevalent in low- and middle-income countries[3], nor the wide range of factors and determinants that act as pre-conditions for people to achieve and maintain good health.

Historically, some groups have experienced long-standing discrimination in access to health including, among others: women, people with disabilities, indigenous peoples, poor people, people in low-income countries, rural populations, slum dwellers, elderly people, children, adolescent and young people, people of low social class or caste and people stigmatized by specific conditions such as HIV/AIDS.

Given the wide range of health determinants and conditions that are at play, the spectrum of research required to address the complex range of factors associated with inequities in access is necessarily very broad. Research can help to identify and address barriers to access of all types (including economic, geographical, institutional, political, socio-cultural and technological barriers) and can help to identify, test and validate measures to improve equity of access for all. The range of people who need to be engaged in such research is also extensive – encompassing not just physical, biological, social and behavioural scientists located in academic research institutions but also health workers, nongovernmental organizations (NGOs), communities, civil society groups and individuals, including representatives of groups on whom the research is focused.

Given the wide range of health determinants and conditions that are at play, the spectrum of research required to address the complex range of factors associated with inequities in access is necessarily very broad

This article considers a diverse array of factors associated with inequities in access to the means to achieve better health in developing countries and summarizes some of the ways in which research is, or could be, playing a role in removing barriers and biases.

Access to the preconditions for health

It is increasingly appreciated[4] that a broad array of non-biological factors act as determinants of health, including those of economic, environmental, political and social origins (Figure 1). Improving health, especially for some of the poorest and most marginalized in society, will require giving much greater attention to these "causes of the causes" of ill-health, with effort needing to be concentrated on securing the human rights on which many of these determinants depend.

Research to examine these wider determinants of health, to understand the causal relationships and to demonstrate ways in which they can be used to improve health status and health equity is scarce and there is a need to begin by establishing the scope of the research agenda, mapping the human and financial resources already available and setting priorities for where and how the most urgent gaps are to be filled. The research agenda on determinants of health must include studies of the extent to which human rights are recognized and upheld, given that health and human rights are inextricably connected.

Among the broad range of determinants, social factors have received most attention recently, particularly through the establishment of a series of Knowledge Networks by the WHO Commission on Social Determinants of Health (CSDH)[5]. The CSDH, created in 2005 to draw attention to pragmatic ways of creating better social conditions for health, aims to promote models and practices that effectively address underlying social inequities, human rights and the broad social determinants of health; to support countries in placing health as a shared goal to which many government departments and sectors of society contribute; and to help build a sustainable

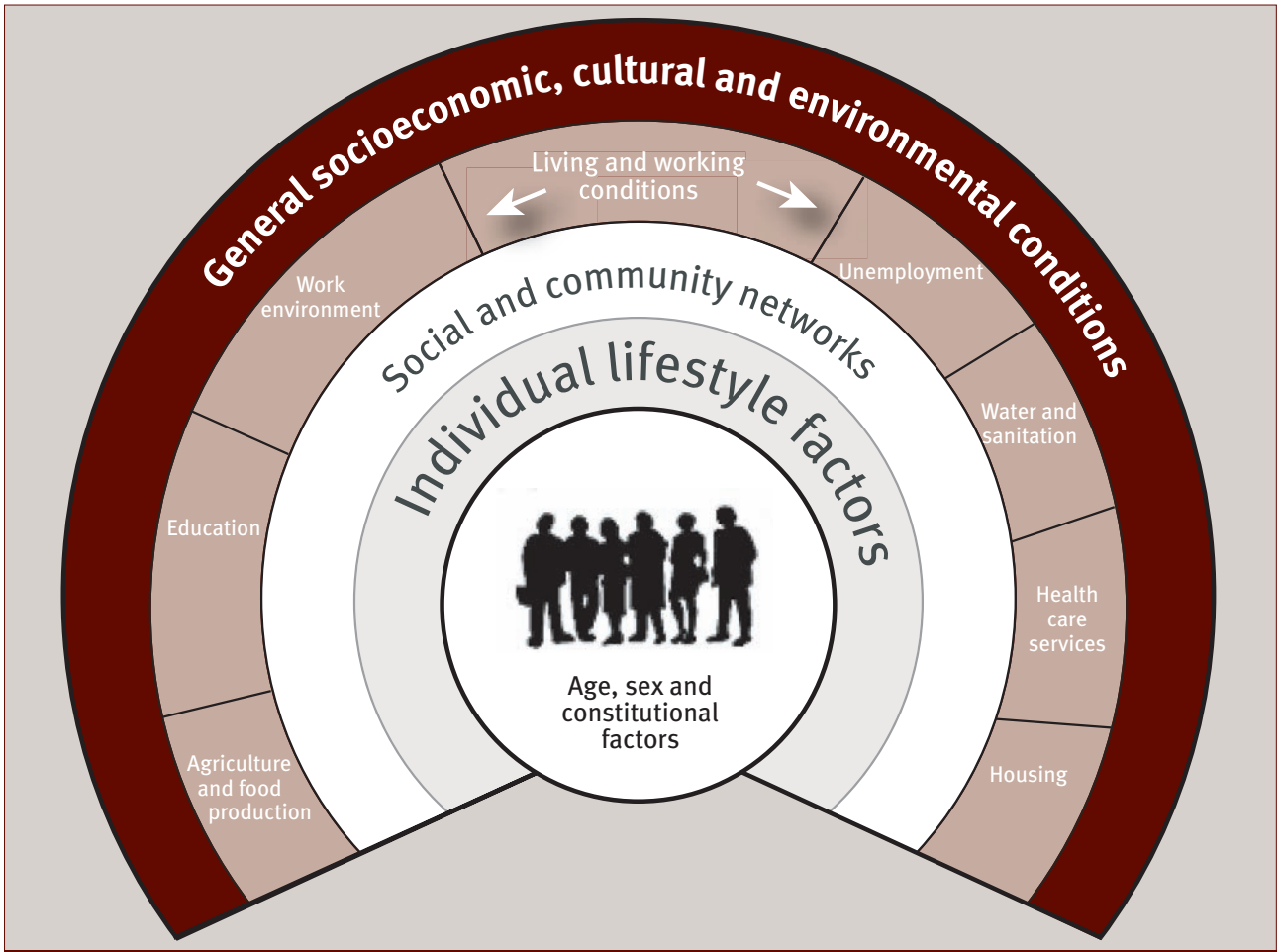

Figure 1: Factors affecting health[4]

global movement for action on social inequities, human rights, and the other broad social determinants necessary to achieve health equity. The Knowledge Networks are building a detailed picture of the linkages between health and the social determinants, and their work should uncover an extensive research agenda that will need to be addressed to accomplish the Commission's overall goals.

Margaret Whitehead[6] has set out a typology of actions to tackle social inequalities in health, which helps to generate a useful framework for a research agenda to support practical and effective policies and programmes. Whitehead's approach begins with identifying the theory underlying interventions: recognizing the logical reasoning that connects intervention programme inputs to intended outcomes (Figure 1) provides a basis for assessing whether there is any reasonable likelihood that programme goals could be achieved and enables the development of appropriate criteria for evaluating success.

Whitehead's typology of actions to reduce health inequalities includes four categories:

- strengthening individuals;
- strengthening communities;
- improving living and working conditions;
- promoting healthy macro-policies.

This framework may also be useful for analyzing and planning research in the field of health inequalities and equitable access.

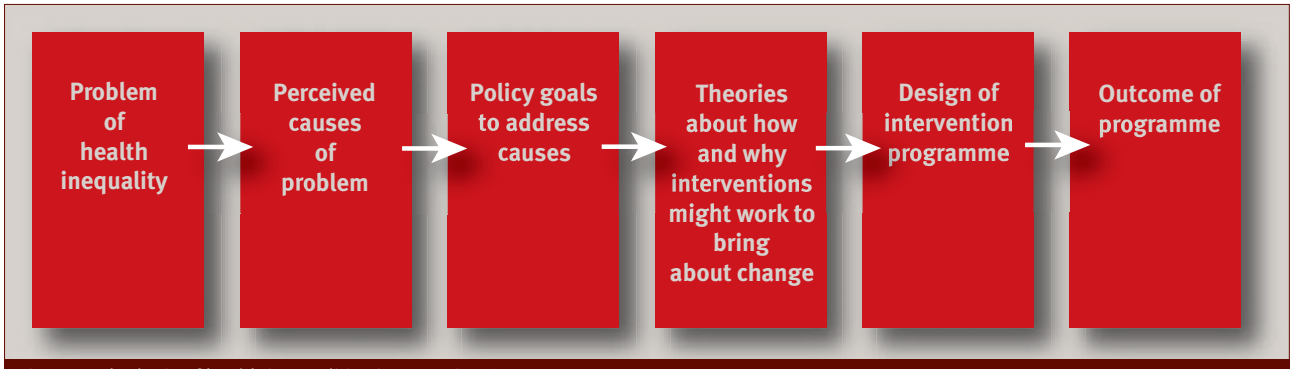

Figure 2: The logic of health inequalities interventions[8]

Type I	Prevalent in both rich and poor countries, with large numbers of vulnerable population in each.
Type II	Prevalent in both rich and poor countries, but with a substantial proportion of the cases in poor countries.
Type III	Overwhelmingly or exclusively prevalent in developing countries.

Box 1: Categories of diseases according to their relative prevalence in higher- and lower-income countries

The role of health systems[7] in challenging inequity has been the subject of study by the CSDH Knowledge Network on Health Systems. The report of this Knowledge Network[8] synthesises a large amount of available evidence on how health systems can contribute to reducing health inequities and provides a policy guide on actions that can be taken to address these inequities, including mobilizing intersectoral relationships, facilitating social empowerment, building up universal coverage, revitalizing primary health care, strengthening the process of developing and implementing policies, and securing international support for nationally-led health system transformation and action. While the focus of the report is on the use of existing knowledge, it identifies many gaps and also serves as a stepping off point for an extensive agenda of new research. This is especially important in the light of the fact that, as the report itself notes, the experience of health systems is always context-specific.

Innovation

Research to improve health is best understood as a process within a chain of health innovation that begins with a concept, question or observation and proceeds through experimental investigation towards the eventual application of the results to the use of a new process or product in the field. Innovation for health equity should not be regarded as being restricted to the creation of affordable and appropriate medical products and technologies[9]. It also includes developing and applying understanding of how to improve equitable access through novel health policies, services and systems, interventions and support mechanisms; and encompasses the application of health technology assessment to assist in selecting the most appropriated and cost-effective technologies to meet health needs, especially of the poor and vulnerable. And it includes innovations in understandings and measurements of health and health equity.

Pharmaceutical products for diseases endemic in developing countries

Diseases have been categorized into Types I to III according to their relative prevalence in higher- and lower-income countries[10] (Box 1).

For a range of diseases that substantially or predominantly occur in poorer countries (Types II and III), access to pharmaceutical products for prevention, diagnosis and treatment has often been very poor. Two major elements of this limited access can be identified:

1. For many of the diseases which have little or no prevalence in high-income countries, there has been a dearth of research and development (R&D) resulting in the registration of new products. Thus, of the new pharmaceutical products registered for human use in the period 1975–1997, only 13 (around 1%) were for tropical parasitic infections[11]. As a result, treatments are either not available or depend on very old generic drugs that may have significant side effects and efficacies that are limited and declining due to emerging resistance. Where diagnostic tools for these diseases exist, they may be slow, insensitive or unsuited to field conditions prevailing in the disease-endemic countries, requiring highly skilled personnel or sophisticated laboratory settings.
2. In cases where newer and more effective drugs, vaccines and diagnostics are available, these have sometimes found relatively low levels of uptake and use in developing countries, due to factors including affordability and the availability of health systems for their delivery.

It is clear that, to a large extent, these two elements are related to a common problem – that of market failure. Substantial R&D investments are needed to create new pharmaceutical products and these are unlikely to be made by the private sector where there is not seen to be a good market for recouping the investments. Drugs created for a market in high-income countries, where per capita expenditures on health run into thousands of dollars per year, may prove too expensive for use in low-income countries whose health expenditures are far less than 100 dollars per capita per year.

Several different approaches have been explored or proposed to solve the problem, varying according to the stage in the chain of innovation and product delivery/uptake at which the market failure is perceived to be occurring:

- For a range of "neglected diseases" – especially tropical parasitic infections, but also HIV/AIDS and TB – investments in R&D for drugs, vaccines and diagnostics has come from the philanthropic sector, with the Rockefeller Foundation taking a lead in the mid 1990s in the creation of product development public-private partnerships (PDPs) beginning with the International AIDS Vaccine Initiative. The Bill & Melinda Gates Foundation has made substantial contributions since 2000. More recently, a number of bilateral donors (e.g. Ireland, Netherlands, Norway, UK) have started to become increasingly significant supporters of this approach[12]. PDPs have generally taken a portfolio approach, creating a pipeline of candidate products in development, some of which are now in or about to enter clinical trials. Since the latter – especially Phase III trials to prove efficacy and involving large numbers of patients in the field – are very expensive, a major challenge now facing the world is how to provide adequate funding to ensure that effective new products reach registration and enter clinical use in disease-endemic countries. Across the range of diseases and products for which support is

required, the levels of funding may well soon exceed the capacities of the philanthropic sector and it will be vital to attract larger investments from the public sector if this "push" mechanism is going to fulfil its promise[13]. It will also be vital to ensure that the efforts of the different philanthropic and public sector donors become better aligned, avoiding duplication or competition to back early "winners" and ensuring that the complete spectrum of "neglected diseases" receives adequate support. The Organisation for Economic Co-operation and Development's (OECD) initiative with the Dutch Government in the "Noordwijk Medicines Agenda" represents one important strand in the current efforts to develop a more coherent and collaborative approach to meeting this challenge[14].

- At the same time, "pull" mechanisms are being developed that are intended to provide incentives for investment, especially by the private sector, to create new products where there has been a market failure. One approach now being implemented is the "advance purchase commitment" (AMC) through which governments guarantee a viable market by means of a binding contract to purchase a newly developed pharmaceutical product if it meets pre-determined criteria. Several countries have recently announced support[15,16] for this approach and, in a pilot case announced in February 2007, an AMC is being applied to a new pneumococcal vaccine[17].
- It has been argued in some quarters that part of the cause of market failure in the creation of drugs for neglected diseases is the patent system which has evolved over the last two centuries. The large investments needed to create high-technology products such as pharmaceuticals are rewarded by the granting of exclusive intellectual property rights for a period of time, during which the inventor can charge high prices in order to recover the initial investment and potentially earn large profits before the patent life expires and generic copies drive prices down. This matter has been extensively debated during the work of the Commission on Intellectual Property Rights, Innovation and Public Health[18] and its successor, the Inter-Governmental Working Group on Public Health, Innovation and Intellectual Property[19]. A number of proposals have been advanced for alternative systems to stimulate and reward innovation and to lower barriers to more collaborative and less competitive efforts. These include creating open access drug companies and patent pools and de-coupling the rewards for invention from the subsequent pricing of the products, rewarding innovation by offering prizes or compensation based on the amount of disease averted in developing countries[20,21]. These variants on the well-established patent system provide a "twist" to supplement the "push" and "pull" mechanisms outlined earlier, which work within the existing regime of intellectual property protection.
- In the last few years, a number of new initiatives have been developed for the purchase of available medicines for neglected diseases. These include new bodies such as the Global Fund to Fight AIDS, Tuberculosis and Malaria and the GAVI Alliance, and fund-creating mechanisms like UNITAID and the International Financing Facility for Immunization[12]. Although they do not themselves fund drug research, the existence of these funds, which assure large-scale finances for the purchase of needed products for a number of years to come, may also stimulate greater investment in R&D to create new products.

Equity in research

The domain of research itself exhibits a range of inequities: imbalances in the allocation of resources to different types of research and to the health problems of people in different situations; limitations of access to decision-making and priority-setting about the use of resources, to participation in research and to the interpretation and use of its results. Thus, while research may be aimed at tackling problems associated with inequities in access to health, the research itself must be rigorously inspected to remove biases that may contribute to the perpetuation of inequities.

The *BIAS FREE* Framework is an analytical tool published by the Global Forum[22]. It has rapidly gained popularity in a number of settings in both developed and developing countries as a powerful methodology for uncovering biases in research due to a wide range of discriminatory factors deriving from social hierarchies.

Across the world, there is broadly a consistent relationship between health status and the availability of skilled health workers, with those countries having the highest levels of burden of disease also being the ones with the fewest trained health-care providers[23]. Increased attention is now being directed towards the crisis in human resources for health, including through the establishment of the Global Health Workforce Alliance[24], with efforts focusing on critical elements of the recruitment, training and retention of health workers in poorer countries. However, an equally stark lack of skilled health researchers – especially in Africa – has received much less attention, as highlighted in an expert consultation on human resources for health research held in 2006 in Nairobi[25].

Enabling research to make a full contribution to addressing health and health equity issues requires ensuring equitable access to a range of resources, including: capacity development and human resources; tools to measure equity; and funding for health research in all its dimensions, including those relating to creating conditions for health, for health promotion, prevention, treatment and care. Access to the process of priority setting is also vital and this needs to involve the application of equity principles and criteria to setting the priorities for use of limited research resources to address health needs, especially of the poor and vulnerable[26].

Decision-making and governance

The research agenda relating to equitable access to decision-making and governance includes examining how:

- policy-making involves all stakeholders (in particular those who historically have been excluded from decision-

making), takes account of all bodies of evidence and is accessible to producers and users of research;

- health research systems can be built on principles of equitable access and can contribute to its achievement;
- greater coherence and coordination among the funders and directors of research at global and national levels can increase equitable access to sustainable basic preconditions for health, health services and products. ❑

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Access to health

Strengthening health systems towards better health outcomes

Article by Chen Zhu

This annual conference of the Global Forum for Health Research is an important event for China and for health improvement across the world. I wish to extend, on behalf of the Ministry of Health of China, warm congratulations on the successful convocation of the Forum. I also wish to take this opportunity to share with you some of my ideas and experiences about the development of the health sector and the promotion of human health.

A brief overview

Improving health is one of mankind's eternal pursuits. To provide each citizen with equitable, accessible, reliable and high-quality health care is an important responsibility of every government and an important condition for promoting health for all. It is also an important indication of a country's economic and social development and level of modernization. Since the beginning of the 20th century, life expectancy has increased greatly and quality of life has improved. Thanks to innovations in medical science and technology, mankind has not only eliminated smallpox but also acquired the technical means to prevent and control many other diseases. The Human Genome Project that began in the late 20th century has enabled mankind to know more about life itself. All this has created favourable conditions for improvements in human health outcomes.

Having said that, mankind still faces serious challenges and harsh realities on the road towards better health outcomes. Health improvement is not yet at the top of the political agendas of countries across the world. Preoccupation with economic growth has resulted in health losses and increasing burdens of disease. Inequity in health has emerged as a major problem. There are big gaps across different regions, countries and groups of people in terms of health resources and health conditions. The environment, climate change, urbanization, industrialization and trade globalization pose new problems for health systems in all countries. Population ageing and rising service costs have exerted greater pressure on health financing systems. There is no room for complacency when it comes to the control of communicable diseases, and the burden of chronic, non communicable diseases is increasing. The achievements of medical science and technology have failed to benefit each and every member of society in a fair and timely manner.

Like many developing countries, China has gained unique experiences in developing its health sector. China has also experienced twists and turns along this path. Under the planned economy, China carried out large-scale patriotic health campaigns organized by the government. As a result, people's living and working conditions improved markedly. By stressing prevention services and appropriate technologies in health, China made significant contributions to the development of the concept of primary health care and to international health. China created a health system suited to its own national situation and put in place a health service network covering both rural and urban areas. It set up a sustainable health financing system with the support of fiscal and collective economic forces. Each of these important measures helped substantially improve health of the Chinese people. In the three decades from the 1950s to the 1980s, the life expectancy of the Chinese people increased by over 20 years. In those 30 years, China enjoyed a faster rate of health improvement and richer labour resources than any other country in the world.

Since China adopted a policy of reform and opening-up to the outside world in the late 1970s, its overall national strength has increased and remarkable achievements have been made in economic and social development. From 1978 to 2006, China's Gross Domestic Product grew at an average rate of 9.7% annually, much higher than the world average of 3.3%. China's economic growth has been a kind of miracle. The fiscal revenues have increased dramatically, reaching nearly 4 trillion Renminbi (RMB) in 2006 (over 500 billion US dollars). The per capita disposable income of those in urban areas and the net income of rural residents have grown at an average annual rate of 7% since 1978. Along with rapid economic growth, China's health sector has also undergone rapid development. The health care network covering both rural and urban areas has further developed and channels for funding have further expanded. The quality of health services has improved, the number of health workers has increased, and the educational level of health workers has improved. China is now facing rare historical opportunities for further developing its health sector.

Recent achievements in China's health development

The Chinese government attaches great importance to the health of its people and to the development of the health sector. In China's 11th Five-Year Plan for National Economic and Social Development, health sector development is listed as a critical step in realizing scientific development and the improvement of people's life. Not long ago, the State Council approved Guidelines for Health Sector Development during the 11th Five-Year Plan period, and the General Office of the State Council issued the National Plan for Food and Drug Safety during the 11th Five-Year Plan period. Since 2003, a series of breakthroughs have been made in the development of China's health sector.

Stepping up efforts to improve the disease prevention system and other public health systems: In 2003, China launched a three-year plan for improving the disease prevention and control system, as well as strengthening systems for communicable disease treatment. So far, the tasks set out in this plan have been accomplished, and over 5000 projects have been carried out with a total investment of 26.9 billion Renminbi. In addition, public health information systems and health supervision systems have been further strengthened. As a result, public health services in both rural and urban areas have been improved along with the capacity of service providers, raising the standards of health services. Tremendous efforts have been made to prevent and control major diseases. The DOTS strategy has been adopted to treat tuberculosis. Medical assistance is provided to those suffering from late stage schistosomiasis. Hepatitis B vaccine has been included in the national immunization plan. The policy of "Four Frees and One Care"[1] has been implemented for AIDS patients and their families. Starting from 2007, China has taken further steps to include vaccines against Hepatitis A, cerebrospinal meningitis, and other communicable diseases in the national immunization plan, increasing the number of vaccines covered under the government's free immunization plan from 7 to 15. With a view to ensuring equal access to essential public health services, China is now working to draw up a list of essential public health services in an effort to fulfil the government responsibilities and effectively achieve the goal of promoting public health.

Strengthening rural health services: Beginning in 2003, the Chinese Government started a new cooperative medical system. The government provides the bulk of funding for this system, with rural residents paying a small amount and rural households forming the main unit of participation. Smooth progress is being made to advance this project. This system has been set up in about 2400 counties and cities with 700 million rural residents participating. Starting in 2005, the Chinese Government has launched another rural health service system development plan. Within five years, nearly 21.7 billion RMB will be invested in the rural health service system. This plan will help upgrade rural health services, improving service quality and making rural health services more accessible and equitable.

Developing community health care in urban areas: The Chinese Government is following a regional plan, adjusting the allocation of health resources to promote health for every household with the support of communities. Efforts are being made to develop a new type of urban health care system based on a community health service model that gives priority to prevention and combines preventive and curative services. Possibilities for a two-way referral system are being explored, along with effective coordination between community health institutions, hospitals, centres for disease control and prevention, and maternal and child health care institutions. By the end of 2006, 278 cities had instituted community based health services, accounting for over 98% of all cities in China. In addition, 23 036 community health service institutions had been set up across the country. Beginning in 2007, the central government has offered financial support through payment transfers to cities in central and western China to help them develop community health services.

Improving the health financing system: In recent years, government inputs to the financing of total health expenditures in China have risen, while residents' individual contributions have gone down. The contribution of the government health appropriation and the social health expenditure to the total expenditure on health has increased from 40% in 2001 to 48% in 2005. Residents' individual contributions have dropped from 60% in 2001 to 52% in 2005. Positive developments are underway in the structure of health financing sources. Approximately 170 million employees in urban areas now enjoy basic medical insurance coverage, with total insurance funds of 174.7 billion RMB in 2006. The State Council has launched pilot projects of basic medical insurance plans for urban residents in the second half of this year. The Chinese Government has also worked vigorously to develop a medical financial assistance system in both rural and urban areas. This system will rely mainly on governmental input to offer financial assistance to low-income families and poor families with large medical expenses. A total of 2.12 billion RMB was spent on medical financial assistance in China in 2006. Commercial health insurance is also growing rapidly, with total revenue reaching 37.7 billion RMB nationwide in 2006.

Tightening regulation of medical institutions and enhancing service quality: A core principle of the Ministry of Health of China is to ensure that health services bring real benefit to the people. As such, the Ministry of Health urges all health service staff to comply voluntarily with public supervision efforts. Since 2005, the Ministry of Health has organized hospitals nationwide to participate in activities with the theme of "putting patients first and improving service quality". These efforts have helped to standardize health service delivery, to enhance service quality, and to improve relationships between medical staff and patients. Efforts have also been made to strengthen pharmaceutical supervision by regulating pharmaceutical production, distribution and prices,

raising public awareness of the rational use of medicines, and upholding the rights and interests of patients.

Strengthening the capacity for innovation in medical science and promoting traditional Chinese medicine: In 2006, the State Council issued its National Outline for Medium- and Long-term Scientific and Technological Development, listing population issues, health and pharmaceutical innovation as top priorities in science and technology. With a growing cohort of medical professionals, China's capacity for health research is also growing. Traditional Chinese medicine is an important part of China's health system. It has played an instrumental role in disease prevention and treatment, rural health development, and urban community health services. Traditional Chinese medicine has its unique advantages in handling difficult and complicated cases, and it is an important part of China's historical heritage. To foster innovation in traditional medicine, in 2007, the Ministry of Science and Technology and the Ministry of Health jointly issued the Outline for Innovation and Development of Traditional Chinese Medicine 2006–2020, charting the course for further development in the traditional medical sector.

Intensifying reform of health system: In 2006, the State Council set up a Health System Reform Coordination Group to promote the development of China's health system; to address issues of access to doctors and hospitals; and to improve the health of the people. The National Development and Reform Commission and the Ministry of Health serve as the coordinators, and they are responsible for organizing more than 10 governmental bodies to address key issues in public health reform. Over the course of a year's work, important progress has been made. We will continue to integrate governmental guidance with market mechanisms, while addressing relationships between fairness and efficiency in health system reform. It is the duty of government at all levels to improve the health of the people, to realize, protect and develop the rights and interests of the people with regard to health. Taking China's realities as a starting point, China must learn from other countries while exploring its own way towards health system reform with Chinese characteristics. We should focus our efforts on institutional innovation, and, at the same time, take effective measures to solve those problems that the people care about most. Efforts will be made to upgrade the health service system in rural and urban areas; to improve medical insurance and its funding mechanisms; to expand medical financial assistance services; and to strengthen governmental supervision and regulation, enabling the health system to operate in a more efficient way.

The health of the Chinese people keeps improving. The average life expectancy in China reached 73 years in 2005, an increase of 4.4 years from 68.6 years in 1990. The mortality rate of children under the age of 5 years dropped from 61 per thousand in 1991 to 20.6 per thousand in 2006. Maternal mortality fell from 80/100 000 in 1990 to 41.1/100 000 in 2006. The overall heath of the Chinese people is leading that of most developing countries. Marked results have been achieved in controlling HIV/AIDS, TB and malaria. The number of people with malaria has been reduced from 24 million in the 1970s to 116 000 in 2006, with malaria endemic areas now much smaller in size. China is taking effective measures to honour its commitment to the United Nations Millennium Development Goals. At the same time, this is part of China's contribution to global health development.

Deepening international cooperation and advancing health research

Since 1963, China has continuously sent medical teams to more than 60 countries and areas in Africa, Asia, Latin America, Europe and Oceania, involving more than 2 million medical staff and treating more than 200 million patients. In recent years, the Chinese Government has increased aid to developing countries, African countries in particular. President Hu Jintao announced at the Beijing Summit Forum on China-Africa Cooperation in November 2006 that the Chinese Government will provide a grant of 300 million RMB within three years to help African countries prevent and cure malaria by providing artemisinin and setting up malaria prevention and control centres. We have provided 30 African countries seriously affected by malaria with artemisinin and sponsored seven training sessions on malaria prevention and control in 2006.

Diseases respect no country borders, as the saying goes. It is the common wish of mankind to effectively control diseases and to improve health. With globalization gaining momentum, it is all the more important to strengthen international cooperation in health. And international cooperation promises great progress in the prevention and control of communicable diseases, in health research, medical education and health systems and policy administration. The Global Forum for Health Research and the World Health Organization should play important roles in guiding and facilitating international cooperation. Effective cooperation between countries is critical to our collective efforts to fight disease, to improve health, to advance the progress of mankind and to uphold harmony and stability in the world.

Promoting health research: All countries are now facing great challenges in health financing and ever increasing health expenditures. Currently, limited funds are available for health research, and this problem is especially pronounced in developing countries. Insufficient investments in research and limited capacity for medical innovation are barriers to scientific decision-making and the development of the health sector, and therefore have a negative influence on the health of the people. All countries need to step up efforts to increase investment in health research, to organize strong systems for innovative research, and to bring value products from scientific research into production. At the same time, full use should be made of scientific evidence, and we should also work to bridge gaps between decision-making and scientific research.

Training more health professionals: Human resources are at the core of breakthroughs in health research, and are the driving force for the sustainable development of the health sector. Most developing countries face a shortage of health professionals, especially health professionals with innovation capacities. There is ample room for strengthened cooperation between developing and developed countries in the area of human resources development. At the same time, developing countries should also strive to create environments that foster innovative talent, to create an atmosphere of respect for medical science, for knowledge and for human resources. This can help reduce the loss of human resources and help attract those who have gone abroad to return to serve their own countries.

Strengthen exchanges and cooperation: Peace, development and cooperation are the core concerns of our time. We in the health research field should deepen cooperation at national, regional and international levels. The success of Human Genome Project is a case in point, as it is the product of close cooperation among scientists from different countries. China is ready to step up exchanges and cooperation with developing and developed countries to work towards the goals of improving human health, advancing health research and making our lives better. ❑

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1. "Four frees" refers to providing free antiretroviral drugs to AIDS patients with financial difficulties and without any medical insurance; free counselling and screening testing for people voluntarily seeking HIV/AIDS counselling and testing throughout China; free drugs for pregnant women infected with HIV to block mother-to-child transmission and free testing reagents for their babies; and free tuition for AIDS orphans during the nine-year compulsory education period. "One care" refers to including AIDS patients with financial hardship in government support programmes, providing them with necessary relief in accordance with relevant regulations, helping those AIDS patients who are capable of working to find jobs to increase their income, and increasing public awareness of HIV/AIDS to reduce stigma and discrimination against people living with HIV/AIDS.

Recent trends in research on health equity

Article by Davidson R Gwatkin

Health equity is increasingly becoming a concern for societies around the world. The mounting research documenting the increasing disparities in health outcomes and access to care, between rich and poor, and across other social gradients, defined by occupations, ethnicity and class, is a testament to this trend.

A search of the US National Institutes of Health MEDLINE electronic data base shows a rapid increase in the number of articles appearing in response to a search using the terms "health equity" or "health poverty". In the decade from 1995 through 2004, the number of citations identified using these terms more than doubled, rising steadily from around 2600 to over 6200 – an impressive 9% annual rate of increase.

To be sure, this trend needs to be assessed with caution. The overall MEDLINE database also expanded rapidly during the same period, at a 7% annual rate that is only somewhat slower than that of health equity research. Also, at least some of the reported increase in health equity research appears attributable to a rise in articles only tangentially related to health equity/poverty, and appearing on the list of citations for possibly questionable reasons: the paper authors' limited understanding of health equity, or their desire to link their work to an issue perceived as increasingly popular. Yet even these uses of the term constitute a tribute of sorts to the growing prominence of work in health equity; and since they are unlikely to constitute nearly all of the increase, they reinforce rather than detract from the conclusion that health equity research has been attracting increased attention.

Much of the recent health equity research covered by databases like MEDLINE has fallen into two broad categories. The first looks primarily to the *social and economic determinants of health* and health inequities among different groups in society, defined by income, occupations, ethnicity, and class. The second deals with the low or differential use of health services among different economic, gender, or other groups.

It is also interesting to note from the literature how researchers have traditionally approached the problem of health equity using two lenses: ex-post lenses focusing on how to improve conditions affecting people's health or access to health care; and ex-ante lenses, focusing on preventing people who are not currently poor from falling into poverty in the future, and/or preventing the poor from becoming even poorer.

The wide range of work undertaken on health equity presents a challenge to easy synthesis. Fortunately, it is possible to provide a flavour of the research undertaken through a description of three prominent initiatives focused on addressing determinants of health equity, on the one hand, and health care access, on the other hand. The first of the three uses both ex-ante and ex-post perspectives because it goes "upstream" to assess the structural factors influencing the determinants of health and health disparities. The second initiative uses a more ex-post approach. The third applies an ex-ante policy perspective as its guiding principle.

Social and economic determinants of health and health disparities: the WHO Commission on the Social Determinants of Health[1]

The WHO Commission on the Social Determinants of Health was formally launched at a March 2005 meeting in Santiago, Chile. It is chaired by Sir Michael Marmot, known especially for his work on social inequalities in health in the United Kingdom. Its 19 other members include a former head of state (Ricardo Lagos of Chile), two current or former health ministers (Charity Ngilu of Kenya, Monique Bégin of Canada), leaders from civil society (e.g. Mirai Chatterjee from India's Self-Employed Women's Association (SEWA), health advocates (e.g. Stephen Lewis), and several distinguished researchers (of whom the best known is probably Nobel Laureate Amartya Sen).

During the Commission's three-year life, its principal aim is: "*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… Success will be achieved if institutions working in health… will be using this knowledge to set and implement relevant public policy affecting health*"[2].

The Commission is not first and foremost a research initiative, in that it is undertaking or funding little new research, beyond its work on measurement and evidence. However, the Commission places a strong emphasis on knowledge for action and is devoting considerable resources to bringing together the available research findings that have a central bearing on policy, for use in achieving its principal objective of influencing policy.

One of its principal mechanisms for bringing together research findings is a set of "knowledge networks," the first of whose four tracks of work is "consolidating, disseminating and promoting the use of knowledge that demonstrates the

imperative for actions on the determinants of health and that informs both policy and effective, equitable interventions on those determinants"[3]. Thus far, nine networks have been established, each with 12 or more individual members supported by a coordinating "hub". The locations of eight were selected through open competition; they deal with early childhood development, globalization, health systems, urban settings, measurement and evidence, women and gender equity, social exclusion, employment conditions. The ninth network, on priority public health conditions, is housed at WHO.

Since these networks have yet to complete their work, the full syntheses of knowledge in their particular areas that can be expected from them are not yet available. However, a sense of the general orientation that they are likely to take is available from the earlier work of Commission Chairman Michael Marmot and his colleagues, which has centrally shaped the Commission's orientation.

At the heart of this work is the idea of a "social gradient" in health, whereby health outcomes become worse as one descends the socioeconomic ladder. This means that not only do the poor have worse health than the rich, but the middle classes have worse health than the more rich as well. While this is itself far from startling, the idea incorporates two other points that are much less intuitively obvious and that greatly increase its significance. One is the finding that these gradients exist not just in poor countries, but also in better-off ones where living conditions among even the lowest groups studied are far above any meaningful absolute poverty line. From this, it is pretty clear that there are causes of ill-health that lie well outside the nexus of poor nutrition, inadequate education, unfavourable environmental surroundings, and the like that is normally blamed for particularly high rates of illness and death among the poor. The second is the identification of psychological factors – degree of control over one's work environment, for example – that appear to be responsible for these high rates, and the delineation of the biological channels through which such psychological and other factors work.

Such findings lead towards an emphasis on social and economic policies, more than on health services, as the most promising approaches to the reduction of socioeconomic health inequalities. One of the several examples that could be cited involves unemployment, which has been shown to affect health not only through loss of income, but also through the anxiety that it causes. Government moves to smooth the business cycle, and to ensure reasonable unemployment benefits illustrate ways of countering ill-health and the other effects of this factor. Another illustration concerns transport, where government policies focusing on cycling, walking, and the use of public transport can promote health by providing exercise, reducing fatal accidents, increasing social contact, and reducing air pollution[4].

Thus far, most work on the social gradients of health has dealt with Northern, developed countries, particularly in Europe. If the Commission is successful, the same approach will be applied increasingly to health equity research and policy development in middle- and lower-income countries over the years ahead.

Health service use among the poor and the better-off: the World Bank's reaching the poor program[5]

The World Bank's recently-completed Reaching the Poor Program (RPP) was initiated in order to find ways of dealing with a disturbing finding from earlier Bank-sponsored research: that basic health services intended for and traditionally believed to be reaching the poor were in fact not doing so. For example, full immunization coverage among children in the poorest 20% of a country's population was typically only one half to two thirds what it was among children in the best-off 20%; a pregnant woman in that poor group was only about one third as likely to be attended at the time of delivery by an adequately trained medical person as a woman in the highest group.

Like that earlier research, the RPP focused primarily on economic inequalities, taking advantage of a recent finding that a household's assets could serve as a reasonable indicator of its overall economic status. This meant that researchers no longer had to rely on data about income or consumption, which are both notoriously difficult to collect, in order to assess households' economic status. Rather, they could use information on such things as sources of water, availability of electricity, and possessions (watches, radios, etc.) that takes only limited time to collect, and that is already being routinely collected through many health surveys.

The RPP investigators commissioned approximately 20 studies – and collected findings from as many other studies as they could identify – that incorporated this approach to the measurement of economic status and sought to determine the distribution of service use across the economic groups thus identified. The interest was the rate of service coverage in the poorest population group, and the proportion of total services benefits going to that group. (This latter dimension – the measurement of the proportion of total service benefits accruing the poor – represented an application of an approach from the public finance field called "benefit incidence"; and one of the RPP's purposes was to call the attention of the public health community to that technique.)

The outcome was the identification of numerous health projects that "swam against the tide" by achieving high coverage among the poor, and/or delivering to the poor a disproportionately high percentage of benefits (i.e. a percentage of benefits higher than the share of the population represented by the disadvantaged group in question). Illustrative examples of such projects included:

- Mexico's "Progresa/Oportunidades" Programme that pays rather than charges poor families for clinic and school attendance. The programme serves over 20 million people, and almost 60% of the people served belong to the poorest 20% of Mexico's population.
- Cambodia's experiment in contracting with non-governmental organizations to operate governmental rural primary health services, under contracts calling for attainment of specified coverage levels among the poor. During the four years of the project, the coverage among the poorest 20% of the population by eight basic services rose from an average of below 15% to over 40% in two

districts with a population of over 200 000. This increase was well over twice as large as that experienced in two comparable districts that continued to provide standard government services.

- Distribution of insectide-treated bednets through measles immunizations campaigns in Ghana and Zambia. In Ghana, the Red Cross and the Government Health Services raised, from nearly 3% to nearly 60%, the rate of treated bednet use among children in the poorest 20% of people in one of the country's Northernmost Ghana. A similar but larger programme in Zambia produced similar results.

The RPP investigators concluded that the numerous experiences like these that they found showed that the unimpressive equity performance of more typical programmes did not have to be accepted as inevitable. Rather, much better performance is possible. But the investigators also noted the wide range of strategies that had proven successful against different settings, as illustrated by the very different nature of the three illustrations given above. This led them to warn against any belief in any single approach or small set of approaches that can be expected to work best in any setting. Rather, they advocated study of the entire range of promising approaches available, and experimentation to determine which among them is likely to work best in a particular setting.

Protection against impoverishment: the Affordability Ladder Program of the Liverpool Faculty of Medicine[6]

While the initiative described above dealt with helping people who are currently poor, the Affordability Ladder Program (ALPS) focuses on preventing people from becoming poor in the future. In so doing, it is working on a set of issues that has attracted increasing interest in recent years as health systems in developing countries have evolved in ways widely believed to increase the vulnerability of households to the economic consequences of ill-health.

The root of this evolution lies in the transition from state-directed to market-led economies during the 1980s and 1990s – most spectacularly in China and the countries of the former Soviet Union, but in many other parts of the world as well.

This shift brought a significant change in outlook to the health sector, where strategies had typically been dominated by the aspiration to provide government-delivered services at no charge to the entire population; and thinking about health service delivery came increasingly to be dominated by thinking about mixed public-private systems, and about government systems that more closely resembled private ones.

Since this shift usually involved increased patient payments for health services, it has given rise to concern that the services might end up impoverishing people as well as improving their health. Thus, the impoverishing impact of illness in general, and of patient payments for health services in particular, began attracting the attention of both policy-makers and researchers. They have been particularly concerned with two related issues: first, determination of how serious the problem is, and what its causes are; and second, identification of solutions to that problem.

While by no means the only research project to deal with these issues, ALPS is the largest known single organized initiative in this area. It is a network of researchers in countries (China, India, Sri Lanka, South Africa, Sweden, Tanzania, Uganda and Vietnam) coordinated by the Liverpool Faculty of Medicine and funded by the Rockefeller Foundation. The network members are working on a wide range of issues within a common framework. The framework starts with a perceived health problem, and tracks how people respond to it through use or non-use of various types of care, with a particular focus on how these choices are affected by the burden of financial payments and on what the resulting health, social, and economic consequences might be.

The programme results available thus far have concerned primarily the first of the two issues referred to above: that is, the dimensions and causes of the problem[7]. Of particular relevance are the findings of a recent programme-initiated paper summarizing the available evidence on the economic consequences of illness and paying for health care in low- and middle-income countries[8].

The findings suggest that that a focus on the impoverishing impact of payments for health services provides only a partial view of illness's consequences in low-income settings. For one thing, the financial impact on households of payments for health care appear considerably smaller than the income lost from illness-induced inability to work. While the amount of work on this point is rather limited, the ALPS authors cite studies suggesting that the income lost from ill-health is on the order of 2 to 3.6 times as large as the amount paid for services. A second issue that the authors note concerns decisions not to use health services because of their cost. In such cases, the cost of services to households or individuals may have no financial impact, but it can obviously have major consequences for health status.

Notwithstanding these important caveats, however, the authors' review of over 60 empirical studies leads to a clear conclusion that "there is growing evidence that some households (even middle-income ones) slide in to poverty when faced with health care payments, especially when combined with the loss of income due to ill-health". They also suggest that illness-related costs diminish the likelihood that already-poor families will be able to move out of poverty[9]. ❑

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Understanding health service access: concepts and experience

Article by Lucy Gilson (pictured) and Helen Schneider

Creating access is generally understood to be a central goal of health systems. However, there is global recognition that health systems in many low- and middle-income countries are far from achieving reasonable levels of access to essential health care[1,2]. Equally important, there is increasing evidence to show that the distribution of health service coverage within low- and middle-income countries is highly inequitable[3,4,5]. Inequitable access produces systematic differences between population groups in the use and experience of health care[6]. Access barriers deter or delay the search for care, particularly among poor or marginalized groups, with consequences for individuals, households and communities.

Commonly, access is understood to be a function of policy decisions such as those about where to locate facilities or how to finance health care-making; that is, decisions about the supply of health care. However, recent research shows that this is a narrow approach. Here we, first, present a broader understanding of access as well as a framework for thinking through the potential policy responses to access problems. Second, we discuss in more detail an often ignored dimension of access, cultural access or acceptability. In these discussions we draw on some recent conceptual thinking as well as presenting relevant research findings. Finally, we consider policy interventions relevant to access barriers and the research needs in this field.

An access framework

There are three key elements to defining access. Firstly, drawing on Donabedian's[7] concept, access is the "degree of fit" between the health system and those it serves; a dynamic process of interaction between health system (or supply-side) issues and individual or household (or demand-side) issues.

Secondly, access has a number of dimensions: [8,9,10]

- Availability (sometimes referred to as physical access) refers to whether or not the appropriate health services are in the right place and at the right time.
- Affordability (sometimes referred to as financial access) refers to the "degree of fit" between the cost of health care and individuals' ability-to-pay.
- Acceptability (sometimes referred to as "cultural" access) is the social and cultural distance between health care systems and their users.

Within each dimension, there are a number of supply- and demand-side factors and multiple layers of determinants underlying each factor. For example, availability includes the location of services, hours during which care is provided and the type, range, quantity and quality of services, each considered relative to the health needs of the population served. The range of services is in turn influenced by the type of staff working in that facility and the scope of practice of each category of health worker, which in turn, are influenced by human resource policies, and so on. The multi-dimensional nature of access has been well articulated by Aitken and Thomas[11] in the context of the Nepalese Safe Motherhood Programme (see Box 1).

Thirdly, the concept of access is distinct from that of utilization. Access is the *opportunity or freedom* to use a health service while utilization is when an empowered individual makes an explicit and informed decision to exercise his/her freedom to use health care. Our definition of access is summarised in Figure 1.

The nature and influence of acceptability barriers

Concern about poor provider attitudes and behaviours towards patients has generated growing interest in the acceptability dimension of access – both in high-income[13,14] and middle- and low-income countries[15]. However, the acceptability definition provided earlier clearly indicates that acceptability concerns go beyond patient-provider interactions. A recent review[16] of available evidence on

> Access is enabled in an environment that encourages people to utilize health services, within any given social context. At its best it is a dynamic, participatory process based on good practice. Access advantageously uses local knowledge, perceptions and values, relevant traditional practices, preferences and beliefs, to enhance knowledge and awareness. Access encourages self-confidence, voice and agency, especially among women. Access embraces financial, institutional and infrastructure factors, including but not limited to funding, transportation and education. Access relies upon good provider attitudes, trust, honesty, responsiveness, accountability and good quality service delivery, both at established facilities and through outreach programmes. Access engages socially marginalized and vulnerable communities, is inclusive and empowering.

Box 1: Multidimensional nature of access. *Source: ref. 11, pg8*

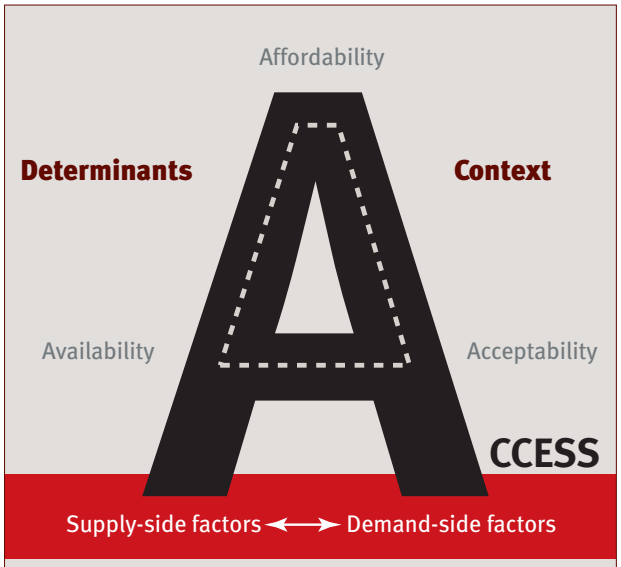

Figure 1: A framework on access. Source: adapted from Thiede et al[12]

acceptability outlines three central elements:

1. The fit between lay and professional health beliefs – covering both patient's perceptions of the effectiveness of treatment and the extent to which their constructions of health and healing match health care provider understandings on these issues.
2. Patient-provider engagement and dialogue – with particular emphasis on the communication practices of providers, the extent to which patients are themselves given opportunities, and are able, to discuss their own care and whether or not providers demonstrate prejudice towards patients, perhaps simply by stereotyping them and their needs rather than listening to each patient.
3. The ways in which health care organizational arrangements influence patient responses to services – for example, fees for service systems often generate patient concern that the provider is more interested in making money than in addressing their needs fully.

All of these elements are themselves influenced by a wider range of socio-cultural factors. In seeking care, people always draw on advice from others in their local community – and this advice is shaped by health beliefs, the reputations of particular providers and rumours about them, trust in medical technology, as well as cost and perceived quality[17-20]. Provider behaviours are, meanwhile, shaped by the emotional demands of their jobs, as well as workloads and other aspects of their organizational and social environments. Poor human resource management practices often frustrate providers and lead them to take their frustrations out on their patients[21]. Providers working in authoritarian cultures are also likely to act in authoritarian ways towards their patients, preventing client-centred approaches to chronic illness care[22]. Indeed, the way in which the power relationship embedded within the provider-patient interaction is managed at both personal and organizational levels is a central influence over whether or not the patient trust in providers that is necessary to effective care is built (see Box 2)[23]. Such trust is not only vital to acceptability but also to protecting patient dignity and the wider social value derived from health care by marginalized groups[24,25].

Over the last 13 years, South Africa has acted to strengthen its health system and address the health and health care inequities it inherited from the past. The range of policies implemented vary from strengthening the primary health care infrastructure to removing fees for primary and maternal health care services and implementing a new Patients' Rights Charter to enable stronger provider-patient relationships. A series of studies[26-28] has, however, shown that, whilst supporting many of the policies in principle, South African health workers are frustrated by the new policies. They commonly feel that these policies are imposed on them without any prior consultation or even warning, requiring them to change their practices and often resulting in increased work. This use of managerial power makes health workers feel that there is a lack of care for them in their workplaces, and they identify poor managerial style as a key factor underlying low motivation levels. Some studies have also shown that health workers themselves admit that, as a result of these experiences, they sometimes then take out their frustrations on their patients, abusing their relationship of power with patients. Not surprisingly, therefore, patients and community members commonly criticize health workers for behaving badly and demonstrating little care towards them. Expressed patient trust in providers appears to be quite limited, and public criticism of the declining quality care provided in the public health sector is widespread.

Box 2: Trust and access to health care in South Africa

Some research evidence also shows that acceptability barriers do directly influence health service equity. In all countries, socially disadvantaged and marginalized groups are most likely to bear the burden of discriminatory provider attitudes and poor communication practices[29,30], least likely to be able to engage with providers during health care encounters[10,14] and most likely to have different health beliefs from those that are dominant within traditional bio-medical health care systems[31]. Indeed, negative health care experiences are an aspect of marginalization within any society. A wide range of evidence, for example, specifically demonstrates the gender dimensions of these experiences, as well as of provider experiences, and their consequences for access (Box 3)[32,33]. European experience meanwhile clearly indicates that despite the wide geographic availability of services and well established risk protection mechanisms, acceptability barriers underpin systematic differences in health care utilization between socio-economic groups as well as between minority groups/migrants and non-migrants, and women and men[30].

The impacts of acceptability problems are, finally, seen in population level health inequities. Acceptability problems are linked, for example, to:

- patient unwillingness to reveal past medical history, making diagnosis and treatment difficult;
- lower rates of referral to secondary and tertiary care, and lower rates of intervention relative to need;
- limited patient adherence to advice or treatment, and

This study investigated the introduction of a new primary health care health worker, the Lady Health Worker (LHW), intended to offset gender barriers to health care access in Pakistan. It found that male health systems managers subjected LHWs to managerial abuse, including sexual harassment. LHWs were also not given resources to do their jobs well and commonly expected to undertake tasks that went against broader societal norms and expectations. Not surprisingly, therefore, LHWs faced hostility from neighbours and family members for taking on these new jobs. The consequences of these experiences only exacerbated existing access barriers. They included absenteeism among LHWs, turnover of staff, malpractices (LHWs sometimes imposed informal charges on patients), and impersonal treatment of patients.

Box 3: Gender dynamics in health care in Pakistan.
Source: Mumtaz et al[32]

failure to follow up, particularly in relation to chronic illness;

- lower self-reported health status (Box 4)[34].

Policy action to address access barriers

Given the dominant understandings of access, most investigations of health service access have led to policy conclusions about the need to extend the health care infrastructure to under-served areas or to address financial barriers to access by user fee exemptions, removing user fees or introducing pre-payment schemes or other forms of insurance[12,35]. However, the many dimensions of access indicate that a wider range of policy interventions is required.

Innovative strategies to increase access reported in both low/middle- and high-income countries include:[16]

- "close-to-client" services in the community including the development of referral networks within and across sectors;[36]
- provision of transport subsidies;[37]
- community action to improve access to and use of pharmaceuticals;[38]
- working with private and traditional providers to improve quality and reduce costs;[39]
- peer empowerment interventions;[40]
- enabling indigenous health systems and promoting an intercultural approach to health care;[41]

In a national telephone survey of 961 adults in the United States, reported distrust of the health system, measured on a Health Care System Distrust Scale was considered relatively high. More importantly there was a significant association between distrust of the health system and self-reported fair/poor health. While the direction of causality – whether mistrust leads to poor health or whether frequent use of the health system because of poor health leads to mistrust – it highlights an important arena for further research and intervention.

Box 4: Self reported health and mistrust in the US health system.
Source: Armstrong et al[34]

- improve contact with and involvement of refugee, minority and marginalized communities; paying attention to the specific needs of minority groups in therapeutic protocols and services; employment of workers from minority groups and marginalized communities in the health system; and improving the cultural awareness and training providers in trans-cultural communication[29].

However, effective action to address access barriers also requires that policy interventions act on the broader organizational and social influences over them. Such interventions are likely to include: strengthening leadership and management within health services, particularly human resource management; developing functioning accountability mechanisms to bring provider and patient communities together in developing health services; and sustaining the wider social mobilization activities that influence health care delivery. These in turn will require dedicated funding sources and political advocacy to sustain interventions[6,16]. It is also important to take into account that the way in which new policy interventions actions are implemented influences provider and beneficiary responses to them. A small but growing body of evidence shows that the processes through which policies are developed and implemented themselves determine these responses and the policies' impacts.

Research needs

Despite its centrality as a goal of health policy in many countries around the world, there has been little systematic empirical work directed to the measurement of access to services and the evaluation of policies aimed at promoting equitable access internationally. A review of the literature has highlighted that most studies claiming to evaluate access, mainly undertaken in high-income countries, focus on measuring differences in health care *utilization* (rather than access) and on identifying a limited number of factors that influence these utilization patterns[42,43,44]. Research in low- and middle-income countries has also focused on assessing inequities in utilization, with a growing number of "Benefit-Incidence Analyses" being conducted, which examine socio-economic differentials in coverage/utilization by specific health interventions[45]. Where studies have directly attempted to "measure" access, these have assessed specific dimensions of access, particularly geography (distance to care facility), cost (user fees) and ability-to-pay (health insurance coverage), rather than adopting an integrated approach to access. In recent years there has been growing interest in questions of affordability, covering financial barriers, including the growing evidence on household cost burdens and health-seeking behaviour[46].

On the whole, however, the evidence base from which to derive policy conclusions remains weak. More research is needed on the acceptability aspect of access and how the various dimensions of access (availability, affordability and acceptability) interact. There is also need for more discussion on the types of study designs required to assess a broad-based and comprehensive approach to access. Finally, greater interaction between researchers in the field would be valuable.

The authors are involved in a number of initiatives addressing questions of equitable access. They include the Health Systems Knowledge Network of World Health Organization's (WHO) Commission on the Social Determinants of Health;[47] the Regional Network on Equity in Health in Southern Africa (EQUINET) (www.equinetafrica.org), the multi-country Consortium for Research on Equitable Health Systems (CREHS), funded by the UK Government Department for International Development (www.crehs.lshtm.ac.uk), and a recently initiated research programme entitled "Researching Equitable Access to Health Care" (REACH) in South Africa. ❑

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Combining health and social protection measures to reach the ultra poor: experiences of BRAC

Article by Syed Masud Ahmed

Poverty is considered as the "biggest epidemic that the global public health community faces" in the contemporary world[1]. Of all risks facing poor households, health "shocks" probably pose the greatest threat to their lives and livelihoods[2]. Moreover, due to the operation of the "inverse care law"[3], the poor who need health care most are least likely to get it[4]. Neglect, abuse and marginalization by the health system are part of their everyday experience[5]. Cost burdens of health care thus deter or delay health care utilization or promote use of less effective health care sources or practices by the poor[6]. Various crisis coping mechanisms such as selling of productive assets, mortgaging land, or borrowing from money-lenders at high interest rates to cover the costs of illness push these households into a "poverty trap" from which they rarely recover[7].

Society in Bangladesh is characterized by substantial socio-economic and gender differentials in health status[8], health care access and utilization[9] and health benefits gained from public and private health expenditures[10], all disfavouring the poor. The poor in rural Bangladesh lack access to quality health care due to both supply-side (e.g., geographical, skilled manpower, supplies, user-fees/"out-of-pocket" costs etc.)[11] and demand-side barriers (e.g., information, financial, socio-cultural barriers, etc.)[12]. Overall, it costs about twice as much to visit a government health service as to visit an unqualified practitioner, and about twice as much again to visit a private qualified practitioner. As a result, either they have to forego any treatment or rely mostly on unqualified or semi-qualified providers in the informal/private sector, who may account for 50–75% of visits outside home[13]. The economic consequences of ill health for the poor households in Bangladesh, especially the bottom 15–20%, is well documented[14]. Thus, enhancing poor people's ability to access quality health care at low cost has a potential poverty-alleviating effect in Bangladesh.

Different types of intervention are suggested for meeting the health care needs of the poor such as universal coverage, cash transfers, voucher schemes, exemption, community-based health insurance, and other strategies such as contracting out services to the private or NGO sector[15]. However, there is scant evidence of the impact of these small-scale interventions on the health of the poor, especially the most vulnerable among them. In this paper we will describe with evidence a programme undertaken by Building Resources Across Communities (BRAC)[16], which combined health and social protection interventions to address the health care needs of the poorest among the poor, besides poverty alleviation.

BRAC's "Challenging the frontiers of poverty reduction/targeting ultra poor, targeting social constraints (CFPR/TUP)" programme

In Bangladesh, the proportion of population falling below the lower poverty line[17] (corresponding to the consumption of 1805 kcal per person per day) are variously termed as "extreme poor", "poorest of the poor" or "ultra poor"[18]. These ultra poor households[19] have few or no asset base, are highly vulnerable to any shock (e.g., natural disaster, illnesses requiring in-patient or costly out-patient care, death or disability of an income-earner), and mainly depend on wage-labour for survival. They comprise one of the major (around 36% of the population) disadvantaged[20] population groups in rural Bangladesh.

BRAC's regular intervention integrates microcredit-based income-earning activities with skill-building and social awareness raising activities, in addition to essential health care services[21] to reduce vulnerability of the households against income-erosion from illness. However, research at BRAC and other similar organizations showed that regular microcredit-based intervention is not enough to effectively reach the most vulnerable section among the poor, i.e. the ultra poor in rural Bangladesh due to various structural factors[22]. This led BRAC to revisit its development paradigm and ultimately develop this customized grants-based, integrated intervention for the ultra poor[23]. Once the grants phase is over, it is presumed that the ultra poor population will attain a foundation for a sustainable livelihood, and be able to participate in and benefit from mainstream microcredit programmes.

The intervention was undertaken as an operation research project to develop a module of integrated health and social protection intervention for the ultra poor. Launched in 2002, the first phase of the intervention covered all the 21 sub-districts (*upazilas*[24]) of the three purposively selected famine and/or flood-prone districts in northern Bangladesh with a high concentration of extreme poor households. The ultra poor households were selected through a meticulous process

combining participatory wealth ranking exercises with the villagers and verification by a brief household survey. A set of inclusion and exclusion criteria ensured that only households which have been by-passed previously by any kind of development inputs from any source are selected[25].

Once selected, the women members of the ultra poor households were provided with two or more income-generating enterprise options including poultry rearing, livestock, vegetable farming, horticulture nursery, and non-farm activities (value range: US$ 50–150). Other non-health inputs were: subsistence allowance (@ US$ 0.17 daily); skill-development training (e.g., poultry/livestock rearing, vegetable cultivation, shoe-making etc.); social awareness development and confidence building training; and pro-poor advocacy for involving the rural elites[26].

The health support was tailored specifically to overcome different demand-side barriers faced by the poor, especially ultra poor, to access health care services[27]. These comprised of: EHC services with free installation of latrines and tube-wells (to develop health awareness and change "unfelt need" to "felt need"), consumer information on locally available health services (to overcome information barrier), identity card for facilitated access to formal health facilities (to overcome social exclusion), and financial assistance for diagnostics and hospitalization, if needed, through community mobilized fund (to overcome financial barrier) [28].

Impact assessment

CFPR/TUP was designed as an experimental programme to address some of the most complex economic and socio-political constraints facing the ultra poor in Bangladesh. The basic model of careful targeting, asset transfer, skills development, intensive technical assistance along with customized health support has in general worked quite well as reflected in the various assessments carried out both internally by BRAC's Research and Evaluation Division[29] and external evaluators[30].

Impact on livelihood

Findings reveal that the majority of the participating ultra poor households improved their poverty status following the intervention. Using the conventional extreme economic

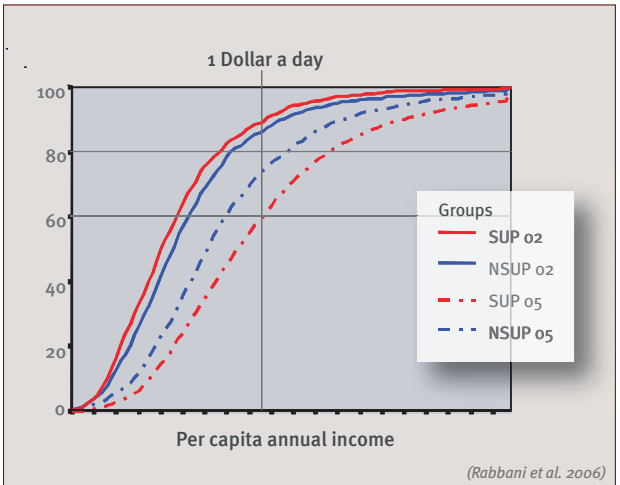

Figure 1: Per capita income in 2002 and 2005

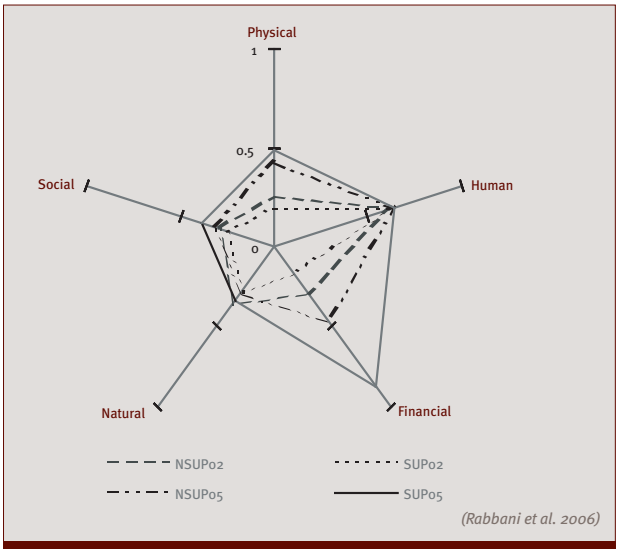

Figure 2: Changes in different assets during 2002–2005

poverty line of one dollar a day, we find that in 2002 the proportions of extreme poor were 89% and 86% for selected ultra poor households, SUP (top 1st line) and not-selected ultra poor households, NSUP (top 2nd line) households respectively (Figure 1). It has gone down to 59% for the SUP (bottom broken line) but only to 73% for the NSUP in 2005 (broken line above the previous line) [31].

Five types of assets formed the basis of a household's sustainable livelihood in this evaluation and is represented in an asset pentagon (Figure 2). These assets are: financial assets (savings and credit), human assets (earner-member ration, average years of schooling of household members, percentage of household members without any disability, percentage of household members who have not suffered any illness in the last 15 days from the day of interview), physical assets (productive assets, furniture, tube-well, ornaments/ jewellery, value of homestead), natural assets (land ownership), and social asset (whether household members received any invitation from neighbours)[32]. The asset pentagon in Figure 2 visually displays the relative changes over the three-year time period of these assets among the SUP and NSUP households. It can be seen that SUP households have overcome their initial deficiencies in most categories except human assets, and have managed a stronger asset base than the NSUP households. The lack of change in this category reiterates the fact that investment in human asset is a long-term process.

Impact on nutrition and food security

Simultaneously, the food security status of the households improved (Figure 3). In 2002, over 60% of the SUP reported chronic food deficit, the rest had occasional deficit, and only a few SUP households broke even. Food deficit is also highly prevalent in 2005, but the extent of chronic food deficiency has fallen for both groups. The quantity and quality of the food consumed also improved during the study period[33]. A 31% increase in food intake, and 9% increase in energy intake occurred in the SUP households while there was only 1% increase in food intake and 10% decline in energy intake for the NSUP households.

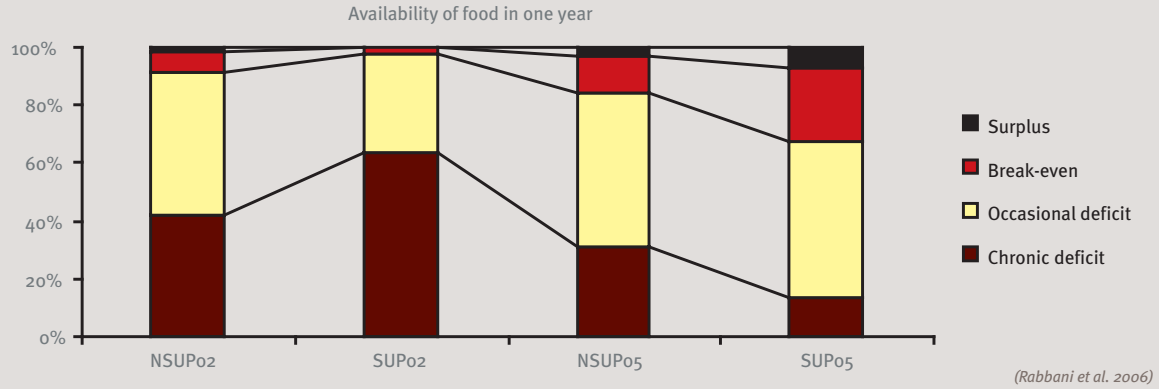

Figure 3: Food security status during last one year

Findings from the impact evaluation studies also revealed substantial improvement in other objective indicators such as children's nutritional status and use of contraceptives[34], and improved quantity and quality of food consumption[35]. The latter study based on the three days recall method found that the intake of energy significantly increased from 1750±650 kcal/day to 2138±704 kcal/day in SUP households where no such significant change was observed in the NSUP households. Also, the percentage of energy coming from cereals decreased from 85% to 78% in SUP households while it remained unchanged in NSUP households. The consumption of fish and oil improved significantly in the SUP households[36].

Self-rated health

When women's self-rated health status during 2002 to 2004 was compared, SUP women fared better than the NSUP women (Figure 4)[37]. They reported better improvements, fewer reported poorer health, and a marginal proportion of SUP women reported good health if it was previously good. The effects of the CFPR/TUP programme remain positive and significant even when factors like marital status, education, age, previous health, disability, occupation, sanitary knowledge and behaviour, family planning and location are held constant[38]. Thus, the programme has a significant effect on women's health.

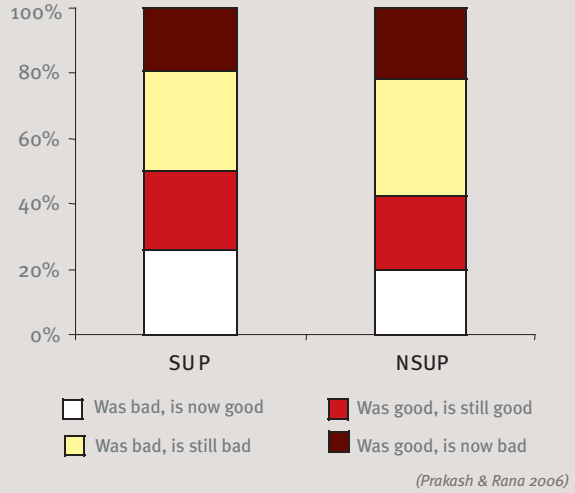

Figure 4: Self-rated health status

Economic consequences of illness

The increase in number of workdays lost to illness could reflect a greater ability for SUP members to take time off to recover rather than attempt to keep working and thus prolong their ailments (Table 1). In 2002, fewer SUP members spent money, and those that did spent far less than the NSUP members. These differences vanished in 2005, showing increased capacity for expenditure on health for the SUP households.

Health care-seeking behaviour

By increasing capacity for health expenditure and facilitating access to formal public sector health care facilities (by use of health card), the CFPR/TUP programme initiated changes in health-seeking behaviour of the ultra poor towards greater use of qualified health care providers and reduction of self-treatment/no treatment[39]. This happened, presumably, through activities in the intervention to overcome specific demand-side barriers (e.g., informational, economic, cultural, and social barriers) for accessing health care. However, gender differences in health care-seeking and health expenditure disfavouring women were also noted.

Importance of the health components

The importance of customized health support to overcome income-erosion is also reiterated in the impact evaluations. Authors of another study on the same group of participating women explored factors underlying change and found that "health is a major factor in determining change in the TUP programme"[40]. They concluded that if participants cannot work due to poor health and nutrition, they are never likely to see significant change that is sustainable. Similar conclusion about the importance of the health component was also reached by an independent mid-term review mission of the CFPR/TUP programme[41].

Sustainable livelihood

At the end of the intervention period, over half (around 54%) of the ultra poor households participating in the intervention were at different stages of joining the mainstream development programme of BRAC and taking microcredit loans to continue with their income-earning enterprises (Figure 5)[42]. They also continued to receive regular EHC services provided by the programme. The authors concluded

	2002			2005			Diff. in diff
	SUP (1)	NSUP (2)	Difference (3=1-2)	SUP (4)	NSUP (5)	Difference (6=4-5)	(7=6-3)
Prevalence of illness (% people sick in last 15 days)	15.21	14.17	1.04*	14.17	14.45	-0.28	-1.32*
Workdays lost due to illness (mean)	1.28	1.47	-0.19	2.96	2.66	0.31	0.50*
Average expenditure on illness (doctors' fees+medicine)	76.26	148.10	-71.84**	127.47	112.64	14.83	86.67**
Average expenditure on transport for medical attention	25.34	52.42	-27.08	27.08	22.48	4.60	31.68*

*, ** *denote significance at less than 5 and 1% level respectively*

(Rabbani et al. 2006)

Table 1: Factors affecting health

that with a lower borrower-member ratio and relatively smaller sized credit taken by these "graduated" ultra poor members, microcredit/microfinance for the poorest may take a longer time to achieve sustainability.

In the CFPR/TUP model, a declining trend in the total cost of intervention per ultra poor household was seen with time (from US$ 344 in 2002 to US$ 287 in 2004) which is expected to go down further to US$ 278 in 2006[43]. The model was concluded as cost-effective considering the impacts on livelihood which were found to be positive (improved income and asset base), comprehensive (economic, social and health changes) and apparently sustainable (maintenance of asset growth after "graduation" and joining regular microcredit/microfinance programme).

Conclusions

Mitigation of the income-erosion effect of illness is an essential pre-requisite for alleviation of poverty, especially for the poorest households in low-income countries like Bangladesh[44]. The findings of this study support the

(Sulaiman et al. 2006)

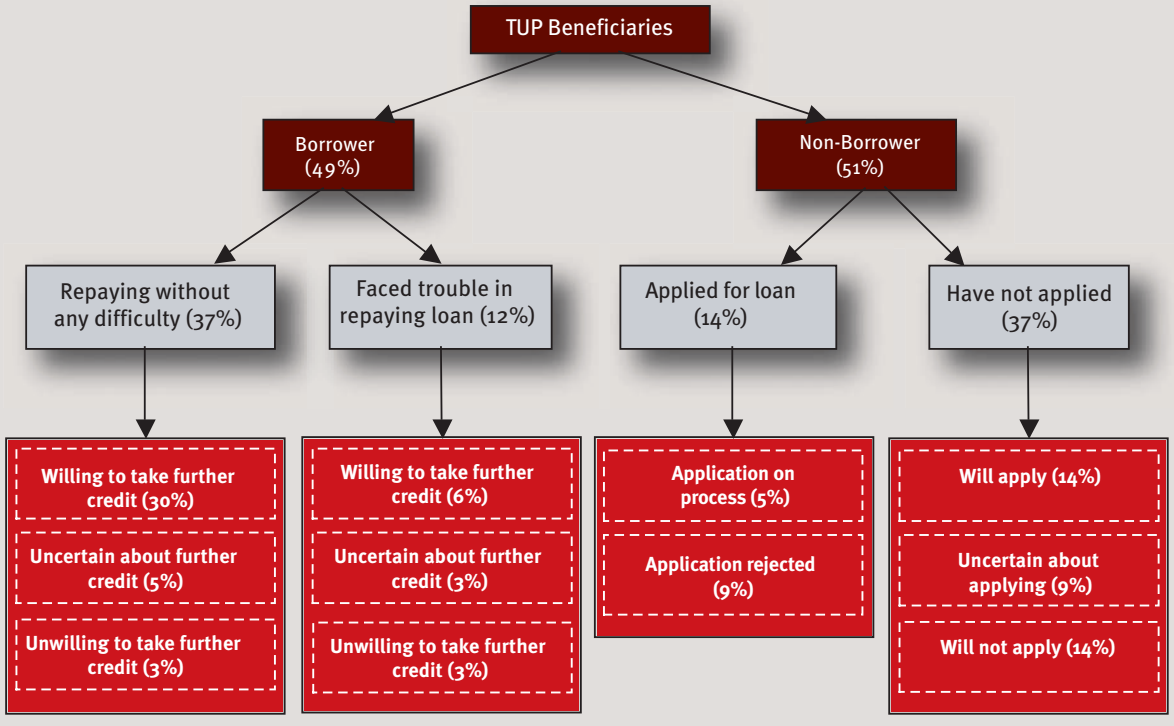

Figure 5: Status of beneficiary households of 2002 (baseline) in February 2005 (one year after completion of intervention cycle)

hypothesis that an intervention that included health and social protection measures in addition to economic resources and capability development typical of microcredit programmes, would be more likely to succeed among the very poor[45]. However, existing evidence indicates that providing health services for the poorest is more expensive than the average cost in any population due to a number of reasons such as cost of targeting, varied service needs and acceptable quality of care to attract people for service use[46]. For scaling up of this kind of intervention, the problem of financing has to be resolved due to large resources needed in the initial phases. This is not the sole purview of health system, but collaboration with other sectors such as education, agriculture, employment generation, small and medium enterprise development, women's affairs etc. is needed. The health system can play a stewardship function in guiding this collaboration. ❑

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Mandatory clinical trial registration: rebuilding public trust in medical research

Article by Trudo Lemmens (pictured) and Ron A Bouchard

At a 2004 Ministerial Summit on Health Research in Mexico, ministers of 52 countries endorsed the idea of registration of clinical trials and called on the World Health Organization (WHO) to develop a uniform registration system[1]. In response, the WHO's Clinical Trials Platform developed a detailed proposal and launched in 2006 an international online registration database[2].

The idea of registering clinical trials was launched decades ago, and has over the years been introduced by various organizations and governmental agencies[3]. But it is only in 2004 that a controversy involving clinical research created a real momentum for the establishment of comprehensive and mandatory national and international clinical trials registries. The controversy involved the alleged hiding of the results of several clinical trials on the use of paroxetine for the treatment of depression in children and adolescents by GlaxoSmithKline (GSK)[4]. According to the accusations in a lawsuit launched by the Attorney General of New York, the company selectively published positive but partial results of one of the trials in a leading medical journal, and used this publication for the promotion of off-label prescription of the product, while hiding results which indicated lack of efficacy and increased risk of harm. The controversy is neither the first nor the last involving misrepresenting, hiding, or delaying publication of important data, with serious consequences for thousands of patients[5]. But the public nature of the lawsuit, the seriousness of the allegations, and the clear public health relevance of the results, made the registration proposal "irresistible"[6]. GSK itself accepted, as part of the settlement of the lawsuit, to make its clinical trials data accessible on a website[7], inspiring other companies to quickly follow suit[8].

More than 150 scientists and several organizations involved in promoting evidence-based medicine also signed in 2004 the Ottawa Statement, calling for the introduction of mandatory and legally enforceable registration of all clinical trials[9]. The International Committee of Medical Journal Editors (ICMJE), an organization of 12 of the world's most influential medical journals, announced in the same year that its members would from then on only consider for publication clinical research studies that had obtained a clinical trial registration number, prior to enrolling human subjects[10]. Trial registration has thus become a de facto requirement for those who want to publish their research in one of the leading medical journals. Registration of clinical trials seems indeed to have taken off. Registration on the US-based ClinicalTrials.gov alone grew from a little over 13 000 trials in 2004 to over 40 000 as of June 2007[11], while WHO's international registry already had over 12 000 entries by June 2007.

Clinical trials registration: what is it?

WHO Clinical Trials Platform defines a clinical trial as "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes". The registration process involves assigning a unique number to a clinical trials protocol, details of which are made public on a central registry at trial onset[12]. WHO Platform provides a unique global identifier, with links to certified national registries, and a one-stop search portal which is freely accessible. WHO's registration system is based on a "minimum data set" of 20 items (see appendix). The advantages of WHO international registry include: equal access to data by sponsors, researchers, regulators and the public, the use of freely available platform software rather than sponsor-specific proprietary software, uniform data recording across jurisdictions and sponsors, and increased transparency and accountability, in comparison with sponsor-organized registries. Nevertheless, industry representatives have opposed mandatory registration of all WHO's proposed registration items, claiming that it would harm market competition and stifle innovation[13]. They suggested that five of the 20 items (official scientific title, interventions, primary outcome, key secondary outcomes, and target sample size) should be amenable to delayed disclosure, expressing concern about protection of intellectual property and decreased competitiveness. Others argue that without these five items trial information becomes meaningless[14].

Ethical and public policy foundations of trial registration

Research involving human subjects relies for a large part on altruism, and is dependent on participants' trust in its contribution to public good[15]. Controversies such as the one mentioned earlier have led to mistrust, not only towards pharmaceutical companies, but also towards the medical research enterprise itself, and to domestic governments, which often rely on industry self-regulation and public-private partnerships[16]. Recent surveys indicate that only 25% of

Americans think that the pharmaceutical industry is doing a good job, on par with their view of the tobacco industry[17]. Trial registration can be seen as part of a crucial effort to restore public trust in medical research[18]. It constitutes a public invitation for further scrutiny and control of publication of research results and as a statement that when it comes to patient and consumer safety, nothing ought to remain hidden behind a veil of corporate or governmental secrecy.

Mandatory registration can also be connected to established moral obligations to research subjects. Research participation is valued by participants as a public service[19]. They expect that the information gathered through their assistance contributes to scientific progress. This is why influential research ethics guidelines or statements such as the Declaration of Helsinki[20] and the Nuremberg Code[21] both require that the design and purpose of studies on humans be publicly available and that the rights of trial participants take precedence over both commercial and career interests[22]. As noted by the ICMJE, research participants "deserve to know that the information that accrues from their altruism is part of the public record, where it is available to guide decisions about patient care, and deserve to know that decisions about their care rest on all of the evidence, not just the trials that authors decided to report and that journal editors decided to publish"[23]. Assuring research subjects that their participation provides a public benefit should also stimulate their commitment towards research[24].

Registration further promotes knowledge transfer. Discrepancies between information gathered in clinical trials and reported results have long been recognized[25]. Mandatory registration enhances dissemination of important clinical information among clinicians, researchers, governmental agencies, and the public. It improves information exchanges, for example, between industry-based and academic researchers and alerts researchers to gaps in the knowledge base[26]. It facilitates knowledge creation and knowledge transfer within the drug development and innovation sector[27] and enables "research into research", both from a clinical perspective and a science and technology studies perspective[28].

From a regulatory perspective, the most important contribution of mandatory registration is that it allows the research community and governmental agencies to better control for bias in clinical trial design and publication[29]. Design bias occurs when a trial is designed with a high likelihood of being positive, for example through careful selection of clinical trial populations. Publication bias refers to the practice whereby studies providing unfavourable or negative result are not published or misrepresented through data selection. Bias can occur because journals are less interested in publishing negative research outcomes. As various controversies highlight, it can also be part of a commercial strategy to hide results that will not support an application for new drug approval or that will undermine the efficacy or safety status of an existing product[30]. Clinical trial registration allows the research community to scrutinize what studies have been proposed, whether the design seems appropriate, how many patients were being recruited, what the intended outcomes were, and whether the studies seem fully reported.

Mandatory registration can also contribute to scientific and economic efficiencies in clinical research. It may reduce risk to research subjects by avoiding unnecessary duplication of efforts and minimizing situations where harm to subjects has not yet been reported[31], while also encouraging appropriate replication and confirmation of results[32]. On a global level, public disclosure of the existence of certain trials fosters both international collaboration among researchers and recruitment to clinical trials which serves to enhance trial success rate[33]. Interestingly, at one of WHO Clinical Trials Platform meetings, patient advocates also suggested that an international central registry will promote trial participation, by providing information for patients who would often be willing to travel to participate in clinical trials. Finally, registration should help domestic and international funding bodies target resources where they are most needed and likely to be effective[34]. Well-coordinated global registration will further help domestic governments, particularly those in resource-poor countries with less mature regulatory regimes to better manage and monitor their clinical research programmes and protect vulnerable trial populations[35].

Promoting public trust, transparency of research and knowledge transfer, respecting research subjects, and facilitating clinical trials thus provide the underlying rationale for registration. It seems clear that meaningful, i.e. substantial disclosure, corresponds most with these values. Any exception to the principle of extensive disclosure of research information ought therefore to be justified by considerations that are equally pressing. What are the concerns about mandatory registration and do they trump the public interest in trial registration?

Registration, intellectual property rights and competitive interests

Patent concerns

The argument that public disclosure of the information requested in WHO clinical trials platform will undermine a potential patent application seems weak. When a novel product or "novel use" of a product is tested in clinical trials, it is usually already protected by a patent. Patent applications are filed as soon as there is an expectation that a new compound or a new use may be patentable subject matter. For a new product, this generally occurs early on in the development process, years before a clinical trial is undertaken. For a new use patent, an application would be filed as soon as there is a realistic expectation that this new use is patentable, again long before it is tested in a clinical trial.

In fact, the existence of patent protection for new products and new uses undermines the arguments against detailed registration and disclosure requirements. Patent applications often contain more information about potential drug development strategies than the summary information required for registration under the current WHO Platform proposal. They will be published in most jurisdictions within 18 months of the application. Domestic patent legislation in several jurisdictions, as well as the 1970 Patent Cooperation Treaty[36], explicitly require publication of the patent application within a short period of time after registration of the patent.

While there are some exceptions to this publication requirement, the patent system itself aims at promoting publicity. Thus, information about development strategies and potential new use strategies for existing drugs can be gleaned from the information contained in patent applications by competitors long before trial registration.

Competitive advantage considerations

Other threats to market exclusivity and loss of competitive advantage have been invoked to justify delayed disclosure of certain clinical trial information in public registries. During the WHO consultation process, industry organizations provided examples of situations in which, it alleged, clear commercial interests are attached to delayed disclosure[37]. In those situations, registry fields would be considered "highly proprietary". This would be the case, for example, when a company is testing a new method of delivery for a patented product, and where competitors may learn about these efforts, speeding up the development of a new delivery of their own competitive product. Delayed disclosure would protect a company's interest in establishing a strong market position through being the first entrant on the market. Another scenario would be that a company is developing a product, new use, or line extension of an existing product, which it does not expect to be patentable. It may be inclined to test this product secretly, again to keep a potential head-start over competitors. Another scenario pertains to orphan drugs. Under certain systems of orphan market exclusivity, an inventor who has developed a product for a rare disorder can obtain market exclusivity, keeping competitors off the market for a given period. A competitor can break orphan market exclusivity, however, if it comes up with a product that is shown to be superior to the product that obtained exclusivity. Under this scenario, an innovator has a financial interest in staying ahead of competitors who could be inclined to attempt the development of a superior product in the same class.

A number of arguments can be invoked to challenge the claim that these scenarios justify delayed disclosure. First, it is worth pointing out that competitive intelligence currently already provides information about a competitor's strategic developments. Pharmaceutical sponsors aggressively gather competitive intelligence on their own, and use due diligence done by patient advocacy groups and individual patients seeking trials involving potentially life-saving therapies. Intelligence may have become easier to accumulate because of the close links between several patient advocacy groups and industry[38]. Second, when research subjects are recruited in clinical trials, there is an ethical and legal obligation to obtain informed consent, which requires that patients receive meaningful and thus reasonably detailed information about the study. Gathering clinical trial information through research subjects rather than through a registry may be more time consuming, but is not impossible for a resource-rich industry. Third, even if access to registry data may affect in one particular trial a competitive advantage of one company over another, the former may benefit in other circumstances of the full disclosure regime. Over time, a level playing field should be established as competition will simply start at an earlier stage. Fourth, the general claim that it will undermine a company's interest in refining and innovating its products remains very speculative. Speculation about potential harm to economic interests is a poor basis for public policies that aim at protecting an important public interest. In the orphan drug context, even more so than in the other scenarios, public interest seems to be hampered by anything less than full disclosure. In fact, healthy and beneficial market competition will be stimulated by the registration of all trial components. So much the better if a competing innovator wants to invest in the development of a superior product. This competitor will still carry the risk that its attempts to develop a superior product will fail. Moreover, as argued under the previous scenario, disclosure of basic aspects of clinical trials is most likely to have occurred already anyway.

The risk of loss of competitive advantage and the speculative nature of the impact on innovative drug development strategies must be weighed against the importance of public access to important clinical trial data. While the development of new therapeutic agents is both desirable and valuable, it seems hard to defend the claim that it is more important to avoid the undefined and seemingly limited risks that full registration may create for the development of these agents than to promote transparency and sharing of information. More importantly, providing adequate information about clinical trials to research subjects is an unavoidable ethical and legal obligation. Registering basic clinical trial information constitutes only one additional step and ought to be seen as a general moral obligation towards the public and towards the goal of transparent and responsible research, whose integrity and reputation is increasingly challenged. It is worth pointing out here also that the TRIPS (Trade-Related Aspects of Intellectual Property Rights) Agreement explicitly allows states to disclose commercially sensitive information of pharmaceutical companies because of public health interests[39]. This constitutes an international recognition of the fact that public health interests trump trade-related interests.

These arguments support the position of WHO clinical trials platform, that full disclosure of all minimal data at the time of registration is essential. But while full disclosure of the minimum data-set is an important first step in the promotion of the integrity and transparency of clinical research, it is not a panacea.

Limits of trial registration

One of the most significant limits of WHO clinical trials proposal is its lack of direct enforceability: the WHO has no jurisdiction to directly sanction or to directly enforce registration through other means. This scenario is analogous to other international quasi-law vehicles such as the United Nations (UN), World Trade Organization (WTO) or World Intellectual Property Organization (WIPO), which depend on so-called "soft law" compliance measures to ensure compliance by member states. The experience with the US ClinicalTrials.gov database indicates what can happen if there is no concrete penalty attached to registration. While the 1997 US FDA Modernization Act[40] requires trials for all life-

threatening and serious conditions to be registered on the ClinicalTrials.gov databank, detailed analyses indicate that a significant number of industry-sponsors do not comply with the requirement[41].

To support WHO's initiative, funding agencies, academic centres, philanthropic organizations, and supportive industrial sponsors ought to develop strict compliance mechanisms. Registration should be imposed as a requirement for research ethics approval. Patient advocacy groups could attach registration as a condition to support and advertise clinical trials. The best approach would be for domestic governments with control over existing primary registries to endow relevant governing bodies with the necessary legal jurisdiction to enforce compliance through sanctions. Given industry's concern about competitive advantage, it seems particularly important to assure pharmaceutical companies that there is a level playing field, by ensuring compliance with registration requirements. Domestic regulations and state control can do that.

Even though the WHO minimal data set extends well beyond information required to be registered in several other registries, some have criticized the WHO initiative for providing insufficient information. The Ottawa Statement, for example, proposes that registration data further include information on the full protocol and consent forms, details of ethics committee approval and other trial design information[42].

Registration of the WHO data set will indeed not resolve all problems associated with manipulation of trial results[43]. It is unclear how the accuracy of registration data that are not peer-reviewed as well as the scientific validity of statistical analyses and interpretations could be validated using information from existing registries or resources. The registration system does not alleviate concerns associated with the fact that sponsors with vested commercial interests still control how research is designed, how subjects are recruited, how data are collected, and how results are presented[44]. The data set does not provide registry staff or researchers with access to protocols or raw data, which significantly hampers independent scientific review of database entries. Without the ability to independently review and validate entries, selective reporting of trial results may still occur. Finally, the basic principles of evidence-based medicine require review of study design and quality in addition to other relevant scientific data prior to drawing conclusions from a single study[45].

Finally, WHO's clinical trials registration system does not impose results reporting. It allows the public, researchers, and governmental agencies to know that research is or has been undertaken, which allows for further scrutiny and questions when publications come out. But it does not provide them with direct access to final outcomes. Several influential organizations have called for public disclosure of results in a manner analogous to clinical trial registration, including the US Institute of Medicine, ICMJE, and researchers[46]. As noted by the ICMJE in their most recent discussion statement on mandatory registration[47], the climate for results registration will likely change dramatically and unpredictably over coming years but is sure to go ahead in some form.

WHO has recognized that this is a next important step in the promotion of research integrity. It has set up a Study Group on the Reporting of Findings of Clinical Trials, which is looking at the development of criteria and standards of disclosure of results[48]. This new initiative will constitute another important step towards more reliable and trustworthy clinical research. Result reporting will only have success, however, if a coherent, comprehensive, and mandatory registration system is in place. It seems therefore crucial that national governments, professional organizations, industry, and researchers commit to such a registration system and fully support WHO in its efforts. ❑

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	Item	Definition/Explanation
1	Primary Register and trial ID #	Name of Primary Register, and the unique ID number assigned by the Primary Register to this trial.
2	Date of registration in Primary Register	Date when trial was officially registered in the Primary Register.
3	Secondary ID#s	Other identifying numbers and issuing authorities besides the Primary Register, if any. Include the sponsor name and sponsor-issued trial number (e.g., protocol number) if available. Also include other trial registers that have issued an ID number to this trial. There is no limit on the number of Secondary ID numbers that can be provided.
4	Source(s) of monetary or material support	Major source(s) of monetary or material support for the trial (e.g., funding agency, foundation, company).
5	Primary Sponsor	The individual, organization, group or other legal entity which takes responsibility for initiating, managing and/or financing a study. The Primary Sponsor is responsible for ensuring that the trial is properly registered. The Primary Sponsor may or may not be the main funder.
6	Secondary Sponsor(s)	Additional individuals, organizations, or other legal persons, if any, that have agreed with the Primary Sponsor to take on responsibilities of sponsorship. A Secondary Sponsor may have agreed: • to take on all the responsibilities of sponsorship jointly with the Primary Sponsor; or • to form a group with the Primary Sponsor in which the responsibilities of sponsorship are allocated among the members of the group; or to act as the sponsor's legal representative in relation to some or all of the trial sites; or • to take responsibility for the accuracy of trial registration information submitted.
7	Contact for public queries	Email address, telephone number, or postal address of the contact who will respond to general queries, including information about current recruitment status.
8	Contact for scientific queries	Email address, telephone number, or postal address, and affiliation of the person to contact for scientific queries about the trial (e.g., principal investigator, medical director employed by the sponsor). For a multi-centre study, enter the contact information for the lead Principal Investigator or overall scientific director.
9	Public title	Title intended for the lay public in easily understood language.
10	Scientific title	Scientific title of the study as it appears in the protocol submitted for funding and ethical review. Include trial acronym if available.
11	Countries of recruitment	The countries from which participants will be, are intended to be, or have been recruited.
12	Health condition(s) or problem(s) studied	Primary health condition(s) or problem(s) studied (e.g., depression, breast cancer, medication error). If the study is conducted in healthy human volunteers belonging to the target population of the intervention (e.g., preventative or screening interventions), enter the particular health condition(s) or problem(s) being prevented. If the study is conducted in healthy human volunteers not belonging to the target population (e.g., a preliminary safety study), an appropriate keyword will be defined for users to select.
13	Intervention(s)	Enter the specific name of the intervention(s) and the comparator/control(s) being studied. Use the International Non-Proprietary Name if possible (not brand/trade names). For an unregistered drug, the generic name, chemical name, or company serial number is acceptable. If the intervention consists of several separate treatments, list them all in one line separated by commas (e.g., "low-fat diet, exercise"). The control intervention(s) is/are the interventions against which the study intervention is evaluated (e.g., placebo, no treatment, active control). If an active control is used, be sure to enter in the name(s) of that intervention, or enter "placebo" or "no treatment" as applicable. For each intervention, describe other intervention details as applicable (dose, duration, mode of administration, etc.).
14	Key inclusion and exclusion criteria	Inclusion and exclusion criteria for participant selection, including age and sex.
15	Study type	A single arm study is one in which all participants are given the same intervention. Trials in which participants are assigned to receive one of two or more interventions are NOT single arm studies. Crossover trials are NOT single arm studies. A trial is "randomized" if participants are assigned to intervention groups using a method based on chance (e.g., random number table, random computer-generated sequence, minimization, adaptive randomization).
16	Date of first enrolment	If the trial is being registered after recruitment of the first participant record actual date of Anticipated date of enrolment of the first participant.
17	Target sample size	Number of participants that this trial plans to enrol.
18	Recruitment status	Recruitment status of this trial. • **Pending:** participants are not yet being recruited or enroled at any site . • **Active:** participants are currently being recruited and enrolled. • **Temporary halt:** there is a temporary halt in recruitment and enrollment. • **Closed:** participants are no longer being recruited or enroled.
19	Primary outcome(s)	Outcomes are events, variables, or experiences that are measured because it is believed that they may be influenced by the intervention. The Primary Outcome should be the outcome used in sample size calculations, or the main outcome(s) used to determine the effects of the intervention(s). Enter the names of all primary outcomes in the trial as well as the pre-specified timepoint(s) of primary interest. Be as specific as possible with the metric used (e.g., "% with Beck Depression Score › 10" rather than just "depression"). Examples: Outcome Name: all-cause mortality, Timepoints: 5 years; or Outcome Name: Mean Beck Depression Score, Timepoint: 18 weeks.
20	Key secondary outcomes	Secondary outcomes are events, variables, or experiences that are of secondary interest or that are measured at timepoints of secondary interest. A secondary outcome may involve the same event, variable, or experience as the primary outcome, but measured at timepoints other than those of primary interest (e.g., Primary outcome: all-cause mortality at 5 years; Secondary outcome: all-cause mortality at 1 year, 3 years), or may involve a different event, variable, or experience altogether (e.g., Primary outcome: all-cause mortality at 5 years; Secondary outcome: hospitalization rate at 5 years). Enter the name and timepoint(s) for all secondary outcomes of clinical and/or scientific importance. Be as specific as possible with the metric used (e.g., "% with Beck Depression Score › 10" rather than just "depression"). Examples: Outcome Name: all-cause mortality, Timepoint: 6 months, 1 year; or Outcome Name: Mean glycosylated hemoglobin A1C, Timepoint: 4 and 8 weeks.

Last update: July 2007. Available: http://www.who.int/ictrp/data_set/en/index.html

Appendix A: WHO Minimum Data Set

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Open access to research protocols and results: intellectual property and the right to health

Article by Rodrigo A Salinas

The human right to the highest attainable standard of health requires for its fulfilment access to good quality health care. Equitable access to health technologies, ranging from health promotion activities to drugs and complex interventions, is a key part of the care provided. An equally important requirement for ensuring good quality care, however, is access to information on the efficacy and safety of these technologies, coming from scientific research. Any barrier hampering access to this information should be considered as dangerous as those barriers preventing access to drugs and other health technologies. The Doha Declaration recognized in 2001 that trade-related intellectual property rights should not conflict with the right to protect public health. Conflict among these rights, however, affects not only access to drugs, as emphasized by those mechanisms created to implement the Declaration, but also access to the information on the efficacy and safety of these drugs, particularly by those provisions contained in article 39.3 of the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement that reward the non-disclosure of the findings of medical research.

The right to the highest attainable standard of health has been recognized as a human right in the International Covenant on Economic, Social and Cultural Rights, adopted and opened for signature and ratification by the General Assembly of the United Nations (UN) in December 1966. In a general comment issued by the Economic and Social Council of the UN in 2000, it is explicitly stated that a substantive issue arising in the implementation of this right is the provision of equal and timely access to basic preventive, curative, rehabilitative health services, regular screening programmes and appropriate treatment of prevalent diseases and disabilities.

The new global deal on intellectual property rights, arising out of the Uruguay Round of Multilateral Trade Negotiations that concluded with the signature of the Agreement on TRIPS, and the creation of the World Trade Organization (WTO), in the eighties, has been denounced in many forums as a barrier for fulfilling this right. The current system of granting patents for new drugs, considered as crucial for encouraging the invention of much-needed medicines by the pharmaceutical industry, has been considered as an obstacle for getting equitable access to drugs in developing countries[1]. These concerns and a couple of much publicized cases, such as the case brought against President Nelson Mandela by the South African Pharmaceutical Manufacturers Association, eventually led the WTO to produce the Doha Declaration on the TRIPS Agreement and Public Health recognizing that:

"…the Agreement can and should be interpreted and implemented in a manner supportive of WTO members' right to protect public health and, in particular, to promote access to medicines for all"[2].

Ensuring access to drugs, notwithstanding, is only one among other requirements needed for fulfilling the right to good quality health care. A much less explored, but equally important domain is the need for ensuring access to information on the efficacy and safety of drugs. Health care, in order to achieve the desirable outcomes it is supposed to get, needs not only careful use of technologies that are applied by health professionals, and provided by health services, but needs also a responsible and accountable decision-making process leading to the prescription of a particular procedure for a particular person. This decision-making process, to be considered a high quality one, needs timely access to adequate and appropriate information on the safety, efficacy and effectiveness of the whole menu of technologies that are available to be prescribed for different conditions. Good quality information on these domains comes, in medicine, from methodologically sound and ethically responsible research. It is reasonable, thus, to conclude, that the materialization of access to health care as a human right, needs not only actual access to technologies but also adequate and timely access to information on those domains that allow appropriate decisions to be made at the points where these decisions occur.

Practising medicine and allied health professions in the 21st century, would be unthinkable without access to good quality data on the efficacy, effectiveness, and safety of health technologies, ranging from health promotion activities to highly sophisticated medical devices. As part of this move towards explicit use of scientific data, evidence-based medicine has been widely accepted as a new paradigm for teaching and practising medicine, de-emphasizing intuition, unsystematic clinical experience and pathophysiologic rationale as sufficient grounds for decision-making[3], and

integrating individual clinical expertise with the best available external clinical evidence from systematic research when deciding about the care of individual patients[4]. This approach has been recognized, also, as a valuable tool for choosing the best strategies for closing the gap between research and practice[5] and for improving health care provision, through the delivery of high-quality care that integrates knowledge coming from evidence-based medicine and the emerging discipline of evidence-based management[6].

A number of barriers exist, however, for getting scientific evidence into practice. They include many factors beyond the control of the practitioner and patient, and the process of linking the outcomes of scientific research with health policy and clinical care requires addressing all of them in a thorough manner. A key step in translating the findings of relevant research into actual benefit to patients is ensuring access of decision-makers to good quality evidence.

Unexpectedly, the global system of protection of intellectual property rights has ended up being a barrier not only for access to drugs, but also a barrier for accessing information on the efficacy and safety of drugs. The TRIPS Agreement not only gives patent protection to innovative drugs, but it has also been understood as protecting from divulgation the information on efficacy and safety that is submitted to regulatory authorities, having the status of undisclosed[7]. The TRIPS agreement states, thus, in its article 39.3:

"Members, when requiring, as a condition of approving the marketing of pharmaceutical or of agricultural chemical products which utilize new chemical entities, the submission of undisclosed test or other data, the origination of which involves a considerable effort, shall protect such data against unfair commercial use. In addition, Members shall protect such data against disclosure, except where necessary to protect the public, or unless steps are taken to ensure that the data are protected against unfair commercial use".

The underlying logic of data exclusivity suggests that it is an expression of trade-secrets more than patents, as expression of intellectual property rights[8]. The role of regulatory authorities in ensuring that the information on efficacy and safety of drugs is adequately analyzed has been seriously challenged in the last years[9]. Some authors have labelled the work of the Food and Drug Administration in USA, as substandard[10], and recent disclosure of adverse events information on drugs such as rofecoxib (vioxx) throws a cloak of doubt over the capacity of regulatory authorities for dealing with safety and efficacy information in a secret manner, and public disclosure of all information concerning drugs has been demanded. A recent advance on this direction has been the general agreement on the need of registering clinical trials, endorsed and supported by the World Health Organization, the International Committee of Medical Journal Editors, and even Pharmaceutical Manufacturers[11]. There are many reasons for endorsing this initiative[12]: a publicly accessible register would help funding agencies in deciding where to allocate the money; a register of ongoing research would help patients interested in participating in clinical trials identifying suitable options, and a register leading to the results of research would help both patients and health professionals accessing comprehensive information on the safety and efficacy of medical interventions. The success of initiatives like The Cochrane Collaboration, aiming at producing periodically updated reviews of all relevant randomized controlled trials of the effects of health care[13], rely critically on public access to all results of research.

Any barrier to public access to the findings of research on the effects of health care may result, thus, in threats to the quality of care provided by health services and professionals, to the effective exercise of autonomy of patients in choosing the most appropriate treatment for their condition and, in a more general way, in a threat to the fulfilment of the widely acknowledged right to the highest attainable level of health. Barriers arising out of trade agreements and any reward to non-disclosure of the results of research protection of intellectual property rights should be identified and adequately addressed. The effects of the implementation of the Doha Declaration should go beyond ensuring access to drugs. They should aim, also, at ensuring access to information on the efficacy and safety of drugs. Those conflicts arising out of article 39.3 of the TRIPS Agreement, preventing public access to research results, threatening the transparency of regulatory authorities' processes, and fostering the non-disclosure of data by pharmaceutical companies, should be denounced and solved in the spirit of the general principles recognized by the Doha Declaration in favour of public health protection. The emphasis on the creation of mechanisms to implement this Declaration has been placed, up until now, in ensuring access. The movement towards free access to the results of biomedical research, including the creation of trials registries and freeing the access to peer-reviewed journals in low-income countries, should consider the existing conflict with extra-patent intellectual property rights granted to non-disclosed information on the efficacy and safety of drugs, and the current confidence crisis on how this information is appraised by the regulatory authorities. ❑

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A social determinants approach to health equity

Article by Sharon Friel (pictured), Ruth Bell, Tanja AJ Houweling and Sebastian Taylor

The Commission on Macroeconomics and Health clearly demonstrated that an investment *in* health was good for the national economy[1]. Investing *for* health arises from a different paradigmatic base and recognizes the pursuit of health and social well-being as a human right and a matter of social justice[2]. Successful investment for health can be measured not simply by economic improvement but, perhaps more importantly for sustainable human civilization, by observable health and social gain.

There is general concurrence internationally that supporting investment for health requires a shift in policy and practice. As the 2003/04 "10/90 Report"[3] summarizes, in the past half century the concept of development has refocused from human capital to be concerned primarily with the provision of necessities fundamental to living, including health. However, not everyone in society has equal opportunity to achieve good health. Gross differences in health, both between and within countries, are observed by markers of social stratification such as income, education, employment, gender and ethnicity[4,5,6]. In developing countries the emerging double burden of communicable and noncommunicable disease[7,8,9] combined with pervasive poverty serve to compound the poor health opportunities for large sections of these populations. Remedying these inequalities in health between and within countries requires an approach that gives serious attention to the social determinants of health.

There is no doubt that poor people suffer from far higher levels of ill-health and premature mortality than rich people, and addressing the health of poor people and nations must be a matter of concern for policy-makers and service providers[10]. Indeed, the introduction of vertical initiatives to control major communicable diseases, such as the Global Fund to Fight Tuberculosis, AIDS and Malaria[11], the WHO "3 by 5" Initiative[12] and the Roll Back Malaria Partnership[13], as well as horizontal initiatives to improve health systems, have substantially redressed the major infectious disease burden and improved average population health in developing countries. The Millennium Development Goals focus attention on eliminating poverty in the world's poorest countries and put health clearly on the international and national development agendas[14].

However, poverty and (lack of) health care do not fully explain the observed inequalities in population health. They do not explain the variation in life expectancy and health status among poor people, with different levels of education or from different ethnic backgrounds[9], nor why groups along the social spectrum differ in levels of mortality from, for example, cardiovascular diseases, cancers and external causes (violence)[6], nor why populations with different living and working conditions have differing health experience[15-18]. Understanding and tackling the persistent inequalities in health, in a sustainable manner, therefore requires recognition and response to not only the poorest in society, not only the gap between rich and poor, but also the gradient in health observed across all groups within and between societies[19,20]. Pursuit of such health equity recognizes implicitly the need to redress the unequal distribution of opportunity to be healthy that is associated with membership of less privileged social groups[21]. This focuses attention not only on the relief of poverty but also on the structural determinants of health, including upstream global and national level social, environmental and economic conditions within which people live, and more intermediate factors such as employment, education, housing, quality of living environments and social relationships[22, 23].

Background to the Commission on Social Determinants of Health

At the 2004 World Health Assembly, WHO's former Director-General Dr Jong-wook Lee announced the beginning of a process to act upon the social causes of global health inequities[24]. As a result the Commission on Social Determinants of Health, hereafter known as the Commission, emerged in 2005 to build on previous and current UN efforts to work towards better health and greater health equity. The Commission's vision is a world where all people have the freedom to lead lives they have reason to value. Working towards this, the Commission places primary emphasis on the underlying factors that determine population health and its distribution within and between societies. It works on the assumption that healthy populations result, largely, from action that is often outside the health care sector.

Within the formal lifetime of the Commission (2005–2008) the aim is to set out solid foundations for its vision: societal structures, conditions and relations that influence health and health equity 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, in health and non-health sectors, at local,

national and global level use this knowledge to set and implement relevant public policy affecting health[23].

The Commission is not only reviewing existing knowledge but also raising societal debate and promoting uptake of policies that will reduce inequalities in health within and between countries. It is doing this through four tracks of work:

(1) **Learning:** organizing, consolidating, disseminating and promoting the use of existing knowledge that demonstrates the causal relationships between social determinants and inequalities in health, and further developing the evidence base on interventions and policies that focus on key social determinants which influence health and health equity;
(2) **Advocacy:** identifying and promoting opportunities for effective action on key social determinants and raising societal debate among policy-makers, implementing agencies, civil society organizations and the wider community;
(3) **Action:** catalyzing and supporting processes and institutions that initiate, inform and strengthen actions to integrate knowledge on social determinants within public policy and institutional organization and practice; and
(4) **Leadership:** supporting and giving profile to the public and political leadership for policy and action on the social determinants of health, and organizing and profiling the work of the technical and institutional drivers that support this leadership.

Strengthening the knowledge base

The need for clear, rigorous evidence to inform and support equity-focused health advocacy, policy, practice and leadership is crucial. Perhaps understanding and addressing the social determinants of health is one of the more challenging areas. Research into public health systems and services and the social determinants of health escalated in the latter half of the 20th century. Recently, comment is often made along the lines of "we know the problem", "we know what needs to do done", "why don't we just do what is necessary". Effective translation of knowledge into policy and practice which improves people's health and reduces inequalities in health has however been inconsistent[8,25]. Gwatkin and colleagues describe in "Reaching the Poor"[10] a number of existing interventions, both policy and practice in nature, that are concerned with health issues of impoverished people. However, as the authors highlight, what remains missing from the evidence base is the knowledge on how to make interventions work. A key lesson from this is the need to consider, in a systematic manner, the nature of knowledge and what is believed to be effective intervention, with thought given to the contextual relevance of evidence and the adequacy and quality of information[26]. Cognisant of this, the learning track of the Commission was developed to consist mainly of nine knowledge networks, organized around select social determinants, including early child development, health systems, employment conditions, globalization, priority public health conditions, urban settings, social exclusion, and two cross-cutting themes of gender and measurement/evidence. These social factors, some described further below, can be characterized as having strong impact on health and health equity, and amenable to action. Indeed the investigations by the knowledge networks are focused on identification of effective intervention and the processes and actors necessary to effect change.

A life-course perspective: early child development

It is generally believed that the persistence and, in some cases, worsening of health inequalities is transmitted from generation to generation through economic, social and developmental processes, and that the advantages and disadvantages are reinforced in adult life. A life-course approach focuses on the different elements of health, from the moment of conception through childhood and adolescence to adulthood and old age. This approach reveals critical points in the transitions from infancy through childhood into adult life, where an individual may move in the direction of advantages or disadvantages in health. The patterns are not uniform, varying by social group.

There are various routes for the transmission of advantage and disadvantage through early childhood conditions and experiences. Of note is how poor childhood social circumstances relate to poor adult circumstances in several ways. For example, education is still the major route out of disadvantage, but poorer children perform educationally less well than better-off children. Children dropping out of school, or not entering employment or training after formal schooling, are a particularly high-risk group. Children from poorer backgrounds are much more likely to get into trouble with the police, to be excluded from school, or to become a teenage parent, all of which make moving up the social hierarchy more difficult.

Physical, emotional and cognitive development patterns have their roots in early childhood, with beneficial or harmful effects on subsequent health. Such findings suggest that developing robust strategies for promoting health equity through social determinants policy requires a specific focus on early child development. Life-course analysis of mainstream policies in health, education and social welfare suggest that insufficient protection is currently provided for people at these crucial turning points[27].

Exposure and vulnerability: employment conditions

Research from the past two decades has demonstrated the importance of the place and content of work and their effects on coronary heart disease, mental health and musculoskeletal disorders, but many workplaces still have unacceptable safety risks and exposures.

The main foci for improvements in work-related health have typically been around the eradication or control of known hazards and improvements in the work environment. But even when these "classic" occupational hazards have been corrected, inequalities in health remain between higher and lower positions in the workforce. Changes in employment status and unemployment have been shown to be linked to changes in health. There is a growing evidence base on the health effects of factors including: psychological stress; physical and ergonomic risks; toxic chemical exposure; and

employment conditions like income, job security, flexibility in working hours, job and task control, and employment-related migration.

The effectiveness of regulatory measures, employment and industrial relations policy, and worker safety legal frameworks – structural interventions that seek to prevent and mitigate the effects of employment and working conditions – should be mapped and analyzed [27].

The rapidly changing living environment: urban settings

The rapid process of urbanization has seen an explosion of "slums" worldwide and more generally urban conditions often not conducive to healthy living, either through the physical, social or economic environment generated in such settings. Urban slums are characterized as unplanned informal settlements where access to services is minimal-to-nonexistent and where overcrowding is the norm. Urban settings and in particular the health challenges of slum-dwellers constitute a vast and growing challenge, particularly for developing countries.

Urban development has historically been seen as both a cause and solution for social inequalities in health. However, social gradients in health within urban areas occur everywhere and are resistant to change. Urban environments, and their effect on health, are influenced by the degree and type of industrialization, availability of sanitary conditions, quality of housing, accessibility of green spaces and by transport, an increasing concern. The urban setting is a lens that magnifies or diminishes other social determinants of health and exposes different population groups in different ways to a whole variety of factors conducive or otherwise to health. Interventions in the urban setting therefore imply the integration of actions simultaneously addressing a range of health determinants. Slum upgrading is an often-used intervention to improve social and environmental determinants of the urban poor. This usually includes: physical upgrading of housing, water and sanitation, infrastructure, and the environment; social upgrading through improved education; violence reduction programmes; better access to and improved health services; governance upgrading through participatory processes; community leadership and empowering civil society through knowledge and information[27].

Globalization in the 21st century

The processes, and nature, of globalization may be regarded as the underpinning structural social determinant of health and health equity. Global processes exert a powerful impact at all levels of the social production of health: on the evolution of sociopolitical contexts in countries; on the nature and magnitude of social stratification; and on the configuration of various specific determinants (e.g. working conditions, food availability). We see the global influence within countries operating both formally: multilateral institutions and processes of engagement, multilateral binding and non-binding treaties and agreements; and informally: cultural production, media and the collapse of "cognitive distance" between global population groups. Among the most relevant aspects of globalization on inequalities on health, with potential for intervention, are: market access, trade barriers and liberalization, integration of production of goods, commercialization and privatization of public services, and changing lifestyle patterns.

While recent years have seen a rapid expansion of interest in globalization and health, numerous important questions remain inadequately explored. There is a need to identify and evaluate policy options through which national policy-makers can respond to the challenges posed by globalization and also capitalize on its opportunities in a health-promoting way. It is necessary to identify and characterize the degree of negative or positive health impact of globalization in specific cases: not only to clarify relevant causal processes, but as a contribution to evaluating the impact of interventions and policies on other social determinants of health[27].

In conclusion, if the major determinants of health and health equity are social, so must be the solutions. Areas requiring research then should be ones which address the social factors which influence the global inequities in health. Each of the nine thematic areas for research and intervention, identified by the Commission on Social Determinants of Health, is relevant in all countries. Such research should seek to highlight the transferability of knowledge, elucidate the conditions, processes and actors necessary for effective intervention, and in a systematic manner compile a knowledge base which will underpin action to improve health, reduce the health gap and redress the health gradient. ❑

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Making human rights work for the public's health: equity and access

Article by Leslie London

In the context of growing global inequalities in health status and in access to health care[1,2], strengthening of equity in health systems has been identified as a key global objective at the highest levels of the World Health Organization, instrumental to the realization of both the Millennium Development Goals and the 3X5 target for HIV treatment[3]. Yet what is meant by health equity, and how best to achieve equity in health, remains a contested area. Recent work suggests that one of the missing threads in these discussions is the role of a human rights framework in shaping appropriate policy and programme decisions. This paper draws on research conducted for the Network on Equity in Health in Southern Africa (EQUINET)[4,5] and in other developed and developing country contexts to highlight the interaction between human rights approaches to health and community agency in addressing the underlying determinants of health inequities. These findings point also to the key roles and responsibilities of governments, multilateral bodies and transnational corporations, within a human rights framework, in promoting equity of access to both health care and to the determinants of health.

Human rights occupy a somewhat fraught place in the evolution of public health[6]. Historically, public health approaches have evolved from relatively authoritarian traditions in placing the public interest, however defined, ahead of the rights of individuals or groups. However, the advent of the HIV epidemic, in particular, prompted a rethinking of the place of respect for human dignity within a population approach to health[7,8] and spurred the growth of a movement for mainstreaming the place of human rights in health[9]. Nonetheless, such trends have not resolved a residual unease experienced by public health planners and governments with a perceived incompatibility between rights claims by individuals and responsibilities of public health systems towards the health of populations. These have been manifested in, for example, claims that approaches based on social justice and public health utility are better suited than human rights to address the challenges of HIV in Africa[10], and in the most recent debates preceding WHO endorsement of routine testing for HIV in public health facilities[11].

Valid as these concerns might be, it is important for policy-makers to realise that the perception of a potential contradiction between rights approaches and public health objectives are premised on a particularly individualist notion of what human rights entail, noted as especially prevalent in discourse on health rights in North America[12-13]. Yet international human rights law explicitly recognizes a range of rights, indivisible in nature, and across a range of cultures and settings, which may guarantee individuals opportunities and access to resources, but which are only realizable through collective delivery as socioeconomic rights. In other words, while an individual may claim a right and hold a duty-bearer accountable, he or she cannot do so in isolation from their group, community and context. Conversely, there is also evidence that redistributive strategies that promote the well-being of populations also protect individuals[14].

This is not to deny potential tension between balancing individual and collective rights. Allison (2002), in researching provision of environmental health services in South Africa, points out that not everyone will identify with community or have common interests[15], particularly where unjust social systems have been at the root of creating conditions of inequality and those unjust systems have evolved based on systematic differentials of power. However, the challenge for public health policy-makers is to identify how best to synchronize health policies and programmes with human rights frameworks[16], because they are ultimately both about maximizing human well-being[6].

The evidence

Analysis of three Southern African case studies for EQUINET[4,5] has illustrated a set of critical success factors for harnessing human rights approaches to health equity objectives (Table 1). Firstly, reliance on a legal framework for rights alone is both insufficient and disempowering, since, in the absence of community mobilization, claims to rights are easily ignored, no matter how legally compelling. Whereas it is true in general that the exercise of rights is beneficial for health, there is also evidence that it is the process of civil society participation that is instrumental to these improvements in health status[14]. For policy-makers concerned about advancing health equity, the active participation of, and engagement with communities should therefore be recognized for what it is – a key element towards realizing health equity, and not an obstacle to efficient governance. Evidence from South Africa suggests that even at very local

- Rights alone are not enough, but need to be coupled with community engagement.
- Rights, appropriately applied, can strengthen community engagement.
- Rights, conceived in terms of agency, are the strongest guarantors of effective equity-promoting impacts.
- Rights should strengthen the collective agency of the most vulnerable groups.
- Rights approaches should aim to address the public-private and global divides in relation to human hights.
- Information and transparency are key to human rights approaches that build equity.
- Human rights approaches provide additional opportunities for mobilizing resources outside the health sector.

Table 1: Human rights and health equity – critical success factors

levels, the erosion of civil society structures post apartheid that accompanied the formalization of local government structures led to a decline in political accountability and alienation of communities from decision-making processes with regard to housing and sanitation[15].

Secondly, rights frameworks provide opportunity to reinforce community engagement by affording a mechanism for input to, and negotiation around health policy. Concern for procedural rights is becoming increasingly important in health[17-19] and development discourse[15,20] and has been recently applied in the Equity Gauge model, which uses policy and monitoring information, channelled to communities and civil society, for political action to influence policy-makers to support a health equity agenda[1]. Procedural rights are therefore key to enabling the realization of other rights, as has been shown in many areas related to health, such as in reproductive health[21] and in housing/sanitation[15].

Thirdly, rights frameworks that address issues of power in recognizing agency of those affected by health policy, are the strongest guarantors of effective equity-promoting impacts. Considerable evidence already exists that the root causes of health inequalities relate to powerlessness of both individuals and groups. Such power differentials give rise to a sequence of processes: social stratification, differential exposure based on social stratification, differential vulnerability given an exposure and differential consequences, which combine to give rise to health inequities[22]. Attempts to redress inequities, which are inherently about social change, therefore have to grapple with questions of power[23], and must consequently seek interactions with communities that focus on empowerment rather than mere participation[24]. Hard as it may be to manage, an active civil society is a better guarantee of health equity than models which frame target groups by need and deliver services and resources to passive beneficiaries. Indeed, in public health debates, there has been an increasing support for a return to the spirit of Alma Ata, to revive the notion of community agency in public health practice, and to take seriously our commitment to community empowerment[25-28]. We hear endless appeals to, and laments about the lack of political will to address key health problems. An active engagement by civil society means we no longer have need to resort to a concept of political will, given we commit to a model where "those who are beneficiaries of programmes… negotiate their inclusion in the health system" constituting "organized and active communities at the centre as initiators and managers of their own health"[28].

Considerable evidence already exists that the root causes of health inequalities relate to powerlessness of both individuals and groups

Fourthly, most evident in the EQUINET case studies was the role of rights approaches as critical to strengthening the collective agency of the most vulnerable groups. Advocacy work in areas such as HIV treatment access and in bringing community preferences to bear on national health policies plays a key role in reversing the "thinness of reserves"[22] characteristic of groups suffering health inequities. In this sense, the public health approach of targeting populations according to need, and the priorization of the most vulnerable and marginal groups as a human rights concern represent a synchrony in approaches. What a rights analysis does is to add the recognition that an inability to exercise power means that the poor and vulnerable cannot change the conditions of their vulnerability, and must remain dependent on others to do so[24]. Institutional frameworks for human rights that preferentially favour access for vulnerable groups, such as, for example, in the identification of evidence in Health Impact Assessments[29] are therefore key to realizing the liberatory potential of rights approaches in health[5].

This leads naturally to the fifth implication – that information and transparency are key elements for the achievement of health equity. Lack of information and transparency undermines community agency, and drives conflict and distrust that prevents redress of inequity. For example, the closure of channels of access to information regarding Poverty Reduction Strategy Papers in Malawi has been interpreted as reversing gains made through interaction with policy-makers over other policies such as the national Patients Rights Charter[5]. It is both at an individual and collective level that information serves to reverse the powerlessness underlying health inequalities. Central to the model of the Equity Gauge[1] is the role of information in empowering community partners to advocate for action. Similarly, in the case studies for EQUINET, civil society was both a user and generator of information, through strategic partnerships with research and academic experts that enabled organizations to lobby for policy change to advance the interests of vulnerable communities[5]. Access to information is thus both a right in itself and an enabling mechanism to realize other rights. Policy-makers can therefore play a critical role in ensuring that information accessibility and transparency are not only part of public life, but are geared towards reaching marginalized, isolated and vulnerable groups as a priority.

A further consequence of rights-based approaches to health equity is the capacity to address the public-private and global divides that may not be initially obvious to law-makers. Illustrated most clearly in the HIV treatment access

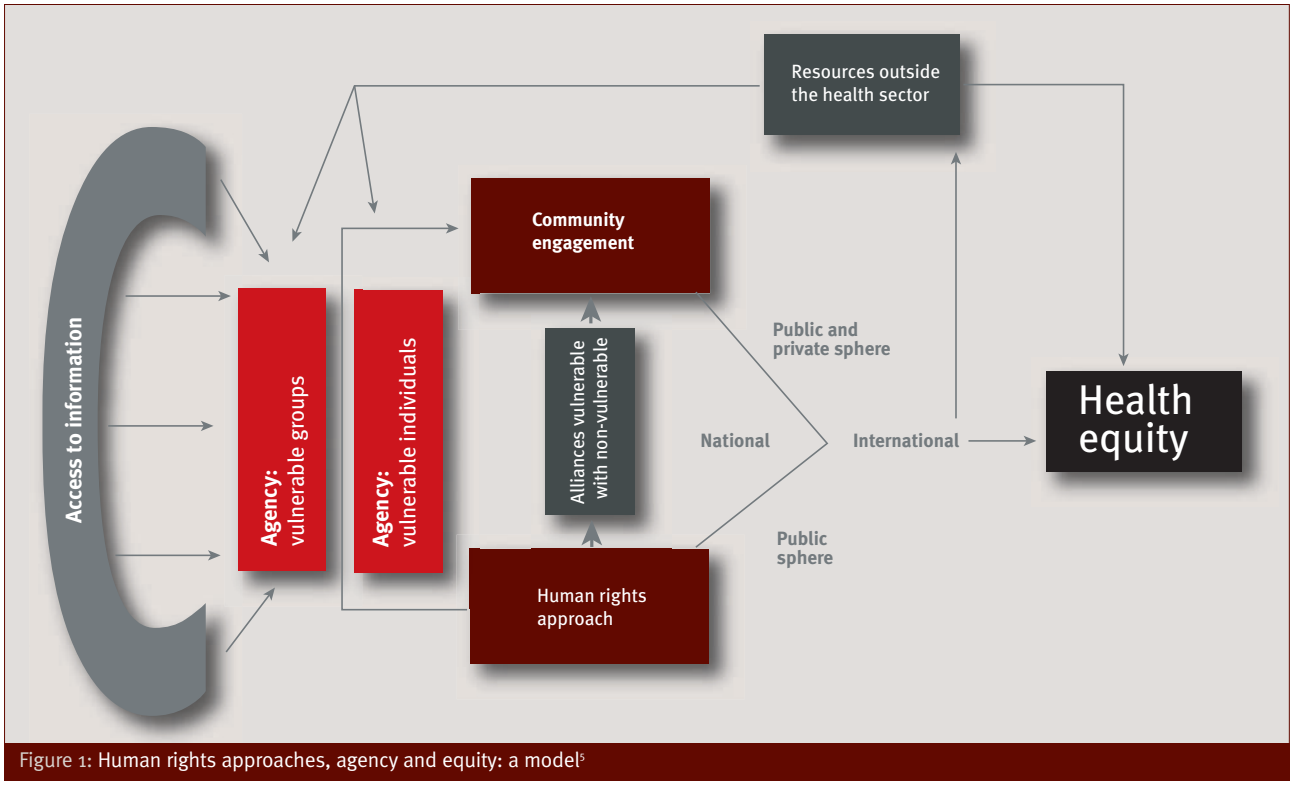

Figure 1: Human rights approaches, agency and equity: a model[5]

movement, human rights campaigns have effectively won victories for expanding access to care for millions worldwide through judicious partnering of governments in court action against pharmaceuticals and in trade negotiations to protect national capacity to invoke special measures for health emergencies[5]. This is particularly important given the trend under globalization towards the weakening of national sovereignty. Even in tackling the thorny issue of human resource migration, the notion of an "international mobility regime" that addresses the critical needs of developing countries[30] will not be effective without a recognition of the inter-relatedness of national obligations of both source and recipient countries to respect, protect and fulfil the right to health and international oversight consistent with provisions of the International Covenant on Social, Economic and Cultural Rights. For that reason, it has been proposed that with the growth of Health Impact Assessments as a tool for assessing health impacts of policies, programmes or projects[31], human rights criteria be incorporated into such tools, bringing accountability to, not only governments, but also trans-national corporations and multilateral bodies[29]. Such strategies provide the opportunity to address global phenomena impacting adversely on health equity such as foreign and trade policy, helping to realize formal global commitments to health as a right[3].

Lastly, the case studies from Southern Africa highlight how human rights strategies provide opportunities for mobilizing resources required for health from outside the health sector. Partly by mobilizng constituencies across sectors and partly because health is itself determined by factors outside the health sector, human rights challenges in areas of housing, social security, water and sanitation contribute to health equity-oriented policies and programmes.

To summarize the evidence: where it is clear that rights approaches are predicated upon understanding the need to prioritize vulnerable groups, where the way rights are operationalized recognizes the role of agency by those most affected, and where rights are conceived as the complete spectrum of civil and political, through to socioeconomic rights, human rights approaches appear to offer powerful tools to support social justice and health equity (Figure 1). Public health concerns for equity then become entirely consonant with human rights-based approaches. The synergy between public health and human rights in relation to equity lie less in the pursuit of individual rights but rather in the way social processes and consciousness are given the opportunity to interface with the state in ways that secure collective rights.

New directions, ongoing challenges

In the context of development economics, Sen demonstrated the link between equity and empowerment[21] and the role of opportunities to develop individual capacity as critical to development and health. Rifkin has built on this theoretical work to develop a framework for understanding the relationship between equity and community empowerment for health, emphasizing the critical importance of active engagement by both individuals and collective to address the situation responsible for their condition[24]. Not only are human rights one of the pillars of the model (the "H" in her acronym CHOICES), but they also inform the applications of the other elements in the model (Capacity-building, Organizational sustainability, Institutional accountability, Contribution, and an Enabling environment).

A second area for further development is the critical need for resource allocation models that incorporate active and

meaningful community input to decision making,[18,19]. Not surprisingly, a recent *World Health Organization Bulletin* has called for papers on exactly this theme, seeking evidence for the application of ethical frameworks for public health decision-making[32].

A third dimension to engagement with this area is how policy-makers, governments and national and international agencies respond to popular movements advancing explicit equity-related agendas. For example, the People's Health Movement, a global network of health civil society groups, has launched a campaign for the right to health[33]. In putting equity and human rights explicitly on to a public agenda, policy-makers will be expected to weigh up competing demands for attention. Of course, finding the path that effectively balances rights and responsibilities is complex, particularly in the context of globalization, where devolving responsibilities to communities risks absolving duty-bearing governments of their obligations[5,15].

Then, there are difficult questions about assessing health policy through a rights lens. For example, in terms of developing basic policies on health worker migration, which present a challenge in balancing health workers' rights to work freely where they wish against the needs of vulnerable groups to health care[30], it appears impossible to begin to engage on the issues without a clear understanding of the nature of a rights framework, the process by which differing and competing rights may be balanced and the procedural standards that must be met when restricting individual rights in the interests of the public good[34]. Models have been developed to assist policy-makers to assess the human rights impacts of health policies, adjudicate between policies and plan appropriately[16,35,36]. Experience in using these models will help to contribute to best practice with regard to public health planning for equity.

Further, individual health workers and managers are frequently set up as gatekeepers or intermediates in contestation over rights of access to health care. This kind of adversarial relationship is not helpful to either users or the health professionals, and unlikely to enable any meaningful progress towards health equity. Patients' rights charters, rather than serving as simply normative standards imposed on dysfunctional health systems, need to be set up so as to enable mutual identification of shared objectives between users and providers, through processes that realize procedural rights as part of a health equity strategy. Of course, health workers need to be mindful of not becoming complicit as instruments of the violations of users' rights, and so need support in situations where they may experience Dual Loyalty conflicts[37], but the strength of a rights approach is that it focuses analysis on identifying system failures rather than branding individuals as the problem. For example, the South African Human Rights Commission recently undertook an investigation into obstacles to access to health care in South Africa as part of its mandate to assess the government's performance with regard to its core obligations on the right to health[38].

Lastly, how can we operationalize a rights system that is not automatically adversarial, and that is able to realise a win-win scenario? For example, Rifkin[24] points out the problems of framing community empowerment as an intervention rather than a political process because it avoids very real conflicts that may arise between communities and those who hold power. Understanding what a human rights framework implies, provides us with a vehicle for explicitly recognizing these differences and provides an accepted framework for managing these conflicts[39].

If national and global policy-makers are to effect a commitment to going "beyond a 'business as usual' approach" in promoting health equity and access to health care[3], we need to think seriously about making human rights work for the public's health. ❑

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Inequality, marginalization and poor health

Article by Lenore Manderson

Variations in health status and outcomes occur in high-, middle- and low-income countries. Economic, political, social and other inequalities between individuals, communities and nations all have profound effects on vulnerability and risk of infection, disease and injury, on access to medical and other care, on treatment, management and outcomes, and on information and interventions designed to maximize well-being. Similarly, such inequalities have profound impact on social health, resulting in individual vulnerability to social exclusion, lack of participation in the social, cultural, religious, economic and other aspects of community life, and differential access to the benefits that derive from these various activities.

The factors that influence health status and health outcomes occur at social, structural, institutional and systems levels in all societies. Gender, differences in ability, race, ethnicity, class and caste are all fields of marginalization, discrimination and personal and structural violence. These differences that result in inequality – gender, ability, age, class or caste, race, ethnicity, sexuality, geography, etc. – co-exist and are inter-related, contributing to poverty in much of the world. Poor people moreover are more likely than others to experience inequality within these social hierarchies, and the co-presence or intersection of various factors that result in inequality compounds the experience and impact of poor health and resultant poverty. These fields of vulnerability are reinforced through structural violence, leading to differences in rates and patterns of infection and illness. For example, people from poor and marginalized communities typically work in industries and occupations and reside in areas that have high risk of illness and injury, they are more likely to be directly exposed to pathogens, to have substandard medical services and poor quality of care, and to lack access to social support mechanisms.

Social inclusion, participation in decision-making, social security, equality, human rights and social justice are key, underlying determinants of health that influence (and are influenced by) education, income and employment

The individual personal, social and economic factors that contribute to inequality, and associated poor health and poverty, result in social exclusion, discrimination and marginalization. Social marginality, discrimination and exclusion affect health negatively in numerous ways, as illustrated by current research on social dimensions of health and illness. Social inclusion, participation in decision-making, social security, equality, human rights and social justice are key, underlying determinants of health that influence (and are influenced by) education, income and employment. Unjust social conditions therefore deprive people of the opportunity to be healthy and often lead to negative health outcomes. In turn, inequitable conditions often limit access to health and medical services, discouraging people who are marginalized or disempowered from presenting to clinics and influencing the quality of care they receive when they do attend. A woman from a minority caste, living in an isolated rural area with physical impairments from polio, is far more likely to be poor, to have poor access to health services, and to receive poor quality of care, than an urban dweller without impairment and from a higher status caste. People with highly stigmatized health conditions (mental illness, leprosy and still, in many cases, HIV), are similarly often denied quality health care. The direct and indirect costs of seeking medical attention, and the humiliation, embarrassment and disappointment experienced when health workers are rude and the necessary equipment, medication or advice are not forthcoming, discourage their continued presentation.

Marginalization affects the health of populations in very different environments. In urban and other densely settled areas, individuals living in poverty, in poor housing, in areas of high population density such as slums or informal (squatter) settlements, or in other unsafe or inadequate living conditions, are disproportionately affected by communicable diseases. Similarly, migrants, nomadic and seminomadic pastoralists and others living in very isolated areas are vulnerable to parasitic and other infectious diseases and may be excluded from health care services run by settled populations. In these circumstances, other environmental conditions, such as poor wet and dry waste management and lack of potable water, also favour vector breeding to promote the spread of infectious diseases. These diseases create social

and financial burdens to individuals, families and communities, and in some cases they accentuate marginalization because the diseases and their consequences are highly stigmatized.

Leprosy and tuberculosis are among the most stigmatized, and individuals known to be infected are often excluded from participating in social, economic and family life. But dermatitis and blindness from onchocerciasis and lymphoedema from filariasis both also result in marginalization, particularly for women with obvious disease who may lose family support and be subject to personal violence. The psychosocial impact of such conditions may lead to reluctance to present for care, although in addition, affected individuals often lack the financial and other resources to seek treatment.

While there has been extensive research on HIV, including in low- and middle-income countries, limited attention has been paid to marginalization and discrimination against people known to be infected, and the health implications of this. While in many countries legislation provides formal protection of their rights, People Living With HIV/AIDS (PLWHA) often face direct and structural discrimination in their daily lives and are severely socioeconomically disadvantaged. This in part is because HIV is typically associated with high-risk, marginalized activities – illicit drug use and sex work. Often people in these categories are discriminated against for other reasons associated with gender, class, caste, poverty and ethnicity. Differential treatment by health staff exacerbates marginality and results in poorer overall health for PLWHA. For example, women who conceive often receive inadequate or no prenatal care and do not disclose their HIV status at delivery; disrespectful and discriminatory treatment at health care facilities is a primary barrier to disclosure and care.

Individuals with physical and intellectual impairments are everywhere poorer, marginalized and disabled by their communities. Social attitudes shape access to care, quality of care, risk factors of complications and co-morbidity. Access to care is often inhibited because of inappropriate communication and discriminatory attitudes, systems and environments. Although disabled people have received relatively little attention by public health services or the medical and health research community, there is growing evidence of their increased vulnerability, including to HIV infection and targeted physical, psychological and sexual violence and exploitation. Disabled people are less likely than able-bodied peers to be included in health education programmes, and information may be inaccessible depending on the nature and severity of their impairments. More generally, there is a lack of information about health and health services in accessible forms for disabled people, there is little accessible information about rights, and poor physical access to services, buildings and transport.

Health status, life chances and life outcomes of individuals are all influenced by such social inequalities and marginalization. Other people from marginalized groups – people who are homeless, misuse alcohol and illicit drugs, or are sex workers, for example – routinely experience discrimination, and again have poor access to health services, receive poorer quality care when they do present, and are at higher risk of infectious disease. Increasingly too, structural violence is punctuated with direct violence – sexual violence, civil war, terror, and the long-term effects of war. This produces further violence and other adverse health outcomes, including increased gender-based violence as a result of war, permanent injuries from bombs and landmines, and the sustained psychological and emotional toll of violent disruption to civil society. In addition, damage to infrastructure and the breakdown of basic services results in an increase in communicable disease, leading to further poverty and inequality.

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One area addressed by the Global Forum for Health Research, where social marginalization has affected health, is in relation to sexual violence. Gender-based violence, including sexual violence, is pervasive, with short- and long-term negative effects on women's physical and mental health. Such effects include reproductive health problems, chronic illness, post-traumatic stress disorder, anxiety and depression. Women subject to domestic violence and sexual violence within and beyond the home are marginalized because of assumptions about their role in provoking the abuse. They often lack access to counselling centres and shelters that could provide short-term protection and ongoing support. Little has been done to address the perpetration of violence and the deeply entrenched and systemic gender biases that excuse – and even legitimize – men's violent and abusive behaviour. Sexual violence in particular had received insufficient attention from researchers, clinical practitioners and policy-makers, and for a long time was ignored as a human rights and health issue. The Sexual Violence Research Initiative (SVRI) of the Forum was launched to support research and advocacy in this area in a variety of settings.

The concept of the "10/90 gap" acknowledges the inequalities in scientific research that exist between countries and the health conditions that affect different populations. But in addition, far less research is conducted about people who are socially marginalized than about those with higher social status: people with physical impairments attract less research attention than those without impairments but with curable conditions; people labelled as having intellectual impairments receive less attention than those with common physical impairments; the elderly less than young adults, and so on. Even less research is done *with* people who are socially marginalized. Rarely are their perspectives, insights and knowledge, and active participation considered when defining the research

questions, developing the research agenda or setting in place research governance structures.

Such marginalization in research agendas contributes further to the "10/90 gap". Redressing the "10/90 gap" involves developing partnerships among marginal communities and researchers, building the research capacity of these communities, and a commitment to a new research ethic that implicitly demands the full and active engagement of these communities in any and all research that pertains to them. Ethical and Human rights principles require fairness and equality not only in access to medical services, but in defining the questions and shaping the information to develop medical and health policy and programmes. Active involvement in research is a critical step to remove inequality and marginality, and to improve the health of all people. ❑

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Discrimination as a barrier to accessing mental health care

Article by Graham Thornicroft

Although each year up to 30% of the population worldwide has some form of mental illness, at least two thirds receive no treatment. This under-treatment occurs even in countries with the best resources[1]. In the USA, for example, 31% of the population are affected by mental illness every year, but 67% of these individuals are not treated[2]. Moreover, in Europe mental illness affects 27% of people every year, 74% of whom receive no treatment[3]. The proportions of people with mental illness who are treated in low- and medium-resource countries (LAMIC) are far less, for example a recent worldwide survey found that the proportion of respondents receiving mental health care over 12 months was as low as 1.6% in Nigeria, and that in most of the 17 countries studied only a minority of people with severe disorder received treatment[4].

A WHO review of 37 studies across the world, for example, found that the proportion of people untreated for particular conditions is: schizophrenia 32.2%; depression 56.3%; dysthymia 56.0%; bipolar disorder 50.2%; panic disorder 55.9%; generalized anxiety disorder 57.5%; and obsessive compulsive disorder 57.3%; alcohol abuse and dependence 78.1%[5-7]. Indeed in one particular study of depressed people in St Petersburg only 3% were treated[8], both because of the low level of coverage of services, and because of demand limiting factors such as the need for out-of-pocket payments to afford treatment.

Two contributory factors towards this degree of neglect are (i) the reluctance of many people to seek help for mental illness related problems because of their anticipation of stigma should they be diagnosed, and (ii) the reluctance of many people who do have a diagnosis of mental illness to advocate for better mental health care for fear of shame and rejection if they disclose their condition[1].

Stigma: a combination of ignorance, prejudice and discrimination

Stigma is a term which has evaded clear, operational definition[9-12]. It can be considered as an amalgamation of three related problems: a lack of knowledge (ignorance and misinformation), negative attitudes (prejudice), and excluding or avoiding behaviours (discrimination)[13-17]. The combination of these three elements has a powerful force for social exclusion[13]. Indeed there is no known country, society or culture in which people with mental illness with a diagnosis are considered to have the same value and to be as acceptable as people who do not have mental illness. Second, the quality of information that we have is relatively poor, with very few comparative studies between countries or over time. Third, there do seem to be clear links between popular understandings of the meaning of a diagnosis of mental illness, if people in mental distress want to seek help, and whether they feel able to disclose their problems[18]. The core experiences of shame (to oneself and one's family) and blame (from others) are common everywhere stigma has been studied, but to differing extents. Where comparisons with other conditions have been made, then people with a diagnosis of mental illnesses are more, or far more, stigmatized[19,20], and have been referred to as the "ultimate stigma"[21]. Finally, rejection and avoidance of people with a diagnosis of mental illness appear to be universal phenomenon, and a recent study of terms used by school children to refer to mental illness revealed 250 different words and phrases, none of which are positive[22].

Limited access to mental health care

It is only recently that the full potency of such barriers to finding treatment and care have been recognized[23]. For example, studies from several countries have consistently found that even after a family member has developed clear-cut signs of a psychotic disorder, on average it is over a year until the unwell person first receives assessment and treatment[24-26]. A survey of almost 10 000 adults in the USA has added more detail to this picture. The results showed that the majority of people with mental disorders eventually contact treatment services, but they often wait a long time before doing so: with average delays before seeking help of eight years for mood disorders, and at least nine years for anxiety disorders. People who wait longer than average before receiving care are more likely to be young, old, male, poorly educated, or a member of a racial/ethnic minority[27].

Where do people go to try to find help? The detailed US survey just mentioned also asked this question and produced some surprising answers. Only about one third (41%) of people who had experienced mental illness in the previous year had received any treatment: 12% from a psychiatrist, 16% from a non-psychiatric mental health specialist, 23% treated by a general medical practitioner, 8% from a social services professional and 7% from a complementary or alternative medical provider. In terms of treatment adequacy, mental health specialists provided care that was at least

reasonable in about half (48%) of the cases they say, while in primary care only 13% of people treated received care that was adequate. Unmet needs were greater for the poor: older people, minority ethnic groups, those with low incomes or without insurance, and residents of rural areas[28]. The study concluded that "most people with mental disorders in the United States remain either untreated or poorly treated".[28]

It is wrong to think that health services are usually the first port of call when people want help for mental illness. In the national survey referred to above, a quarter of people who sought help first went to a member of the clergy. This pattern seems to be remarkably stable: and applied to 31% in the 1950s and to 24% in the 1990s. Indeed more people first went to a faith leader for help than went to a psychiatrist (17%), or to a general medical practitioner (17%) [29].

On what basis do people judge where to go for help? A large national survey in Germany described vignettes of people with depression or schizophrenia and asked about how to find help. Revealingly the general public thought that mental health staff are useful for treating people with schizophrenia, but not for depression. The reason for this is that most people felt that schizophrenia was caused by biological or uncontrollable influences, while they understood depression to be a consequence of "social disintegration" (including unemployment, drug or alcohol misuse, marital discord, family distress or social isolation) so that people with depression were more often recommended to seek help and social support from a friend or confidant [30].

This may go some way to explain why depression is essentially untreated in some countries. An international study of depression found that 0% of people with depression in St Petersburg received evidence-based treatment in primary care, and only 3% were referred on to specialist mental health care [31]. But the major barrier to care in that Russian site was money: an inability to afford treatment costs was the main barrier to care for 75% of the depressed Russian patients studied.

Even under better resourced conditions, it is known that most people with a mental illness in the USA do not seek assistance. An early national survey found that fewer than one third of all mentally ill people received assessment and treatment, although the rate rose to 60% for people with a diagnosis of schizophrenia[28,32,33]. It is a paradox that even though two thirds of all adults with a mental illness went untreated, a half of those who did receive treatment did not have a clear-cut mental illness[34]. Interestingly, the idea that conditions which are less stigmatized (for example, depression compared with schizophrenia) are those which are seen to be more treatable is not supported by the findings of these surveys[35]. So no single factor is enough to explain complex patterns of help-seeking. Nevertheless, the weight of evidence does suggest that even when there are no major financial barriers to care, that many people do not seek help or minimize their contact with services in an attempt to avoid being labelled as mentally ill[36].

Particular groups may have even lower rates of treatment for mental disorders, and this applies in particular to African Americans in the USA or to Black Caribbean groups in the UK[37]. Several American studies suggest that African Americans receive mental health care about half as often as white people [38-40], even though they have higher rates of some mental disorders [41,42]. Several important barriers to care can increase the impact of mental illnesses among black communities in Britain and the USA. These factors have been described as: socio-cultural (health beliefs and mistrust of services), systemic (lack of culturally competent practices in mental health services)[43], economic (lack of health insurance) or individual barriers (denial of mental health problems)[44].

The interplay of these factors produces the contradictory situation in which black groups may have higher rates of many mental illnesses, lower rates of general referral and treatment, but higher rates of compulsory treatment and forensic service contact[45;46]. In the USA patterns of contact with mental health services are in some ways different for black and white people. Black people with a mental illness are more likely to seek help if their families are supportive, and if a family member has had a positive personal experience of mental health care. In one study they did not view mental health on a continuum of well-being, but tended to think of themselves as either mentally healthy or mentally ill. Many interviewees said they did not think they were "crazy", therefore they did not seek mental-health services[47]. Also there was little information about mental-health services in the African-American community. Most people interviewed did not learn about available mental-health services until their conditions had become severe[42]. There is an important general point here that we shall return to repeatedly in this book: that most people of all cultures have relatively little accurate and useful knowledge about mental illness.

Such feelings, at best of ambivalence, and at worst of deliberate avoidance of treatment and care for fear of stigma, have been found throughout the world. For instance, a study of Muslim Arab female university students in Jordan, the United Arab Emirates and Israel, for example, found that for most of these women their first resort was to turn to God through prayer during times of psychological distress, rather than to seek help from health or social care agencies[48]. A strong reluctance to be seen as mentally ill appears to be a universal phenomenon.

Even in battle-hardened soldiers stigma is a powerful factor. Over 3000 military staff from US Army or Marine Corps units were anonymously surveyed three to four months after their return from combat duty in Iraq or Afghanistan. They were assessed for depression, anxiety or post-traumatic stress disorder (PTSD). Most of the unwell soldiers (60–77%) did not seek mental health care, largely related to concerns about possible stigmatization[49].

Why do so many people try so hard to avoid contacting psychiatric services? People who are starting to have symptoms of mental illness are also members of the general population and share the same pool of information about psychiatric disorders. The following common beliefs are likely to reduce their likelihood of seeking help: that psychiatric treatments are ineffective[50]; that others would react with avoidance; or that a person should solve their own problems[51]. At the same time, strong family

"Two months ago I went to my home village. I went for a coffee at a café. Most people there, of those who were aware of my problem, call me 'mad'. More specifically they said 'Here is the lunatic'. That incident made me very sad, I quickly finished my coffee and I left". *Tom*.

encouragement to go for mental health assessment and treatment does often work[52].

It is fair to include not only individual but also systemic factors in trying to understand the puzzle of under-treatment. In the USA the National Depressive and Manic-Depressive Association undertook an investigation to explore why "there is overwhelming evidence that individuals with depression are being seriously under-treated". They concluded that the "reasons for the continuing gap include patient, provider and health care system factors. Patient-based reasons include: failure to recognize the symptoms, underestimating the severity, limited access, reluctance to see a mental health care specialist due to stigma, noncompliance with treatment and lack of health insurance. Provider factors include poor professional school education about depression, limited training in interpersonal skills, stigma, inadequate time to evaluate and treat depression, failure to consider psychotherapeutic approaches, and prescription of inadequate doses of antidepressant medication for inadequate durations. Mental health care systems create barriers to receiving optimal treatment"[53].

Are people in rural areas better or worse served than those in towns and cities? The evidence here is patchy but a clear outline does tend to emerge. If a person with a mental illness wants to keep personal information confidential, this seems to be more difficult in rural communities. A study in Arkansas, for example, compared over 200 urban and rural residents' views about depression and its treatment. The rural residents with a history of depression labelled people who sought professional help more negatively than their urban counterparts. By the same token, those who labelled depression more negatively were less likely to have sought professional help[54].

Similar findings also emerged from a study in Iowa where people living in the most rural environments were more likely to hold stigmatizing attitudes towards mental health care than people in towns, and such views strongly predicted willingness to seek care[55]. Perhaps for these reasons, a survey of rural residents in Virginia found that over a third of the population had a diagnosed mental disorder, but only 6% subsequently sought help, that those who did not go for treatment said that they "felt there was no need"[56]. Evidence from Tennessee also showed that among people who were mentally unwell, those more likely to seek help were women, younger people and those who had been treated for a mental illness previously[57].

There is some evidence that these factors also prevent rural children with mental illness from having access to mental health care. A study of parents in rural areas of North Carolina concluded that although as many as 20% of children had some type of treatable mental illness, only about one third of them received help from the mental health system[58,59]. The researchers found that one of the main barriers to care was stigma towards the use of the mental health care.

So it seems to be true that stigma about mental illness is no less in many rural areas, and may be even stronger than in towns and cities. In part this may be based upon fears that a rural community will learn details about a period of mental illness, while it is easier in cities to remain anonymous. But relatively little research has been done in rural areas to understand these processes in more detail. This is especially important because there are relatively high rates of suicide among male farmers in many countries [60-67].

In summary, this paper shows that stigmatization against people with mental illness is common wherever it has been studied, and that these processes present formidable barriers both to social inclusion and to proper access to mental health care. As the disabilities associated with mental illness exceed those of most other disorder groups[68,69], now is the time to: (i) undertake evidence-based interventions to reduce stigma; (ii) increase access to mental health treatment and care; and (iii) to scale up the available services in proportion to the magnitude of the need[70]. ❑

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"In my village they don't know that I am living at a group home and that I am on medication. I have told them that I am working at a shop in Athens. My close relatives know it and some of them were more supportive after I got sick than before. In my village I don't want them to know about it because I don't want people to say things about me". *Diana*.

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The diverse pathways from globalization to health

Article by Maud MTE Huynen (pictured), Pim Martens and Henk BM Hilderink

Achieving good health has become an accepted international goal. In our attempts to realize this goal, however, we have to recognize that our (future) health increasingly depends on the globalization process. This was, for example, clearly demonstrated by the rapid global spread of SARS in 2003. On the other hand, the growing global interconnectedness also means that we have more capacity than ever before to respond to such health treats. Due to the increasing geographical scale of important health issues, the call for a global approach to health becomes stronger. What this exactly means, however, remains unclear[1]. The multiple pathways from globalization to health are surrounded by uncertainty[2]. In the resulting polarized debate about the health effects of globalization, it is difficult to discuss how globalization should move forward[3]. In order to improve our understanding of the diverse pathways from globalization to health, we describe a conceptual framework for the effects of globalization on population health[2].

Conceptual framework for globalization and health

Health can be perceived as the integrated outcome of its multidimensional determinants[4]. The nature of these determinants (institutional, economic, socio-cultural and environmental) and their level of causality (proximal, distal and contextual) can be combined into a basic framework that conceptualizes the complex multi-causality of population health. Figure 1 and Table 1 provide an overview of the wide range of health determinants that can be fitted within this framework[2]. This framework illustrates the broader context within which the health of a population develops.

Globalization is increasingly perceived as a comprehensive phenomenon that is shaped by a multitude of factors and events, and that is reshaping our society rapidly. Based on the work by Scholte[5], Held et al.[6] and Rennen and Martens[7], we define globalization as "a process characterized by a growing intensity, extensity and velocity of institutional, economic,

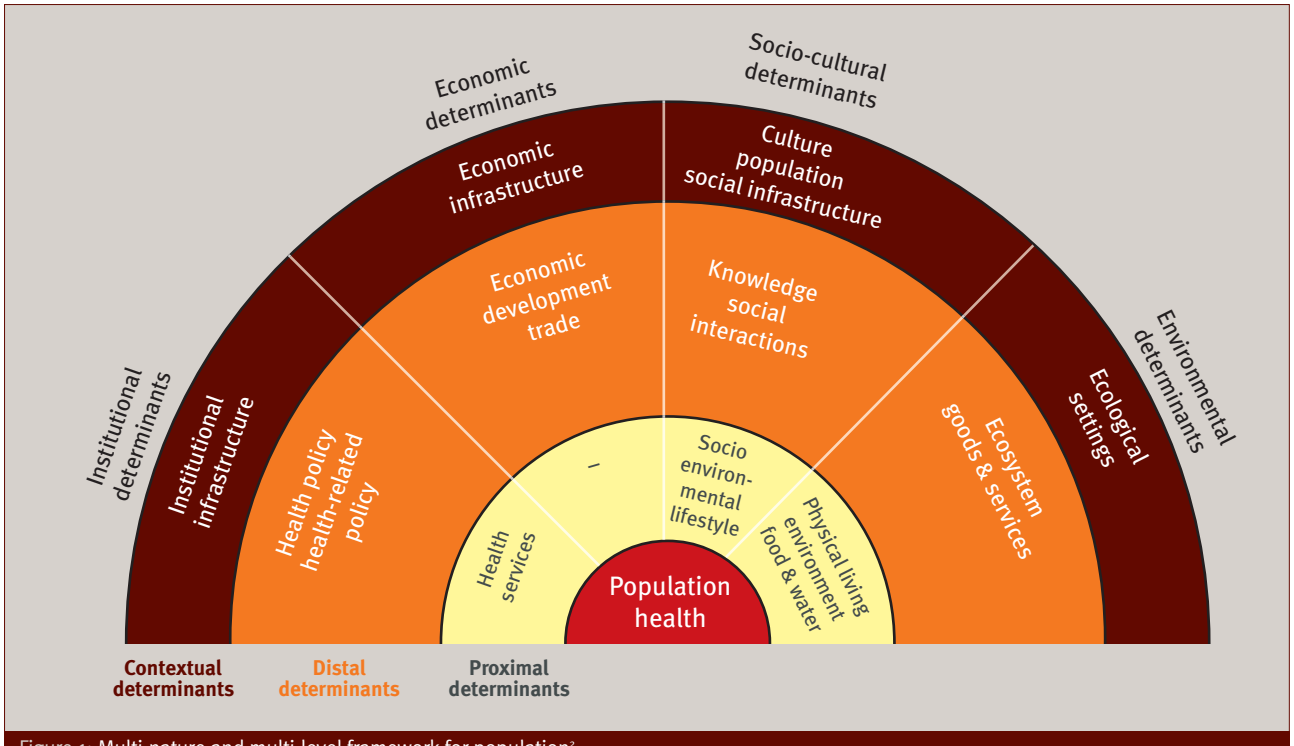

Figure 1: Multi-nature and multi-level framework for population[2]

socio-cultural and ecological interactions, resulting in transborder processes and effects"[2]. In order to focus the conceptual framework, however, the following important features of globalization are identified:

- global governance structures;
- global markets;
- global mobility;
- cross-cultural interaction;
- global environmental changes.

Based on Figure 1 and Table 1, it can be concluded that these features all operate at the contextual level of health determination, influencing the distal health determinants. In turn, the changes in distal factors have the potential to affect the proximal determinants and, consequently, health. Figure 2 links the above-mentioned features of the globalization process with the identified health determinants[2].

Globalization and distal health determinants

Figure 2 shows that the processes of globalization can have an impact on the identified distal health determinants. Below, the implications of the globalization process on these distal determinants will be discussed in more detail.

Health (-related) policies

Global governance structures are increasingly gaining importance in formulating health (-related) policies. Important institutions in global health governance include the World Health Organization (WHO) and the World Bank (WB)[8]. The latter plays an important role in the field of global health governance, as it acknowledges the importance of good health for economic development and focuses on reaching the Millennium Development Goals. The WB also influenced health (-related) policies together with the International Monetary Funds through the Structural Adjustment Programmes[9] and the Poverty Reduction Strategy[10]. In addition, the policies of the World Trade Organization (WTO) are also increasingly influencing population health[9,11,12]. Fidler[13] argues that "from the international legal perspective, the centre of power for global health governance has shifted from WHO to WTO". Opinions differ with regard to whether WTO agreements provide sufficient possibilities to protect the population from the adverse (health) effects of free trade or not[14]. In

Level/ Nature	General determinants	More detailed determinants
Contextual level		
Institutional	Institutional infrastructure	Governance structure Political environment System of law Regulation
Economic	Economic infrastructure	Occupational structure Tax system Markets
Socio-cultural	Culture	Religion Ideology Customs
	Population	Population size Structure Geographical distribution
	Social infrastructure	Social organization Knowledge development Social security Insurance system Mobility and communication
Environmental	Ecological settings	Ecosystems Climate
Distal level		
Institutional	Health policy	Effective public health policy Sufficient public health budget
	Health-related policies	Effective food policy Effective water policy Effective social policy Effective environmental policy
Economic	Economic development	Income/wealth Economic equity
	Trade	Trade in goods and services Marketing
Socio-cultural	Knowledge	Education and literacy Health education Technology
	Social interactions	Social equity Conflicts Travel and migration
Environmental	Ecosystem goods and services	Habitat Information Production Regulation
Proximal level		
Institutional	Health services	Provision of and access to health services
Economic	–	–
Socio-cultural	Lifestyle	Healthy food consumption patterns Alcohol and tobacco use Drug abuse Unsafe sexual behaviour Physical activity Stress coping Child care Lifestyle-related endogen factors (blood pressure, obesity, cholesterol levels)
	Social environment	Social support and informal care Intended injuries and abuse/violence
Environmental	Food and water	Sufficient quality Sufficient quantity Sanitation
	Physical living environment	Quality of the living environment (biotic, physical and chemical factors) Unintended injuries

Table 1: Determinants of population health[2]

2001, WTO ruled that the French ban on the import of all products containing asbestos was legal on health grounds, despite protests from Canada[15,16]. However, protecting citizens against health risks in cases of scientific uncertainty is still difficult, as WTO is reluctant to accept precautionary trade restrictions[17].

Economic development

Opinions differ with regard to the economic benefits of economic globalization. On one side, "optimists" argue that global markets facilitate economic growth and economic security, which would benefit health (e.g. Frankel[18], Ben David[19], Dollar and Kraay[20] and Feachem[21]). On the other side, "pessimists" are worried about the health effects of the global market. Baum[22] states that "the current forms of globalization are making the world a safe place for unfettered market liberalism and the consequent growth of inequities…posing severe threats to people's health". The 2005 Human Development Report[23] argues that one of the prevailing "myths" of economic globalization is that open markets will result in an era of convergence; trade liberalization "has done little to slow down the marginalization of sub-Saharan Africa" and the current "trading system favours the developed world". In fact, notwithstanding some spectacular growth rates, especially in East Asia, incomes declined between 1965 and 1997 in 16 of the world poorest countries[24].

Trade

Due to the establishment of global markets and a global trading system, there has been a continuing increase in world trade. According to the WTO, total trade multiplied by a factor of 14 between 1950 and 1997[25]. More recently, the year 2004 saw an impressive growth in trade, which exceeded average growth recorded over the preceding decade[26]. Today all countries trade internationally and they trade significant proportions of their national income. The array of products being traded is wide-ranging; from primary commodities to manufactured goods. Besides goods, services are increasingly being traded as well[27]. In addition to legal trade transactions, illegal drug trade is also globalizing.

Social interactions: migration

Due to the changes in the infrastructures of transportation and communication, human migration has increased at unprecedented rates. According to Held et al.[27], tourism is one of the most obvious forms of cultural globalization. However, travel for business and pleasure constitutes only a fraction of total human movement. Other examples of people migrating are missionaries, merchant marines, students, pilgrims, militaries, migrant workers and Peace Corps workers[27,28]. Besides these forms of voluntary migration, resettlement by refugees is also an important issue. The UN Population Division estimates the global migrant population in 2005 at between 185 and 192 million people[29]. However, the concerns regarding the economic, political, social and environmental consequences of migration are growing[30] and many governments are moving towards more restrictive immigration policies.

Social interactions: conflicts

In the aftermath of the terrorist attacks on September 11 2001, many questioned the possible links between globalization and the risk on conflicts. On the one side, globalizations can decrease the risk on tensions and conflicts, as societies become more dependent on each. Others argue that the resistance to globalization has resulted in religious fundamentalism, and worldwide tensions and intolerance[31]. According to Huntington[32], the increasing cross-cultural interactions will result in a "clash of civilizations". Nassar[33] describes globalization as a process that leads to a "migration of dreams" in which the world's poor are able to learn of the luxuries of the western world; the increased degree of relative deprivation results in growing tensions. In addition, Zwi et al.[34] identify several other factors that are associated with both globalization and the risk of conflicts, such as increased global trade in arms and inadequate policies.

Social interactions: social equity and social networks

Global communication, global mobility and cross-cultural interaction can also influence cultural norms and values about social solidarity and social equity. It is feared that the self-interested individualism of the marketplace spills over into cultural norms and values resulting in increasing social exclusion and social inequity. Exclusion involves disintegration from common cultural processes, lack of participation in social activities, alienation from decision-making and civic participation and barriers to employment and material sources[35]. On the other hand, however, the geographical scale of social networks is increasing due to global communications and global media. Like-minded people are now able to interact at distance through, for example, the Internet. The women's movement, the peace movement, organized religion and the environmental movement are good examples of transnational networks[27]. The digital divide between poor and rich, however, can result in social exclusion from the global civil society.

Knowledge

The knowledge capital within a population is increasingly affected by global developments in communication and mobility. The term "globalization of education" suggests getting education into every nook and cranny of the globe. Millions of people now acquire part of their knowledge from transworld textbooks. Most universities work together with academics from different countries, students have ample opportunities to study abroad and "virtual campuses" have been developed. In addition, television, film and computer graphics have greatly enlarged the visual dimensions of communication. Many people today "read" the globalized world without a book[36]. Overall, it is expected that these developments will also improve health training and health education (e.g. Feachem[21] and Lee[37]).

Ecosystem goods and services

Global environmental changes are affecting the provision of ecosystem goods and services to mankind. The

Intergovernmental Panel on Climate Change (IPCC)[38] concludes that climate change can result in significant ecosystem disruptions and threatens substantial damage to the earth's natural systems. In addition, several authors have argued that maintaining a certain level of biodiversity is necessary for the proper provision of ecosystem goods and services[39-42]. The Millennium Ecosystem Assessment warns that the ongoing degradation of ecosystem functions poses a growing health risk[43]. Several ecosystem functions are important to sustain our physical health. First, ecosystems provide us with basic human needs like food, clean air, and clean water. Second, they prevent the spread of diseases through biological control. Finally, ecosystems provide us with medical and genetic resources, which are necessary to prevent or cure diseases[44].

Globalization and proximal health determinants

Figure 2 shows that the impact of globalization on each proximal health determinant is mediated by the above-discussed changes in distal factors. The most important relationships will be discussed in more detail below.

Health services

Health services are increasingly influenced by globalization-induced changes in health care policy, economic development and trade, and knowledge, but also by migration. Although WHO aims to assist governments to strengthen health services, government involvement in health care policies has been decreasing and, subsequently, medical institutions are more and more confronted with the neo-liberal economic model. According to Collins[45], populations of transitional economies are no longer protected by a centralized health sector that provides universal access to everyone and some groups are even denied the most basic medical services.

The increasing trade in health services also has some profound implications. Although it is perceived as improving the consumer's choice, some developments are believed to have long-term dangers, such as establishing a two-tier health system, movement of health professionals from the public sector to the private sector, inequitable access to health care and the undermining of national health systems[9,11]. The illegal trading of drugs and the provision of access to controlled drugs via the Internet are potential health risks[46]. In addition, the globalization process can also result in a "brain-drain" in the health sector as a result of labour migration from developing to developed regions[47]. However, increased economic growth is generally believed to enhance improvements in health care. Increased (technological) knowledge resulting from the diffusion of information can further improve the treatment and prevention of diseases.

Social environment

One central mechanism that links the social environment to health is "social support", the transfer from one person to another of instrumental, emotional and informational assistance[48]. Social networks and social integration are closely related to social support[49] and, as a result, globalization-induced changes in social cohesion, integration and interaction can influence the degree of social support in a population.

Another important factor in the social environment is violence, which often is the result of the complex interplay of many factors. WHO[50] argues that globalization gives rise to obstacles as well as benefits for violence prevention. It induces changes in protective factors like social cohesion,

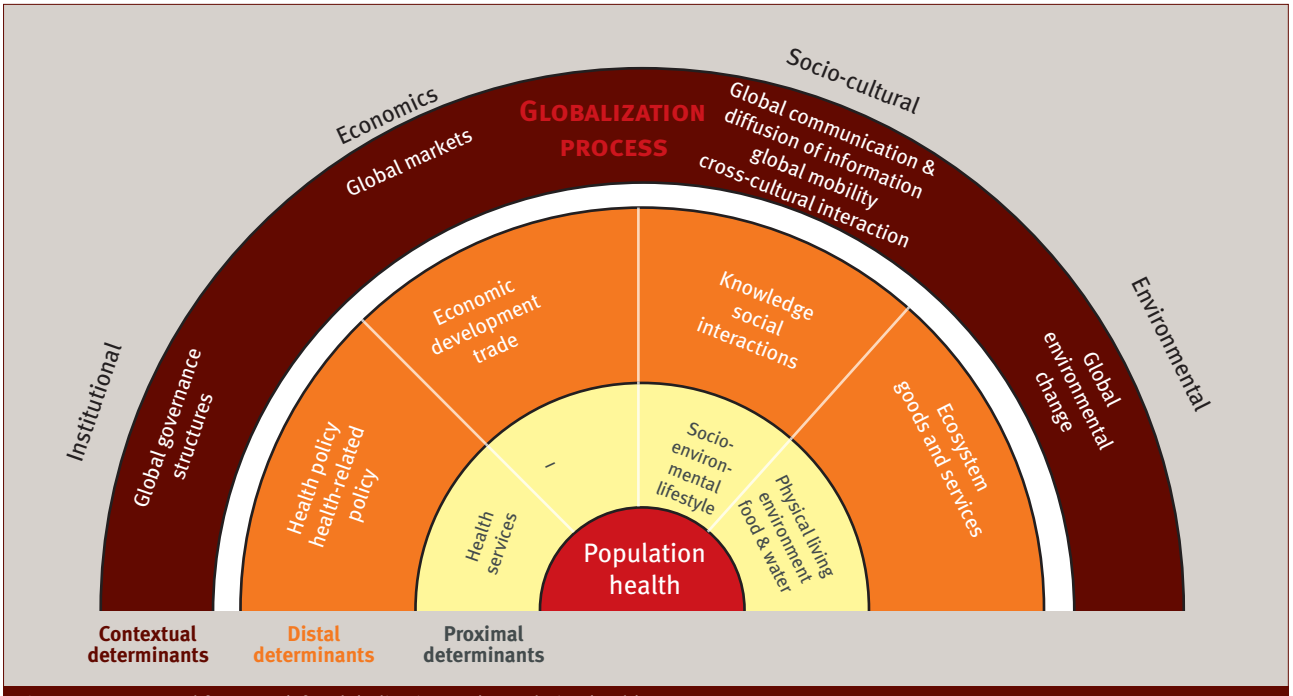

Figure 2: Conceptual framework for globalization and population health[2]

knowledge and education levels, and global prevention activities. On the other hand, it also influences important risk factors associated with violence such as income inequality, collective conflict, and trade in alcohol, drugs or firearms.

Lifestyle

Due to the widespread flow of people, information and ideas, lifestyles also spread throughout the world. It is already widely acknowledged that several modern behavioural factors such as an unhealthy diet, physical inactivity, smoking, alcohol misuse and the use of illicit drugs are having a profound impact on human health[51-54]. Individuals respond to the range of healthy as well as unhealthy lifestyle options and choices available in a community[55], which are in turn determined by global trade, economic development and social interactions. Although the major chronic diseases are not transmittable via an infectious agent, the behaviours that predispose to these diseases can be communicated by advertising, product marketing and social interactions[56]. Global trade and marketing developments drive, for example, unhealthy developments in diet[53,55], tobacco use[53,57], and alcohol consumption[58].

However, health education can play a role in promoting healthy lifestyles by improving an individual's knowledge about the health effects of different lifestyle options. Besides health education, (global) policies can also directly discourage unhealthy behaviour by means of economic incentives (e.g. charging excise on tobacco) or other legislation. An effective implementation of WHO Framework Convention on Tobacco Control (FCTC)[59] is expected to have profound implications on tobacco related-policies and, hopefully, tobacco use.

Physical living environment: infectious disease pathogens

The spread of infectious diseases is probably one of the most mentioned health effects of globalization and past disease outbreaks have been linked to factors that are related to the globalization process (e.g. Newcomb[60]). The SARS outbreak demonstrated the potential of new infectious diseases to spread rapidly in today's world. The combination of movement of goods and people, and profound changes affecting ecosystem goods and services all contribute to increased risk of disease spread. For example, the globalization of food production, trade and consumption has been associated with the increased spread and transmission of food born diseases[61].

The global spread of knowledge and technologies, however, can improve the outbreak surveillance and monitoring of antibiotic resistance[21], increasing the speed of responses in some cases. Wilson[28] states that responding to disease emergence requires a global perspective. Hence, the policies and actions undertaken by WHO are becoming increasingly important in controlling infectious diseases at a global level. For instance, WHO played a critical role in controlling SARS by means of global alerts, geographically specific travel advisories and monitoring[62].

Food

Food trade has become an increasingly important factor with regard to food security worldwide. At present, however, the developed countries still subsidize their agricultural sectors, and tariffs for agricultural products remain relatively high. Economic liberalization policies are expected to have profound implications on food trade and, subsequently food security[63]. Some argue that free trade will create access to better and cheaper food supplies via food imports and can stimulate more efficient use of the world's resources, as well as the production of food in regions that are more suitable to do so. Accelerated economic growth can also contribute to food security[63, 64]. According to *The State Of Food Insecurity in the World 2005*[65], accelerating the progress towards an open and more equitable trading system is one of the key elements in the worldwide reduction in hunger.

On the other hand, trade could also endanger food security (e.g. Lang[66]). For many countries the increasing dependence increases their vulnerability to shocks arising in global markets, which can affect import capacity and access to food imports[63]. Many food insecure countries are not able to earn enough with exporting goods in order to pay for the needed food imports[67].

At the global level, there are increasing international efforts to achieve widespread food security. In 1996, the World Food Summit, for example, stressed the right of everyone to have access to safe and nutritious food. Globalization can also enhance the knowledge of foreign nations about the usefulness of food aid. Additionally, the globalization process can facilitate the worldwide implementation of better technologies and improved knowledge. At the same time, however, the natural resource base for food production is increasingly threatened by compromised ecosystem functioning due to global environmental change.

Water

Globalization also raises concerns over water security. The globalization process is accompanied by privatization policies affecting the provision of water. Governments and international financial institutions promote privatization, as they believe it will promote market competition and efficiency. Others are less optimistic about the effects of privatization. In fact, some cases show that prices and inequalities in access even rise[68]. The virtual trade of water is also believed to be of increasing importance, The water that is used in the production process of a commodity is called the "virtual water" contained in that commodity. Therefore, the increasing global trade of commodities is accompanied by an increasing trade in virtual water[69].

In addition, the globalization process can increase water security by facilitating the worldwide implementation of better technologies and improved knowledge. At the same time, the natural resource base is increasingly threatened as, for example, global climate change and deforestation profoundly affect our ecosystems' ability to provide us with sufficient and adequate fresh water. On a global scale, there are increasing efforts to set up global guidelines or policies with regard to fresh water, however, none of the international declarations

and conference statements requires states to actually meet an individual's water requirements.

Global health: the way forward

Global health research addresses the ways in which globalization is impacting on both health determinants and outcomes[1]. This is a rather new, but very exciting research field. The small number of persons, groups and institutions that is tackling this topic is steadily growing. A next step in this evolution of interest is the recognition that much of the research needs to be conducted within a systems context. Global processes, and their health impacts, do not occur in isolation. Many of the modifications of, for example, infectious disease transmission, lifestyles, health care, or food security are the result of coexistent and often interacting developments. The discussed framework provides valuable insights in how to organize the various factors involved in addressing global health. It clearly demonstrates that an integrated approach is needed, drawing upon the knowledge from relevant fields such as epidemiology, sociology, political sciences, (health) education, environmental sciences and economics. We need to step away from business-as-usual attitudes, sectoral-based solutions and short-term remedies. This will require integrated initiatives organized around the health challenges posed by globalization rather than around specific research disciplines or policy sectors.

Additionally, global health should concern everybody's health. The SARS outbreak demonstrated that when an epidemic threats the affluent countries, the response is fast and well-funded[70]. The current lists of global health priorities primarily focuses on selected conditions around infectious diseases (e.g. HIV/AIDS, malaria and tuberculosis), reflecting health-related problems in the developing world that are perceived to threaten the vital interests of industrialized countries[71]. This illustrates the existing inequalities in power over agenda-setting on global health, with "dominant interests framed as globally shared"[1]. We need more research addressing the complex linkages between global processes and the multiple disease burdens in the developing world. As the geographic scale of important communicable and non-communicable health issues increases, countries are progressively dependent on each other in establishing good health. Exploring the impacts of globalization requires capacity building in developing regions and transborder collaborations between scientists, policy-makers, and other stakeholders. Global health should be inherently concerned with reducing the burden of disease in populations worldwide, and, consequently, with narrowing the 10/90 gap and strengthening research capacity in low-income countries. Additionally, priority setting should not only consider current disease burdens and inequities, but must also anticipate possible global health challenges in the future. ❑

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Innovation

Towards the development of a Health Innovation Strategy for South Africa

Article by Glaudina Loots

South Africa is currently at a significant set of crossroads due to the great need for health innovation to combat the tremendous health challenges in our diverse society. The health needs should be addressed in such a way that the serious inequalities of our society at large are encompassed and negated. This means that the medication that is developed should be appropriate, accessible and culturally acceptable to the population. This issue then needs to take into account various major challenges such as appropriate health medication, health infrastructure and also appropriate needs-oriented research. This article will give a broad and brief overview of the progress towards the establishment of a Health Innovation Strategy for South Africa from the perspective of the South African national government Department of Science and Technology.

The meaning and need for a Health Innovation Strategy

The continuous need for new drugs, vaccine and diagnostics and new processes in engineering and manufacturing, as well as new approaches to health systems and services within developing countries[1] is driving the need for the development of health innovation strategies. Within this context there is a need for an overarching framework that can facilitate this process – this is where an appropriate Health Innovation Strategy fits into the picture.

An area of global concern is that only 10% of the global health research and development budget is being spent on 90% of the global health problems[2]. This unequal flow of resources has since been referred to as the "10/90 gap". Health in the developing countries is no longer the concern of the developed countries; however, there is growing recognition internationally that the health of more than 80% of the world is a matter of concern to all who inhabit this world. One of the crucial factors responsible for this "10/90" gap is the lack of integration of health research into national and international research systems.

India, Brazil, China and South Africa are currently seen as the leading innovative developing countries. Of the four, South Africa's Health Research and Development (R&D) budget as a percentage of public health expenditure is the lowest and falls behind that of India and Brazil. For South Africa to be on par with the other three countries, a concerted effort needs to be made to increase the government R&D expenditure.

It is increasingly being recognized that health research exists within the broader context of research systems which, in turn, function within the specific socio-political and economic context of the relevant country[3].

Similarly, health innovation systems operate within a given country's education, manufacturing, research and development system – guided, naturally, by regulatory systems, intellectual property policies and market forces, domestically and internationally.

It is within this complex context that the South African government and, in particular, the Department of Science and Technology, is engaged in establishing a national framework that will enable research, development and innovation.

Research, development and innovation within the South African context

The National Research and Development Strategy (2002)[4] (NRDS) in South Africa was adopted by Parliament as a strategy geared towards the establishment of the necessary enabling environment. The NRDS recognizes the complex interplay and the synergies that can be created through co-ordination between sector specific research systems and the National System of Innovation that includes the universities, the various national science councils, government and the private sector.

The NRDS sees the Department of Science and Technology (DST) playing a strong role with regard to health research and health technology in South Africa. Health-related research should soften the devastation caused by diseases.

The NRDS recognizes that the following issues, although not exhaustive, should form the core of the health research effort:

- Understanding the social impact of disease.
- Creating an environment and technologies to reduce the effect of poverty on the spread of disease.
- Developing care and support strategies.
- Understanding the challenges in providing access to prevention and care measures.
- Developing innovative preventative strategies.
- Developing novel therapeutic regimes, including the utilization of indigenous knowledge.
- Developing preventive and therapeutic HIV/AIDS vaccines.

- Creating a viable vaccine manufacturing industry.
- Appropriate forms of telemedicine could assist in transforming rural health care provision[4].

The role played by the Department of Science and Technology will be in conjunction with the other major players in health research such as national and provincial government departments of Health, the Health Research Committee (HRC), the Medical Research Council and various institutions that conduct health research and develop or improve health technologies. The Science and Technology Interventions for Health Innovation can therefore be seen as interventions that have a long-term time frame, constituting a high risk and dependant on disruptive and innovative technologies.

The priorities outlined in the NRDS also find support from the Millennium Development Goals. The Report highlights the need for research into HIV/AIDS, tuberculosis and malaria and mentions that: "Science, technology, and innovation policy needs to be oriented towards finding vaccines and cures for these diseases, while creating new institutional frameworks from which new research collaborations can spring"[4].

In defining the role of DST in health innovation, two critical issues have been considered: the first deals with the scope of the work that will be undertaken, and the second deals with criteria defining research areas that are of critical importance to South Africa.

Taking cognisance of the international trends, the South African National Research and Development Strategy and also the health research priorities for South Africa, it is considered appropriate that the role of DST in health research can be broadly defined as *the* promotion of the development and exploitation of new technologies and the advancement of basic knowledge of biology and human behaviour. The DST should consequently be primarily involved with science interventions with regard to vaccine development, issues of drug discovery, the development of new diagnostics, as well as the development of medical devices and treatment regimes.

In order to insure that the research is sustainable and is translated into appropriate social and economic benefit, DST should actively participate along the entire length of the Innovation Chain. For South Africa, this Innovation Chain encompasses capacity development, technology development, including basic science and frontier programmes, biotechnology, nanotechnology and technology transfer, including clinical trials, commercialization of Intellectual Property and implementation through pilot programmes.

Determining health research priorities in South Africa

Based on these broad guidelines and to ensure focus on the country's available resources, it is essential that the health research expenditure is (and remains) highly focused. Various other attempts have been made to identify national health research priorities for South Africa; these include, *inter alia*:

- the health research priorities listed by the Department of Health in their Essential National Health Research conference held in 1996;
- the March 2006 Health Research Conference;
- the National Research and Technology Foresight project of the Department of Arts, Culture, Science and Technology (1998) that identified specific research and technology priorities for the health sector.

In the 2003 Initial Burden of Disease Estimates for South Africa 2000, the South African Medical Research Council identified the top 20 specific causes of premature mortality in 2000 (see Table 1).

Rank	Cause of death	%
1	HIV/AIDS	39.0
2	Homicide/violence	7.5
3	Tuberculosis	5.0
4	Road traffic accidents	4.1
5	Diarrhoeal diseases	3.8
6	Lower respiratory infections	3.8
7	Low birth weight	3.3
8	Stroke	2.7
9	Ischaemic heart disease	2.4
10	Protein-energy malnutrition	1.4
11	Suicide	1.4
12	Diabetes mellitus	1.2
13	Hypertensive heart disease	1.1
14	Fires	1.0
15	Septicaemia	1.0
16	Chronic obstructive pulmonary disease	0.9
17	Neonatal infections	0.8
18	Asthma	0.8
19	Nephritis/ nephrosis	0.8
20	Bacterial meningitis	0.8

Table 1: Top 20 specific causes of premature mortality

Based on the priorities and information from these exercises, certain health areas have been identified as priority areas for the development of Department of Science and Technology interventions (see Table 2).

Approach to health research, development and innovation in South Africa

The South African Science and Technology Interventions for Health Innovations will concentrate on the research and innovation that leads to discovery and evaluation of new drug and treatment regimes, the development of new vaccines and new robust diagnostics for the identified diseases or conditions, as well as the development of medical devices. The range of research activities will include the interrogation of indigenous knowledge, basic molecular science and genetics, chemistry and bio-chemistry, biotechnology, nanotechnology, nuclear physics, ICT, manufacturing processes and engineering.

Consortia of researchers are encouraged to develop a specific research strategy per intervention area. These consortia will have to be representative of most of the researchers/research institutions in South Africa that are dealing with that specific disease or technology area. The consortia will have to appoint a manager/coordinator. One of the universities/science councils will then take responsibility for the management of the consortia and the coordinator will be appointed on contract basis at the specific institution.

Major classification	Disease/Intervention area	Research areas
Major infectious diseases	HIV/AIDS TB Malaria	Vaccine development, Microbicides, Drug discovery and evaluation Drug discovery and evaluation, Diagnostics, Vaccine development Drug discovery and evaluation, Diagnostics, Clinical epidemiology, Vector interaction
Noncommunicable diseases and disabilities	Cancer Diabetes Hypertension/heart disease/stroke	Diagnostics, Imaging, Drug discovery and evaluation Diagnostics, Drug discovery and evaluation, Medical devices and self-management tools Diagnostics, Drug discovery and evaluation, Medical devices & self-management tools
Mental health	Mental health/nervous system disorders	Imaging, Drug discovery and evaluation, Medical devices and self-management tools
Nutrition		Food security research, Food supplementation
Other infectious diseases	Respiratory infections, incl. COPD and asthma Endocrine and metabolic diseases Zoonoses, new and emerging diseases Diarrhoeal diseases	Drug discovery and evaluation, Medical devices and self-management tools Drug discovery and evaluation, Diagnostics Diagnostics, Drug discovery and evaluation Diagnostics, Drug discovery and evaluation
Injuries	Trauma, including burns	Imaging, Medical devices, Drug discovery and evaluation
ICT in health	Health informatics, telemedicine & e-health, Biostatistics and bio-informatics	

Table 2: Health areas identified as priority areas for the development of Department of Science and Technology interventions

Research institutions with higher levels of expertise will be encouraged to partner with institutions with limited capacity in order to build research capacity at these institutions. Examples of these consortia are the South African Aids Vaccine Initiative, South African Malaria Initiative and the Brain and Behaviour Research Group.

The progress with regards to the expected outcomes will be evaluated on an annual basis, with biennial conferences and workshops to showcase the progress and to re-align the research efforts.

Existing and future trends in health research, development and innovation

In their article, Morel et al[1] highlighted a number of determinants for Health Innovation Systems that will enable a developing country to maximize its ability to address diseases of the poor, namely:

1. creating capacity for and undertaking R&D.
2. creating and sustaining capabilities to manufacture products to appropriate standards.
3. promoting and sustaining domestic markets.
4. promoting and sustaining export markets.
5. creating and implementing systems for Intellectual Property (IP) management.
6. creating and implementing systems for drug, vaccine, diagnostic and device regulation.

Currently the main focus of the Research, Development and Innovation Strategy of South Africa is on the strengthening of R&D capacity, as well IP management. The local manufacturing of products is also receiving more attention. The Medicines Control Council of South Africa is a well-established entity and falls under the jurisdiction of the national Department of Health. All new drugs and vaccines need to be approved by the Medicines Control Council before they can be introduced to the market in South Africa. It is noteworthy that a similar system for medical devices is also envisaged.

Total South African R&D expenditure: 2005/06

The Department of Science and Technology conducts an annual Research and Development Survey, based on the Frascati Manual[i] of the Organisation for Economic Co-operation and Development (OECD).

Data extracted from the 2005/06 Research and Development (R&D) Survey results database, indicated that in South Africa the total spend for R&D in 2005/06 was R 14 149 239, with reported direct health R&D expenditure approximately 10.6% at R 1523 billion (Figure 1).

In 2005 the total South African Health Care System contributed approximately 8.1% to South Africa's GDP[7]. As the GDP for 2005[8] was estimated at ZAR 1 539 billion, then the total South African Health Expenditure is estimated at R 125 billion. The Health R&D expenditure is then approximately 1.2% of the total South African Health Expenditure for 2005/06. This is, however, still below the 2% target that was set by the South African Government.

The analysis of the 2005/06 R&D Survey indicated that private companies were responsible for approximately 44% of all Health R&D being conducted in South Africa, while Universities accounted for approximately 36% of the health research (Figure 2).

However, the 2005/06 results reflect that 67% of all health researchers are working at universities (Figure 3).

This discrepancy between the percentage R&D funds versus the Health Researchers per sector illustrates there is

[i] The **Frascati Manual** was developed by the Organisation for Economic Co-operation and Development and sets out the methodology for collecting and using statistics about research and development in countries that are members of the OECD.

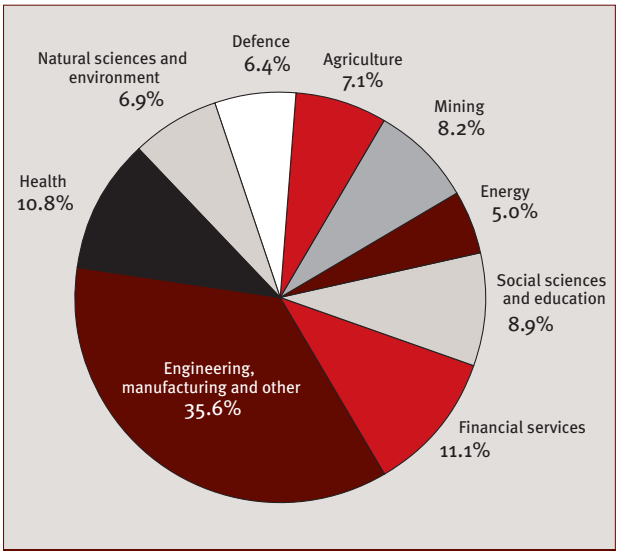

Figure 1: Total South African R&D expenditure 2005/06

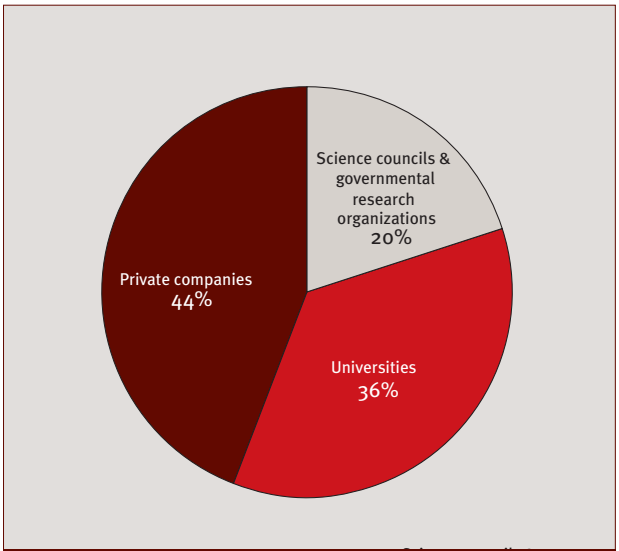

Figure 2: Health research expenditure per broad sector 2005/06 (%)

probably a large amount of intersectoral cooperation between the private sector and the universities. There is a tendency for private research organizations to contract university researchers to conduct their research.

When analysing the research outputs of the university-based researchers, there was a steady increase in publications during the past 15 years. This development is very encouraging. However the national trend of the "greying" of the scientists in South Africa is a worrying factor[9].

The specific fields of science in line with the definitions[ii] of the Global Forum for Health Research within Health R&D that the health researchers are specializing in are illustrated in Figure 4.

The low percentage of research funding for clinical research and chemical sciences research is a worrying factor and would need specific interventions. The research funding with

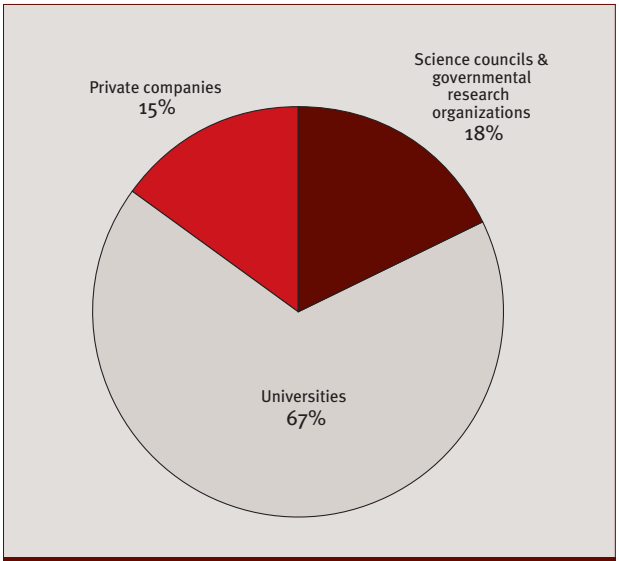

Figure 3: Health researchers per broad sector 2005/06 (%)

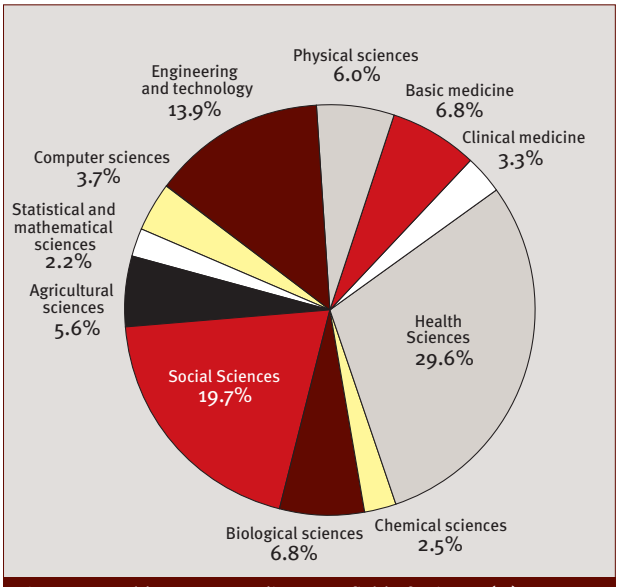

Figure 4: Health R&D expenditure per field of science (%)

[ii] **Basic medicine** – anatomy, cytology, physiology, genetics, pharmacy, pharmacology, toxicology, immunology and immunohaematology, clinical chemistry, clinical microbiology, pathology, biomedicine.
Clinical medicine – anaesthesiology, paediatrics, obstetrics and gynaecology, internal medicine, surgery, dentistry, neurology, psychiatry, radiology, therapeutics, otorhinolaryngology, ophthalmology.
Health sciences – public health services, social medicine, hygiene, nursing, epidemiology.
Chemical sciences – chemistry, and other allied subjects.
Biological sciences – biology, botany, bacteriology, microbiology, zoology, entomology, genetics, biotechnology, biochemistry, biophysics, other allied sciences, excluding clinical and veterinary sciences.
Social sciences – economics, health economics, psychology, educational sciences, political science, sociology, anthropology, demography and geography.
Agricultural sciences – agriculture, forestry, fisheries, horticulture and veterinary medicine.
Statistical and other mathematical sciences – mathematics and other allied fields.
Computer sciences – information and communication technology and software development (hardware development should be classified under engineering fields).
Engineering and technology – civil engineering, electrical engineering, computer engineering (hardware only), and other engineering sciences (such as chemical, mechanical, and metallurgical and materials engineering, the science and technology of food production).
Physical sciences, and earth and related environmental sciences – physics and other allied subjects, geology and other earth sciences, and meteorology and other atmospheric sciences such as climatic research and vulcanology.

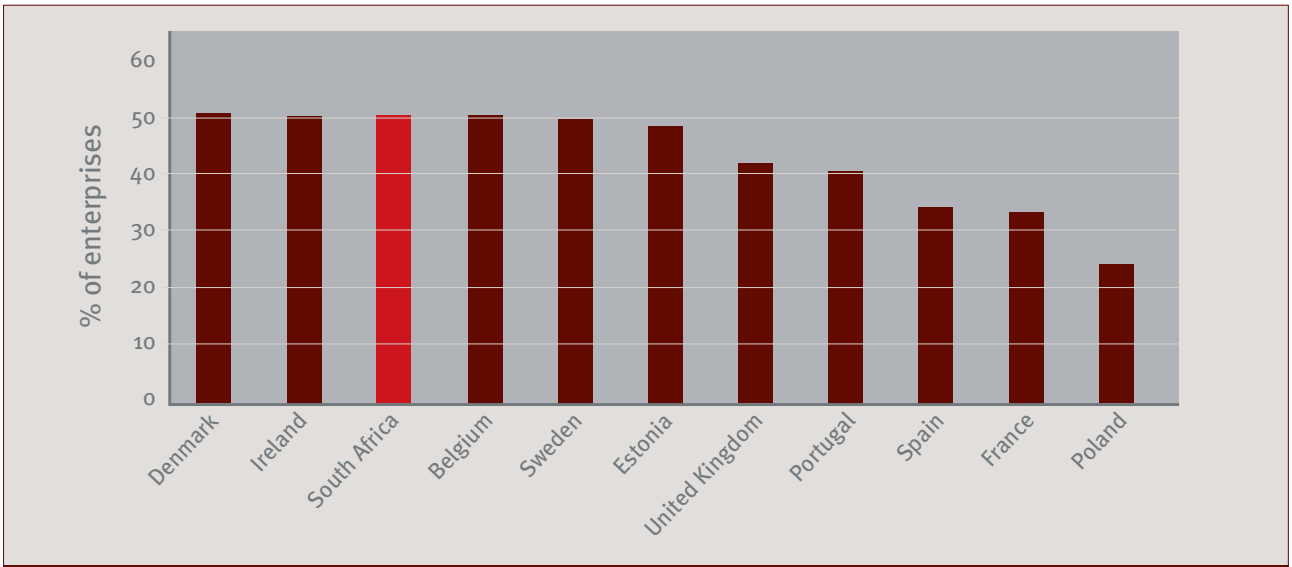

Figure 5: Share of enterprises with innovation activities (%) 2002–2004

engineering and technology interventions for health is quite encouraging and this might be explained by the fact that this type of innovation is encouraged within the South African context.

Innovation

In addition to the Research and Development Survey, the South African Department of Science and Technology also commissioned the South African National Innovation Survey 2005[10]. This survey found that nearly 52% of the enterprises surveyed reported innovative activities. The 52% of enterprises which reported technological innovation activities, comprising both products (goods and services) and process innovations, is at the same level as that recorded in Denmark and Ireland and slightly more than Belgium (51%) and Sweden (50%) (Figure 5).

Companies have to be innovative in order to keep abreast of developments in health innovation – this innovative energy should then be channelled towards appropriate research that addresses the complex needs of our changing society. This competitiveness is a key to economic survival in an increasingly globalized world.

In order to stimulate the biotechnology industry and innovation in South Africa, a specific biotechnology strategy was developed with the aim to focus on those areas where there is likely to be a comparative advantage in biotechnology, as well as to establish new programmes and technology platforms that will harness existing national scientific and technological competencies. It is believed that biotechnology can make an important contribution to our national priorities, particularly in the area of human health (including HIV/AIDS, malaria and TB), food security and environmental sustainability. This National Biotechnology Strategy is one of the building blocks of a wider health innovation strategy.

Conclusion

Based on this brief analysis of the South African Health Innovation scenario, it is clear that a more specific health innovation strategy needs to be developed to address all the aspects of health innovation and that, although some attention is paid to research and development, the commecialization aspects thereof need to be encouraged in order to ensure that South Africa can be more competitive in health innovation. ❑

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She is also responsible for the South African Women in Science Awards, as well as addressing issues pertaining to gender and disability in the Science, Engineering and Technology sector in South Africa. She currently acts as a strategic advisor to the newly-merged University of Limpopo.

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Using the power of intellectual property to strengthen equitable access

Article by Anatole Krattiger

Over the last decade, many countries around the world revised their laws related to intellectual property (IP). These changes were driven by a true "explosion of IP legislation at the international level"[1]: in the last 15 years ten new IP specific treaties were concluded[2], and nearly every international treaty today includes IP clauses.

Because of its feared impact on low- and middle-income countries, the most discussed treaty in the context of health research and development has been the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). Whether or not and to what extent TRIPS will impact the pricing and availability of health products are certainly legitimate concerns. But access to health products and services depends on many factors. One key factor is the successful innovation of new technologies, either as new drugs, vaccines, or services, or as adaptations of existing products to the contexts and frameworks of low- and middle-income countries.

Indeed, innovation management is a complex endeavour. Government and institutional leaders need to address a wide range of issues, ranging from policy choices to implementation strategies. Some of the most important elements to consider in this context are:

1. Intellectual property is just one of several factors that determine innovation in health research and development (R&D).
2. When assessing the impact of legislative and policy choices, intellectual property must be considered in the context of other competencies:
   a. Supportive R&D policy
   b. National health programmes that sustain domestic markets, including distribution systems in both the public and private sectors
   c. High-quality manufacturing standards for drugs and vaccines
   d. Effective regulatory systems
   e. Mechanisms to facilitating trade in health products and technologies
3. Mechanisms and best practices to harness the global IP regime in a manner that promotes both private and public interests, including the improvement of poor populations' access to health products.

As a pre-requisite for countries to participate in the global marketplace and benefit from emerging technologies, strong institutional IP capabilities are needed. This should be coupled with careful consideration of the tremendous latitude provided by TRIPS in terms of national implementation. These should be coupled with national policies and practices that support the public sector's endeavours to meet the needs of the poor. These need not be compulsory licensing that may bring advantages in the short term. Such approaches are unlikely to be effective in the medium- to long-term in enabling – let alone sustaining – collaborative efforts between the public and private sectors.

It is not argued here that the IP rights system is perfect. It is a compromise and an imperfect solution[3]. IP rights systems represent the search for balance between making all knowledge freely available within the *public domain* and granting *ownership* of valuable discoveries to the inventors. Historically, we have seen that this balance encourages investment – and reinvestment – in innovation, primarily by the private sector. Unfortunately, this innovation is too infrequently directed towards the needs of the poor. The failure is not in the IP rights system *per se*, but in part due to the fact that insufficient attention has been paid by the public sector to managing intellectual property. This lack of focused attention must be corrected.

Legislative frameworks

The IP legislative explosion mentioned above has unsurprisingly led to suspicions about IP rights, which are often viewed as controversial and complicated. Indeed, if one considers these numerous treaties from a purely legal perspective, one easily gets entangled in legalities requiring a cohort of lawyers (and, arguably, very deep pockets). Yet this view perhaps misses the point of what IP rights are all about. First and foremost, they are intended to encourage investments in innovation. Second, IP rights systems were created to regulate access to and sharing of the less familiar "intellectual" form of property. Put differently, IP systems today are meant to enable the orderly conduct of business in the realm of intellectual property. The purpose of statutory IP rights, the related contract laws, and the court systems is to enable predictable, transparent business dealings between and among institutions and individuals.

The changes in international IP legislative frameworks through treaties are rapidly changing national legislation. And these changes are profoundly affecting how health innovations reach the poor and how public and private research and development institutions pursue their work. IP rights are sometimes viewed as barriers to innovations in health and other areas. In some circumstances, they are. But this paper argues that overall it is not intellectual property, *per se*, that obstructs access, but rather *how* intellectual property is used and managed. What matters most is how creatively public sector institutions integrate IP considerations into their overall business models and approaches. Seen in this light, the legislative framework provides a solid foundation for a stable, predictable judiciary, which also allows the public sector to use a national IP system as a tool to achieve its goals. A stable IP system empowers the public sector to imagine, anticipate, and act.

The policy choices

Determining how institutions can adopt and adapt the advantages conferred by TRIPS and other legislative initiatives is crucial. For example, government policies are hugely important for establishing to what extent public sector institutions will practise IP management. In the United States, no other policy choice had a more significant impact than the Bayh-Dole Act and other legislative and policy decisions in the early 1980s. They created conditions that spurred investment in biotechnology R&D, leading to numerous health innovations. But above all, these policy choices greatly affected how universities and public sector research institutions manage intellectual property and their relationship with the private sector.

Although the circumstances of countries vary enormously, the following set of questions are nearly universally relevant: when should public sector R&D centres or universities seek patent protection for their inventions? What information related to research should they keep confidential, if any? Under what circumstances should the public sector grant access (in other words license) their intellectual property? And under what terms? And to whom? These questions do not have simple answers. This is largely because the answers will depend on the context in which they emerge. Even within the same institution, the answers may be diametrically opposed for different types of inventions. Given these complexities, what should be the government's role in the area of policy?

First of all, establishing an open, transparent government policy for the ownership of publicly funded research is an important foundation for building sound institutional IP management. Institutional leaders have little latitude when the underlying rules are opaque or not spelled out.

Second, the policy rationale for technology transfer in public sector institutions should not be based on anticipated revenue flows; instead, long-term national, social, and economic objectives should structure policy decisions – with public benefit as the key factor. Indeed, since government funds much research at national R&D and academic institutions, it has the prerogative to mandate certain conditions for the benefit of these institutions' public missions. Policy-makers have a lot of latitude when it comes to ensuring that investment in research is returned as a public benefit. They could certainly require, for example, that products developed and marketed commercially from publicly funded research have some provision for delivery to the poor.

In the United States, no other policy choice had a more significant impact than the Bayh-Dole Act and other legislative and policy decisions in the early 1980s

Third, governments can also strengthen the courts and recognize their important role in balancing conflicting IP policies. Such efforts will provide useful guidance with regards to business, technology, and science planning and strategy. Not every dispute, however, should be resolved in court. For public research and product development in general, and for equitable access and meeting the needs of the poor in particular, governments have tremendous opportunities to promote policies that foster alternative dispute resolution procedures[4]. Such approaches are often preferable for settling differences between parties. Court action is often stymied because of cost, length of procedure, legal uncertainty, a decision-maker's lack of expertise, conflicts between confidentiality and publicity, the difficulty of seeking action in foreign jurisdictions, and the negative impact on existing business relationships. Arbitration is an attractive option for all of these reasons, and while it is a private mechanism, it is not altogether free from regulation by national laws. Governments and public institutions can help make arbitration or mediation procedures accessible and available by identifying and supporting neutral institutions that can provide cost-efficient, timely dispute resolution services. Such approaches would also take much of the negative public perception out of IP rights, especially from legal disputes that can deter increased private participation in meeting the needs of the poor.

Finally, it should be recognized that Product-Development Partnerships (PDPs) allow the private sector to invest and apply its expertise to address the needs of the poor. Many such PDPs are now driving the drug development pipeline in neglected disease R&D. A pioneering new institutional structure, PDPs will become increasingly prevalent in developing countries and contribute to the development of products in less viable markets. National governments have tremendous opportunities to promote policies and capacities that facilitate these innovative partnerships, especially in such areas as effective clinical trials and ethical review capacities, appropriate regulatory bodies for clinical research and product approval, and national and institutional IP policies that stimulate health and agricultural R&D.

Institutional strategies

Whatever the impact of TRIPS and of strengthened patent regimes, institutional IP management capacities will need to be strengthened so that the legislative and policy changes can

be adapted – and harnessed – to a nation's advantage. In the increasingly interconnected global network of science and innovation better IP management at the institutional level enables earlier and easier access to indispensable emerging tools, technologies, and know-how.

Better IP management can be achieved through capacity-building efforts. And these can be sustained through sound national and institutional IP policies. Specific initiatives at the institutional level should include capabilities for negotiating contracts, streamlining statutory protection (copyright, patents, trademarks, and dealing with confidential information), patent searching and filing, freedom to operate reviews and strategy (a particular challenge for public sector institutions)[5], technology valuation, and business strategy development. Governments should be cautious, however, not to develop policies that mandate public research institutions and universities to adopt a single approach. IP management is very context specific, and flexibility is a precondition for its creative and successful use.

Further, the increasingly ubiquitous PDP works by building on the comparative advantage of public and private sectors and managing that interface authoritatively. Any institution that wishes to participate needs, at a minimum, to be in a position to negotiate complex contracts, manage newly generated intellectual property, and respect third party intellectual property. This requires mastery of a range of specifics, from laboratory notebook policies to good practices in managing confidential information to name but two.

Since the mission of many public institutions is increasingly shifting from purely academic research to making a social and economic impact at the local and national level, IP management is an even stronger imperative. It is an integral part of a public sector's toolbox that allows it to meet its entire mission more effectively to create hitherto unsuspected opportunities.

One such opportunity lies in the manner in which drug and vaccine development is changing shape in developed countries. The blockbuster-focused business model of multinational pharmaceutical companies is fundamentally being reshaped[6]. The drivers for this change are complex but due in part to emerging opportunities offered from novel technologies (diagnostics for personalized medicine, gene therapies, and so forth). As a result, a new range of mergers and acquisitions are taking place. In due course, an entirely new array of alliances will be created to further multinationals' quest to create niche remedies that target much smaller populations than blockbusters did in the past. Conceptually, there is nothing that stands in the way for a multitude of developing country institutions, including public sector ones, to participate in this new business model and concurrently gain advantage in serving their own local national niche markets. But it will require some institutional changes.

Institutional culture and individual mindset

To harness the power of IP, management capacity and skills are fundamental. Such skills make it possible to get earlier access to emerging tools, technologies, and resources that can dramatically improve the health and welfare of their citizens. For example, the private sector in India has taken quick advantage of TRIPS by a) channelling its resources into the research and development of drugs for diseases that dominate in developing countries and b) building IP management capacity well before the entry into force of TRIPS[7]. This dual approach provided many companies in India with substantial foreign investments and access to foreign markets. In fact, more drug approvals are being submitted to the US Food and Drug Administration (FDA) from India than from all other foreign companies combined. Similarly, effective IP management can also be made to benefit public research institutions. Without knowledge of sophisticated IP management techniques, however, such efforts to enter into effective public-private partnerships that can direct the power of industry to the needs of the poor will be stymied.

As previously mentioned, innovation in health relies on sophisticated, global IP rights systems and on science that is increasingly complex, specialized, and globalized. This complexity requires a more open system of knowledge sharing than previous research and development programmes, and many studies suggest that successful innovation requires developing clusters of institutions, businesses, and personnel. "Location, location, location," the battle cry for real estate agents everywhere, is increasingly becoming the key word in studies of innovation dynamics and knowledge-based growth. Prime locations in R&D are referred to as "clusters" – groups of similar-minded institutions and individuals who grow together. Although companies and various not-for-profit entities in the same sector or product market have traditionally located themselves in specific geographic regions (rather than spreading out evenly across a country), the deliberate search for ways to encourage clustering has only recently begun. Institutions have much to gain from being located in clusters or strongly linked with them. Indeed, this strategy is one of the most effective ways to bring about institutional change and attract entrepreneurs.

Governments have an important role to play in the process of cluster formation. In order to create clusters, governments could usefully redirect some of their funds from bricks and mortar and product investments towards soft investments in institutions and platforms that create collaborations. Local and national governments can also foster cluster formation by, for example, offering tax incentives to companies to set-up their operations within a defined zone of geographical proximity. It is universities, however, that have the power to lead the way in supporting productive research networks. These networks have the potential not only to generate new knowledge but also the ability to bring in and adapt global knowledge to local needs. Indeed, research collaborations are important both for a university's academic status and for the commercial and economic prospects of a research-based cluster. Universities should strive, therefore, to encourage and support research that engages with the larger community.

Putting the power of intellectual property to work for the poor

As mentioned, when it comes to combating diseases and

promoting health in developing countries, the past decade has seen an unprecedented pace of change. One big change is the range of new actors – particularly the private sector – contributing to this agenda[8]. To ensure that this agenda is sustained, the private sector must continue to be engaged *by* the public sector to achieve public sector goals.

For intellectual property to be put to work by the public sector for public sector goals, an urgent reconceptualization of the relationship between the IP system and developing countries is needed. This requires, first and foremost, best practices in IP management by and for the public sector[9]. Much can be achieved with this relatively simple emphasis – as opposed to efforts aimed at changing international treaties or negotiating yet another global treaty with impact only in the long term, if any[10]. Broad access for the poor can be strengthened significantly – with tangible and near-term benefits – through creative IP management and licensing practices.

Good institutional IP management capabilities, strengthened IP court systems and patent offices, and policies that encourage meeting the needs of the poor are the tools that will create more effective R&D endeavours and provide equitable access to valuable health innovations. ❑

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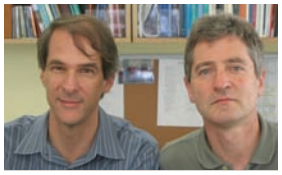
Financing of vaccine R&D – gaps and opportunities for innovation



Article by Paul A Wilson (left) and Robert Hecht (right)

The purpose of this paper is to identify gaps and deficiencies in existing funding for vaccine research and development (R&D) and explore ways that innovative financing mechanisms could fill these gaps. Our focus is on AIDS vaccines, but new funding mechanisms could also support development of vaccines for other diseases that primarily affect the developing world, such as malaria and tuberculosis. We begin to construct an analytical framework and use it to characterize and evaluate funding mechanisms for vaccine R&D.

There has been considerable innovation in global health financing in recent years, including the establishment of the Global Fund for AIDS, Tuberculosis and Malaria (the "Global Fund") and the GAVI Alliance (formerly the Global Alliance for Vaccines and Immunization)[1]. GAVI itself is now funded in part by an innovative mechanism, the International Finance Facility for Immunization (IFFIm), which raises resources through the sale of bonds backed by future donor commitments[2]. In the R&D area, public-private product development partnerships (PDPs), which first appeared in the mid-1990s and are supported primarily by grants from governments and foundations, are another important new funding mechanism[3]. A pilot Advance Market Commitment (AMC) for pneumococcal vaccines, intended to spur private sector investment in development and manufacture of vaccines for developing world markets by creating a substantial subsidized market for these products, was announced earlier this year[4].

Despite this dynamism, funding of global health R&D remains inadequate. Innovative financing mechanisms could accelerate R&D by increasing the total volume of funding and by improving its *focus, flexibility,* and *predictability* and thus easing some of the inefficiencies that currently hamper progress. Innovative financing could also help to mitigate the scientific and commercial risk associated with drugs and vaccines for diseases of the developing world and in this way allow the private sector to contribute more to the development of these new technologies.

Current investments in AIDS vaccine R&D

Funding for AIDS vaccine R&D has grown substantially in recent years. Between 2000 and 2006, funding from the public and the philanthropic sectors rose from US$ 327 million to US$ 854 million, as existing funders increased their contributions and were joined by new donors[5]. If private commercial funding is included, total spending on AIDS vaccines reached $933 million last year (Figure 1). Public sector funders continue to provide the large majority (83%) of resources for preventive HIV vaccine R&D, while in 2006 the philanthropic sector provided 8.4% and the commercial sector accounted for the remaining 8.4%.

Where are the gaps in vaccine R&D financing? How could innovative financing make a difference?

While financial resources devoted to AIDS vaccine R&D have increased substantially, there are a number of deficiencies that must be addressed:

- **Insufficient volume of funding.** The Global HIV Vaccine Enterprise estimated in 2005 that US$ 1.2 billion is needed annually to speed the search for an HIV vaccine. Current spending is thus about US$ 270 million less than what is required. Moreover, sustained support at even current levels is by no means assured: in recent years, the overall NIH budget has levelled off, and one-time grants from foundations cause funding from this sector to fluctuate from year to year. There are strong arguments for expanded government funding of vaccine R&D: vaccines are in important respects "public goods", in that by interrupting disease transmission they indirectly benefit people who are not themselves vaccinated. Moreover, many people who need these health tools are very poor, which further weakens the power of market forces alone to drive their development. Short political cycles and immediate pressures to spend on today's health care services can make it difficult for governments to devote adequate resources to longer-term investments in new drugs and vaccines.
- **Allocative inefficiencies.** Certain activities are inadequately resourced, leaving gaps in critical parts of the R&D continuum. Under-funded areas include *applied research* to address key scientific constraints, such as the challenge of finding a vaccine capable of eliciting broadly neutralizing antibodies; *translational research* and design of novel vaccine concepts; and trial capacity sufficient to conduct several proof-of-concept efficacy trials in parallel[7]. These gaps mean that scientific knowledge is not being

efficiently converted into candidate vaccines and that candidates are not being efficiently tested and compared. In the case of early stage research, we believe that new funding mechanisms are needed to encourage experimentation and support ideas that existing funding sources were not designed to target. Such mechanisms should be able to respond rapidly to opportunities, have a high tolerance for risk, and reach beyond the mainstream of HIV research to bring in ideas from other areas of virology and immunology. A related inefficiency stems from the fact that existing R&D funding mechanisms are mostly national in scope and primarily support research and product development within individual OECD countries (Organisation for Economic Co-operation and Development). In light of the growing science and technology capacity of certain developing countries such as Brazil, China, India and South Africa, there is a need for truly global funding mechanisms that could support neglected disease R&D wherever it can be done.

- **Technical inefficiencies.** Most funding for AIDS vaccine R&D comes from national research bodies such as the USA's National Institutes of Health (NIH), the UK's Medical Research Council (MRC) and France's Agence Nationale de Recherche sur le Sida (ANRS), which award grants directly to researchers and product developers; or from government and foundation grants channelled through public-private partnerships like the International AIDS Vaccine Initiative (IAVI). Recently, the Bill & Melinda Gates Foundation has also made grants to applied research consortia composed mainly of academic investigators. Funds from these national research bodies tend to be relatively *short-term*, typically three years in the case of NIH, while financing from Gates or IAVI may extend somewhat longer. In both cases, the duration of funding is not always consistent with the long-term investments that complex vaccine research projects require or with product development through proof-of-concept stage, which can take five years or longer.

In addition, existing research grants tend to cover only a fraction of the total cost of a scientist and his laboratory. Scientists therefore have to divide their time among several projects and are not able to focus as they could if their entire research programme were covered by a single large vaccine R&D grant. This *fragmented* system of financing can undermine the technical efficiency of resource use.

This analysis suggests that new financing mechanisms could make AIDS vaccine R&D faster and more efficient by expanding the volume of funding; encouraging researchers to focus full-time in large labs and laboratory consortia on key scientific challenges; stimulating more biotechnology companies to develop new vaccine concepts and platform technologies suitable for an AIDS vaccine; and supporting the development of clinical trial sites in high-incidence population cohorts where rapid Phase II proof of concept and larger Phase III efficacy trials could be conducted.

A framework for assessing vaccine R&D financing options

In the previous section we outlined current funding for AIDS vaccine R&D and identified some important gaps that new kinds of support might fill. To give structure to our discussion of innovation in R&D financing, we focus on three dimensions of financing mechanisms: source, use and financial modality.

Source

Funding for R&D can come from the public sector, from the commercial private sector or from foundations. Moreover, especially in the case of public funds, the source can be a national body such as the NIH or an international institution such as the World Bank or a United Nations agency. Sources of commercial private funding of R&D include the pharmaceutical industry, venture capital and private equity firms, and individual investors. A growing number of foundations are now backing R&D activities too, along with philanthropic initiatives of for-profit firms.

It is sometimes useful to distinguish between proximate and ultimate sources: for example, PDPs like IAVI act in part as financing intermediaries, channelling resources raised from national governments and foundations to specific R&D projects along with scientific and technical support. Most

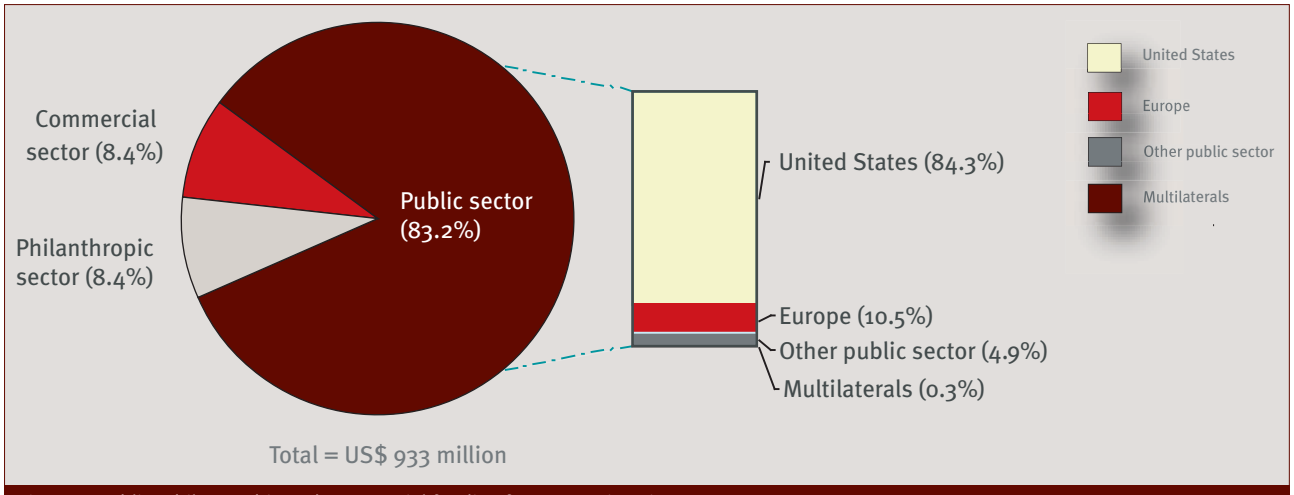


Figure 1: Public, philanthropic and commercial funding for HIV vaccines in 2006

Financing mechanism	Ultimate sources of funds	Intermediary	User	Use	Financing modality (to/from intermediary)	Predictability & flexibility (for intermediary/user)
RECENT						
Global Fund	Donor governments, foundations	Global Fund	Developing country, governments, NGOs	Drugs, bednets, health services	Pooled donations/ grants	Weak/moderate
IFFIm	Bondholders, with government backing	GAVI	Developing country governments	Vaccine purchases	Bonds/grants	Strong/moderate
Pilot AMC	Donor purchase commitments	GAVI	Industry for R&D/developing countries for vaccines	Product development/ new vaccine purchases in future	Product purchase commitment/ purchase subsidy	Strong/moderate
PDPs	Donor governments, foundations	PDPs (IAVI)	PDPs and partner organizations	Vaccine R&D, advocacy, etc.	Grants/grants	Weak/moderate
NEW OR PROPOSED						
R&D window in existing global health fund	Various	GAVI, PDPs	PDPs and science partners	Vaccine R&D	Variable (grants, bonds, taxes)/grants	Variable – depends on source of financing
Vaccine R&D Bond	Bondholders, with government backing	PDPs, other?	PDPs and science partners	Vaccine R&D	Bond/grants or equity	Strong/strong
AIDS Vaccine Innovation Fund	Gates Foundation	IAVI biotechs	IAVI and vaccine R&D	Early stage or equity	Grants/grants	Medium/medium

Figure 2: Key dimensions of innovative financing for health

recent innovation in sources of financing for global health has involved the establishment of new financing intermediaries, including the PDPs as well as the Global Fund and the GAVI Alliance, which pool funds from established sources. The newly launched UNITAID is an interesting exception; although its funds come from established donor nations, they derive ultimately from a new earmarked tax on airline tickets.

Use and user

R&D financing mechanisms can also be distinguished by the activities they fund and by the organizations that carry out these activities. Since different classes of organizations specialize to a degree in different stages of R&D, there is a rough relationship between use and user: financing mechanisms aimed at earlier stages of R&D tend to focus on academic labs and biotechnology companies, while support for later stages generally targets larger firms.

Financing modality

Funding for vaccine R&D can also take a variety of financial forms or use different financing tools to generate resources. The public and non-profit sectors have typically supported R&D through grants or tax concessions. Both approaches partially or fully subsidize R&D with no expectation of financial return. Private investors generally expect a return and fund R&D through debt or equity investments. Each of these financial instruments can be structured in many different ways.

PDPs also support vaccine R&D through grants but typically expect in return a mechanism to ensure that developing countries would have affordable access to a vaccine if it is developed.

Purchase funds or advance market commitments seek to stimulate product development in the private sector by creating a subsidized market. Choices among technologies and product candidates are left to firms and the committed funds are spent only if the desired product is developed, produced and purchased in eligible developing countries.

In comparing the benefits and effectiveness of these financing modalities, several characteristics should be considered. These include the duration and predictability of financing for both the intermediary and for the end user; the flexibility of the funding and the user's ability to target money to its specific R&D needs. In addition, R&D users benefit from funding tools with fewer associated administrative and reporting requirements, while donors naturally prefer mechanisms that make use of existing administrative infrastructure to those that require new institutions and procedures. Other important considerations are the incentives the financing modality creates for recipients and how it distributes risk between ultimate funders, intermediaries and users.

Figure 2 describes several recently established and possible

future global health financing mechanisms using a simple framework based on these dimensions of source, use, user, and financing modality.

Possible new financing mechanisms for vaccine R&D

R&D windows in existing global health financing mechanisms

One possible new source of funds for vaccine R&D would be existing global health financing institutions, which could broaden their scope to support the development of new health technologies. Among the institutions that might open such new "windows" for R&D are the Global Fund, UNITAID, the GAVI Alliance and the World Bank. The strongest argument for such an expansion of the mission of these institutions is that investment in R&D now can increase the payoffs from future spending (or cut costs) by making more effective vaccines available sooner.

For example, an effective vaccine against HIV could save billions in annual treatment costs. The IFFIm mechanism which currently funds GAVI was designed to allow the frontloading of expenditure on immunization, yet the benefits of spending now rather than later are even more compelling for R&D expenditure.

The most suitable use of new resources from these institutions might be to fund clinical trials in developing countries, since this would constitute less of a departure from their current activities. The new funds for R&D could be channelled through PDPs and other organizations sponsoring trials or through national governments where the trials will take place. New resources for efficacy trials would help to fill one of the critical gaps in current vaccine R&D financing. Moreover, financing from UNITAID or GAVI could be more predictable and longer-term than most existing funding, since both UNITAID (through the airline tax) and GAVI (through the IFFIm mechanism) have access to dedicated, predictable resources.

Government-guaranteed bond financing

A different kind of financing innovation would be to draw on the international bond markets to support vaccine R&D, just as the IFFIm has done to pay for expanded purchase and delivery of existing childhood vaccines. Such a fund, the International Finance Facility for Neglected Diseases or IFFnd, has recently been proposed for drug R&D; the concept could apply equally well to vaccines[10]. As with IFFIm, borrowing at competitive rates would be made possible by donor government guarantees. Unlike payment for vaccine purchase, however, investment in vaccine R&D could ultimately lead to a vaccine with commercial potential. Thus donor repayment commitments could potentially be offset in part by product royalties. Nonetheless, donor governments could expect to be responsible for the bulk of repayments, and might reduce their current or future support for vaccine R&D through other channels in return for backing the R&D bonds.

Funds raised through a government-backed bond issue of this kind could be disbursed through an institution such as GAVI. Alternatively, the resources generated through the bond sales could flow through PDPs. In either case, funds raised in this manner would help to assure sufficient volume and greater predictability of financing. There is no theoretical reason to limit the use of funds from a bond issue to a particular stage of R&D, although an expectation from donors that their obligations would be reduced by sales revenues might create pressure to focus on later-stage or less risky projects, or on those more likely to be used in rich world markets as well as low-income countries.

Targeted approaches to financing scientific innovation

Another class of innovative financing mechanism would focus specifically on early stages of R&D – on fostering and translating innovation – and thus aim to fill the gap between public funding of university research and later-stage development work carried out by industry, PDPs, or in some cases, public sector institutions. We will mention three promising ideas.

Innovation funds administered by PDPs: IAVI will soon launch a fund, co-funded by IAVI and the Gates Foundation, to provide small grants to biotechnology companies (and perhaps some university labs) to test ideas considered too risky to attract venture capital or other private sector support and not appropriate for standard public sector research grants[11]. By drawing on the expertise of experienced fund managers and its own knowledge of the relevant science, IAVI also hopes to be able to evaluate projects more rapidly than traditional mechanisms. Until now, nothing of this kind has existed for vaccine R&D and no innovation fund has been set up and managed by a PDP. Although mechanisms of this kind represent a departure from the traditional role of PDPs in supporting mid and later stages of product development through partnerships with industry, they have the potential to feed new ideas and candidate products into the PDP pipeline.

University/industry matching funds: while most scientific innovation occurs in university labs, breakthroughs are not always efficiently transferred to industry where they can be developed into useful products. The Swiss government's Commission for Technology and Innovation is attempting to foster early collaboration between university researchers and biotech companies by providing grants to academic labs on the condition that the money is matched by an industry partner, which then receives preferential access to intellectual property that is created[12]. This system could be modified to target AIDS and other neglected disease vaccine R&D, perhaps by reducing the contribution required from the private sector partner. The Wellcome Trust's Seeding Drug Discovery initiative, which funds translational research on unmet medical needs and pairs researchers with experienced industry advisors, could be another model for bridging this gap[13].

Subsidized venture capital funds: venture capital funds are an important mechanism for financing early-stage R&D in the private sector – in 2004 they mobilized $3.7 billion for the biotechnology industry[14]. Venture capital firms have so far shown relatively little interest in AIDS, malaria and TB vaccines, however, because the likely markets for these products are seen as insufficiently attractive or too uncertain to offset the scientific risk, which, especially in the case of AIDS vaccines, is seen as unusually high. One way to offset

some of this risk might be to match private sector venture capital investments in vaccine R&D for certain diseases with public sector funds or to provide grants to venture capital firms that fill a certain fraction of their portfolio with investments in these areas.

These ideas merit further investigation, although it is not clear from initial consultations with venture fund managers that subsidies of this kind would substantially change the risk/reward calculations of potential investors. Moreover, venture capitalists were skeptical of the idea of a venture fund that blended AIDS/TB/malaria vaccine projects with other biotech activities[15]. This is because venture investors would prefer that all projects in a fund be evaluated relative to the same objectives (i.e., financial returns or contribution to a social goal), rather than by different and potentially incompatible criteria.

If successful, venture capital subsidy or matching schemes would have the potential to bring private sector capital as well as private sector project evaluation and management expertise to early-stage vaccine R&D.

Conclusions

Global health has moved to centre stage in recent years, as health care is increasingly recognized as a critical part of efforts to reduce poverty and improve the quality of life of billions of people, and as a powerful way to harness science and technology to the pursuit of social goals.

There has been substantial innovation in global health financing recently, especially in creating new sources, intermediaries and financial modalities for the purchase of existing drugs and vaccines and the delivery of health services. Although there has been less change in the funding of health R&D, the establishment of PDPs and the launch of a vaccine AMC are important developments.

Despite these advances, there are still significant gaps and deficiencies in vaccine R&D financing, including insufficient volume, focus, flexibility and predictability. In this paper we begin to develop a framework for characterizing and assessing the strengths and limitations of financing mechanisms for vaccine R&D and propose some new financing approaches that might address the deficiencies that we have identified. ❑

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He also served as an Associate Director of the Joint United Nations Programme on HIV/AIDS (UNAIDS) from 1998 to 2001, where he managed technical units based in South Africa, Côte d'Ivoire and Thailand, as well as in Geneva.

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Dr Wilson spent much of his career as a scientist. Before moving to Columbia to work on global health policy, he was an Assistant Professor of Cell Biology at the Cornell Medical College. Dr Wilson holds a PhD in Zoology from the University of California at Berkeley, an MSc degree in Economics from the London School of Economics and an undergraduate degree in Physics from Princeton University.

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Child immunization: accelerating equitable access through innovative financing

Article by Alan R Gillespie

In November 2006, the launch in London, UK of the inaugural US$ 1 billion bond of the International Finance Facility for Immunization (IFFIm) changed the frame of reference for development financing. This breakthrough has brought radical alteration both to the scale and timeframe of immunization programmes, and to the long-term predictability of aid funding.

IFFIm is a new international development institution designed to accelerate the availability of funds to be used for health and immunization programmes. It is the result of an innovative public-private partnership between the development sector, finance communities and donor governments[1]. It works in partnership with the GAVI Alliance, itself another leading-edge hybrid of public and private concerns, working through its partners to implement child health and immunization programmes in 70 of the world's poorest countries[2]. Itself only seven years in existence, the GAVI Alliance has quickly demonstrated that the effectiveness of development assistance depends on making the funds targeted, and on building flexibility into the process.

IFFIm has put unprecedented financial weight behind prompt, near-term action to accelerate vaccine access and health system strengthening for the poorest countries. The placement of this bond was the first use of the international capital markets to fund grants for one specific development purpose and reflects the aim of the Facility: to frontload aid to help meet the Millennium Development Goals. It therefore represents two important drives: to get very significant volumes of aid quickly to where they can be most influential; and to do so within a structure that clearly demonstrates the long-term and predictable nature of support.

The first of these: significant aid, quickly delivered. The first full year of IFFIm proceeds will fund critical global infectious disease reduction programmes as well as supporting immunization safety and new vaccine programmes in GAVI countries (see Figure 1)[3]. By the end of 2007, through IFFIm, an estimated 14.5 million additional children will have been reached with vaccine against hepatitis B, 4.4 million children with vaccine against yellow fever, and 3.8 million children with vaccine against *Haemophilus influenzae* type b (Hib)[4].

Over the next 10 years, the anticipated IFFIm investment of US$ 4 billion is expected in total to provide immunization for an additional half a billion people and save as many as 10 million lives.

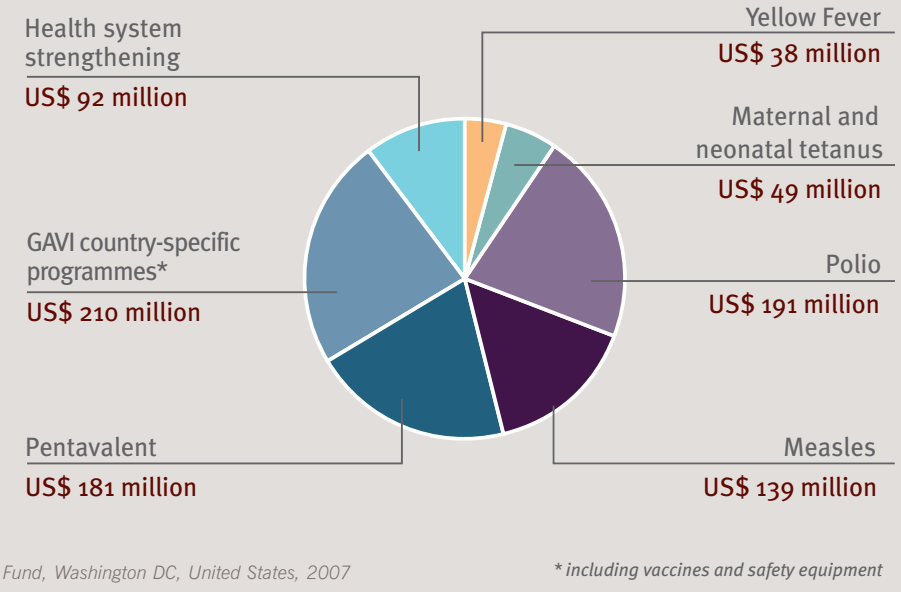
Importantly, IFFIm funds are also helping countries to address as quickly as possible health system "bottlenecks" that currently limit their ability to get vaccines to children. To date the IFFIm Board has approved US$ 117 million to be used for health system strengthening. This represents more than 10% of the inaugural bond amount of US$ 1 billion. Of this, GAVI will have applied US$ 92 million before the end of 2007.

Ethiopia provides a good example of how to tackle these bottlenecks effectively. Ethiopia's per capita gross national income is US$ 160. It is one of the world's poorest countries. It shares the "catch 22" plight of most of the countries in this situation: a high child mortality rate (under five mortality of 145 per 1000 live births), critical gaps in the health workforce, and the consequent vicious circle of ill health and continuing poverty that make it impossible to devote more resources to health.

For Ethiopia, the key is to address inequitable access to basic health services. Health worker density is currently at 0.6 per 1000 inhabitants. The plan to train 30 000 "health extension workers" is the centerpiece of the health component of the national poverty reduction strategy. When roll-out is completed in 2008 the programme will have placed two freshly trained health extension workers in each of Ethiopia's around 15 000 communities, providing services including immunization to community members. Beyond the training, the programme will also finance establishing management/supervisory capacity and infrastructure such as the construction of health posts, and supply/distribution/maintenance systems.

What is IFFIm's role in this? Through frontloading the funding needed to support the five-year plan, the whole project has been massively accelerated – and fully funded.

During 30 years in the financial markets, assisting governments and companies to raise capital, I have never been involved in any transaction so thoroughly worthwhile and rewarding



Source: The GAVI Fund, Washington DC, United States, 2007

** including vaccines and safety equipment*

Figure 1: Expected IFFIm disbursements, 2006–2007

Ethiopia will receive a total of US$ 76.5 million for health system strengthening for 2007–2009, with the majority – US$ 56 million – arriving in 2007.

The predictability of this funding is an essential part of its value. Fragile economies cannot give firm assurances of consistent financial support to long-term plans. But plans involving human resources training have to be sustained. Breakthrough funding like this from IFFIm makes all the difference: it assures the whole period.

Equally essential in this mix is a solid national plan that can bear the strain of such dramatic acceleration. And the end result has to bring the widest possible range of benefits. Tedros Ghebreyesus, Ethiopian Minister of Health and GAVI Alliance board member, described the critical significance of the new programme to improving his country's health services. He said, "Our vehicle has not been strong enough to carry all the programmes we have loaded on it. Now we are working to strengthen the vehicle so that it can carry all our programmes, the vaccines and the other health care interventions, to every corner of this vast country."

The benefits of this type of funding go beyond providing stability to developing country plans. It also has market-shaping potential – a vital component in the endeavour to increase access to new and better vaccines through using market forces and economies of scale to stimulate demand and reduce product prices.

By signaling financial stability and long-term committed financing, it is also possible to spur larger markets, accelerate vaccine development, and promote increased production, availability and lower prices.

For example, IFFIm funds are being used to stimulate increased demand for combination vaccines not currently produced in sufficient quantities. US$ 181 million of IFFIm funding has allowed the GAVI Alliance to make a binding commitment to purchase "5-in-1" pentavalent vaccine at a reduced price by making a longer-term commitment. This product provides, in a single shot, protection against five diseases: diphtheria, tetanus, pertussis, hepatitis B and Hib. The availability of IFFIm funds over the next decade supports security of supply: it also provides an incentive to new manufacturers to enter the market, a dynamic which can further reduce vaccine price.

This dynamic – the "pull factor" of having long-term, substantial funding ready – has already worked very well in support of the global polio eradication campaign. In a WHO-led initiative, a stockpile of completely new monovalent vaccines to secure the post-eradication phase is being generated. The IFFIm funding was essential to spur manufacturers rapidly to manufacture and evaluate the new vaccines that are critical to this process. Demonstrating the asset of flexibility, when the eradication campaign alerted the Boards of the GAVI Alliance to a critically damaging funding gap, reprogramming of IFFIm funds allowed (exceptionally) this crisis to be averted and the campaign to continue unimpeded.

Through the GAVI Alliance, the catalytic funding IFFIm offers is quickly channelled to where it will have most impact. In line with the concept that early intervention with vaccination incrementally saves lives in infectious disease epidemics, an early investment was in a stockpile of yellow fever vaccine, working through the Yellow Fever Initiative.

This was rapidly useful when, three months after IFFIm was launched, Togo reported an outbreak of this highly infectious and lethal viral disease. In the first two weeks of February 2007, a broad range of partners, led by the Ministry of Health in close collaboration with WHO, worked together to bring yellow fever vaccine to 1.33 million Togolese in 11 districts of the Savanes and Kara regions.

In a further benefit, the risk assessment activities undertaken as part of the Initiative in 12 countries in Africa,

are revealing previously unrecognized populations at risk and therefore significantly increased the demand for the vaccine – something that usefully allows supply market stability, better forecasting and production scale-up, with benefits to both producers and purchasers. The result: a marked reduction in the size and frequency of yellow fever outbreaks in Africa in the immediate future and increased availability of vaccine where most needed.

IFFIm has also contributed strongly to the work on the reduction of measles deaths globally. Again on the principle of early, robust action, US$ 139 million of IFFIm support went to the Measles Initiative in February 2007. Nearly 240 million children will have been immunized against measles in supplementary campaigns in 2007. This is a very successful initiative, which has already seen a reduction in global measles deaths from 480 000 in 2003, to an estimated 170 000 in 2010. The vaccination campaigns do more than save lives from measles; they also provide the opportunity for insecticide-treated nets that protect against malaria to be distributed, and other aspects of child health to be targeted, with de-worming tablets and vitamin A supplements.

In each of these areas, in protecting and fostering healthy children, IFFIm is contributing in valuable ways to building up the bedrock of a healthy economy.

IFFIm's origins and its special context go back to the late 1990s, when G8 governments looked back at the past 50 years of giving, and recognized that what was needed was a more focused purpose. This resulted in the Millennium Development Goals. At the same time, Bill & Melinda Gates were searching for a focus for their philanthropy. One of the answers was immunization – and a new model for more efficient delivery. Their initial US$ 750 million dollars gift founded that model in 2000 – the GAVI Alliance. Six years later, that proven concept provided the match IFFIm needed for the prompt execution of its funds. The Gates' "demanding dollar" in many ways was the trigger for others, like Gordon Brown, then UK Chancellor of the Exchequer, to pay close attention to how to get better value for aid and to lead the international support for this new funding facility.

On the face of it, IFFIm investors are rational investors, responding to an impressive offer – a triple-A-rated bond offering a good return. The bonds were priced comparably to other sovereign/supranational issuers, and the initial offer was well over-subscribed with almost US$ 2 billion of demand.

The defining difference – that which sets it apart from the others – is IFFIm's goal. It is not just an investment end in itself. It has a greater purpose: one that allows bond investors to give directly to the frontier of health care, one that has inspired individuals and companies to work *pro bono* to bring this idea to fruition. It makes a profound difference.

Health extension worker 18-year–old Ajebush Wakalto (right) prepares to vaccinate young Brucktayet Teshome (far left, in her mother's arms) at the local health post in Timbicho, Ethiopia. She, and 30 000 others like her in the programme, form the centrepiece of the health component of the country's poverty reduction strategy, bringing a range of health advice to local communities and providing essential basic preventive care, such as immunization.

The bonds were subscribed for not only by the traditional types of investors such as central banks, pension funds, money managers, and insurance companies, but also, in a reflection of its fundamental humanitarian purpose, by individuals such as His Holiness Pope Benedict XVI.

It is the hope and the intent of all of us who are associated with this new instrument that it will make the necessary impact. July 2007 was the mid-point in the MDG timeframe. It is generally acknowledged that progress towards the health-related goals is too slow and too little. Initiatives like the International Finance Facility for Immunization and the GAVI Alliance are two strong allies in the efforts to speed up progress, confronting and offering solutions to the core challenge of inequitable access. ❑

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1. IFFIm's sponsor governments include France, Italy, Norway, South Africa, Spain, Sweden and the United Kingdom. Brazil has announced its intention to join. IFFIm issues triple-A rated bonds with a financial base consisting of long-term (10–20 years) legally binding commitments from sovereign donors. The borrowings and risk are handled under prudent financial policies, with the World Bank acting as Treasury Manager. Goldman Sachs acted as Financial Advisor in establishing IFFIm and Deutsche Bank and Goldman Sachs lead-managed the inaugural bond issue.
2. The GAVI Alliance was created in 2000 as a public-private partnership accelerating delivery of life-saving immunization to the world's poorest children. The Alliance includes a wide range of development partners, developing country and donor governments, WHO, UNICEF, the Bill & Melinda Gates Foundation, the vaccine industry, research and technical agencies, public health institutions, nongovernmental organizations and the GAVI Fund (the resource and funding arm of GAVI).
3. GAVI's "country-specific" programmes include the provision of immunization safety equipment such as single-use syringes and disposal boxes, as well as the provision of new and underused vaccines such as those against hepatitis B, yellow fever, rotavirus and pneumococcal disease.
4. WHO projections.

Being healthy: the role of research

Article by Andrew Y Kitua

Living a healthy life is the ultimate common desire of human beings and is what has driven individuals and communities to search for medicines and other health remedies. Improvements in health research methodologies have helped us to test beliefs, myths and theories for their validity and reliability, which has led to the generation of new knowledge and in turn to new or improved tools. As a result of better research and innovation, we have accumulated vast knowledge about the determinants of disease and ill health, prevention measures and cures of diseases. Our medicines and health interventions are unquestionably better and safer than they were 50 years ago. It is indeed scientific research that has continuously transformed or revolutionized the way we live and has been a key determinant of the rate of modernization and human development.

Access to and utilization of the new knowledge and the resultant new or improved tools has not been equal among the countries that form our global community. Because technology has greatly influenced economic power, countries with greater technological advancement and greater research capacity have conspicuously better health status than countries in transition towards acquiring technology and with weaker research capacities. There is vast heterogeneity of health status today between continents, countries and even within countries. Whether measured by life expectancy at birth, infant and child mortality, maternal mortality, malnutrition, or disease patterns, the health status of a country's population reflects the status of its technological and economical advancements, which in turn reflect its capacity to effectively access and use new knowledge and tools for human development.

Risks for ill health

Health research has greatly advanced our knowledge of risk factors for diseases and ill health. Health risk as a measure of the probability that an adverse event for health will occur following exposure to a certain factor has been used to measure the health status of individuals and communities. It is well known that although there are no individuals or communities devoid of health risks, and risk factors are widely distributed globally, there are global differentials in the level or position of individuals and populations on the risk scale for a particular factor[1,2,3], along the divide of developing and developed countries.

The pattern of morbidity and mortality differs remarkably among countries at different levels of technological and economic status, such that low-income countries, or least developed countries, bear higher mortality from preventable conditions, while high-income countries bear the burden of higher consumption and lifestyle risks[2].

Risks of dying at different age categories from birth, and the causes of such risks, differ greatly among low-, middle- and high-income countries. In low-income countries, the majority of deaths occur at very young ages, before reaching age five. Once individuals have avoided death at this level, they are almost assured to survive the adolescent period between five and twenty years, where the risk of dying is lowest. With the current levels of spread of HIV/AIDS, the previously most fit and productive age between 15 and 45 years has now become highly risky. Mortality in this age group has increased remarkably, bringing down previous gains in life expectancy. In contrast, the majority of deaths occur after the age of 60 years in high-income countries[3].

In low- and middle-income countries, the main risk factors for death are: underweight, resulting mainly from malnutrition and infections; unsafe sex; unsafe water; poor sanitation and hygiene; and smoke from solid fuel[3]. Most of these are avoidable due to availability of knowledge and effective tools to prevent them. Recent studies have shown that 87% of mortality occurring in children below the age of five in low- and middle-income countries is avoidable[4]. In the same category of countries, 63% of males and 84% of females aged 5–29 years die of avoidable factors. The higher proportion of deaths among females is due to avoidable pregnancy-related and child birth-related causes. Avoidable deaths due to communicable diseases account for 90% of all mortality in all sex and age classes, excluding middle-aged men in whom their contribution is 80%.

In high-income countries, mortality is mostly at old age. The relatively few deaths that occur in younger life are concentrated in the neonatal period and are mainly due to congenital malformations. Mortality risk factors are mainly tobacco use, high blood pressure, obesity and alcohol consumption. Road traffic accidents have a significant contribution, and this trend is also increasing in middle-income countries [1].

The picture is reflective of the power of knowledge ownership and capacity to both generate and utilize available

Developing countries	%	Developed countries	%
High-mortality countries		Tobacco	12.2
Underweight	14.9	Blood pressure	10.9
Unsafe sex	10.2	Alcohol	9.2
Unsafe water, sanitation and hygiene	5.5	Cholesterol	7.6
Indoor smoke from solid fuels	3.7	Overweight	7.4
Zinc deficiency	3.2	Low fruit and vegetable intake	3.9
Iron deficiency	3.1	Physical inactivity	3.3
Vitamin A deficiency	3.0	Illicit drugs	1.8
Blood pressure	2.5	Unsafe sex	0.8
Tobacco	2.0	Iron deficiency	0.7
Cholesterol	1.9		
Low-mortality countries			
Alcohol	6.2		
Blood pressure	5.0		
Tobacco	4.0		
Underweight	3.1		
Overweight	2.7		
Cholesterol	2.1		
Indoor smoke from solid fuels	1.9		
Low fruit and vegetable intake	1.9		
Iron deficiency	1.8		
Unsafe water, sanitation and hygiene	1.7		

Adapted from The World Health Report 2002. Preventing Risks and Taking Action, *pp. 161-163*

Table 1: Leading 10 selected risk factors as percentage causes of disease burden measured in DALYs

knowledge. Those with greater ownership and hence easier access to knowledge and tools because of their technological advancements are at a different level of risk than those who depend to a greater extent on knowledge and tools developed elsewhere. Such goods are not readily available and accessible in many low- and middle-income countries, due to low purchasing power and basic infrastructure for their effective application.

With better technologies and greater research participation, access to information and its use is greatly enhanced. Preventable diseases and ill health conditions are significantly reduced and therefore deaths or disabilities due to preventable conditions such as vaccinable infections and sanitation-related diseases, like cholera and diarrhoeas, are totally absent or occur at very minimal levels.

Similar differentials can be found between populations and communities within a country. Although the general health status of individuals and communities in high-income countries is generally better than lower-income countries, the rich and poor within each of the above communities enjoy a different level of health status. Education status also has a strong influence on individuals' and communities' power to access and use new knowledge.

Success and failure stories

Smallpox eradication stands today as one of the greatest human achievements in the fight against agents of disease. This journey of discovery ensued from the curiosity-driven experiments of Edward Jenner. His experiments were probably triggered by the knowledge he acquired from a peasant who told him, "I cannot take that disease", meaning smallpox, "because I have had Cow Pox"[5]. This took him through what may appear today as a dangerous experimentation period of trying to validate the acquired knowledge and improving the methods, until it was possible to proceed to mass introduction and adoption of vaccination as a public health tool. It took effort and determination to demonstrate the effectiveness of the new knowledge to the extent of influencing governments to support vaccination, through the enactment of legislation and provision of funds for intervention. It also required a high level of advocacy to raise awareness and funding of the global campaign for the purpose of eliminating a major killer disease. This campaign was a good demonstration of the power of concerted action to avail resources for the application of new knowledge globally, without any discrimination, and regardless of economic status. Smallpox was a major global threat in the form of epidemics with widespread distribution that terrorized the global population. It was difficult to eradicate, but eradication became possible because of the availability of an effective tool and the willingness of the global community to put together resources towards its elimination. The terror it caused was probably a highly motivating factor. Global commitment ensured that the tool was availed in sufficient supplies to reach effective coverage levels, and sustained sufficiently until total eradication was achieved.

The knowledge generated from understanding the mechanism of action of the vaccine approach opened many doors in immunology and extended the use of this knowledge to the protection of populations, not only from infections caused by other viruses, but also by bacteria.

Onchocerchiasis elimination in West Africa and current efforts to eliminate it from other parts of Africa and the Americas is another example of the good will and commitment of the global community to eliminate a terrible health problem, even when it was affecting African and Latin American populations and none of the developed world[6,7]. Here the value of public-private partnerships in research is demonstrated by the willingness of a rich patent holder to donate freely a tool to help poor populations, which would have otherwise never been able to afford the costs of purchasing and sustaining use of the tool, to have sustainable access to it. The drug was actually developed for other uses in rich countries and it continued to make a profit to the patent holder through its sale and use in such countries. In 2002, WHO reported that 18 million people had grown up free of the threat to river blindness, in the Western African countries, where the disease had previously been endemic[7]. In this case, the participation of endemic countries' governments has been critical. Had this problem been left solely to the low-income endemic countries, we would never have achieved this success to date because, given their economical status, they would not have been able to mobilize sufficient resources for the task. However, the world provided the financial and technical support and endemic countries' governments provided the political commitment and established the programmes, contributing their own resources. The programmes were built within the health systems, strengthening them in the process and providing sustainability.

The failed effort at malaria eradication provides an example of premature, nonevidence-based decision-making by the global community, against a noble commitment at a time

when much progress and achievement had been made towards global malaria control. The global community had seized the opportunity to use concurrently two very effective vector control tools: the newly discovered DDT and drainage of swamps, in conjunction with mass prophylaxis and prompt case identification, and treatment using chloroquine. It was the first time malaria was being attacked globally with multiple tools and the operations were military-like. Within a short period, malaria had been eradicated in Europe and America and transmission had been reduced significantly in many parts of Africa and India, with some countries coming close to eradication. However, following the disease eradication in Europe, and considering the costs of maintaining the operations in the remaining parts of the world, quick, nonevidence-based decisions were taken and the eradication campaigns were abandoned followed by abrupt withdrawal of the funding support to countries. It was believed that malaria eradication in the developing world, and in particular Africa and India, was not achievable given the vastness of the terrain and there was a global atmosphere of despair and loss of direction. This is an example of poor monitoring of activities. It was as if the world had given up on malaria, leaving the plight of the poor to themselves now that the rich countries had rid themselves of the disease. The ensuing results were catastrophic, and malaria came back in the form of epidemics in countries which had achieved good transmission reduction and were near to eradication. We learnt later that this was a result of loss of natural immunity following the transmission reduction and that, in such cases, withdrawal of vector control activities should not have been effected so abruptly.

Lessons learnt

The above examples have taught us that global problems require globally concerted efforts. When such efforts are directed at evidence-based interventions, and are given sufficient resources to reach and maintain high levels of coverage, success is assured. The decisions to continue or stop an intervention should be guided by evidence. The cost of making the wrong decisions in public health are very high. It is important to integrate programmes within existing health systems to ensure governments' commitments and long-term sustainability.

Had research been applied to evaluate the achievements made in large parts of India, Madagascar and Africa, and in particular the cases of projects like the Pare-Taveta Scheme[8], malaria eradication efforts would probably have not been abandoned. The research would have revealed that it would have been totally unethical to do so, and would likely have led to further research on how to maintain the operations at lower costs.

Current challenges

The new millennium has brought with it new determination and commitment by the global community, in face of the still intolerably high disease burden and preventable deaths, despite huge technological advancements. The ambitious Millennium Development Goals[2] (MDGs) indicate the sense of urgency and anxiety that the global community is experiencing over the continuous suffering of the majority of the global population. Regions have risen to the occasion and made serious commitments to work together, while countries have set their own targets and committed themselves to allocating sufficient resources to achieve the targets.

Africa has also responded by forming its own mechanism to enhance research and technological developments as means for achieving the MDGs. New Partnerships for Africa's Development (NEPAD) is a promising innovative mechanism, capable of accelerating African achievements.

The challenges facing all these efforts include ensuring:

- availability of effective and affordable tools which are accessible to those who are at greatest risk (those who need them most);
- accessibility and utilization of such tools by populations of endemic countries;
- research on the effective application of multiple tools;
- integrating strategies within the health systems;
- strengthening health systems to allow rapid scaling-up of interventions;
- research capacity-strengthening in endemic countries to enhance discoveries, knowledge utilization and ownership of new and improved tools.

Conclusions

While the above challenges are formidable, there are promising opportunities for making the world a healthier place to live in. In the first place, effective interventions and tools are available for the conditions causing the greatest disease burden. Effective vaccines for childhood diseases are available. Water sanitation technology has been there ever since the cause of cholera was discovered. Safe delivery methods are available to prevent maternal mortality. Secondly, there are signs of increased awareness of inequities in health. The risk of spreading infections to the rest of the world is real and imminent, given current climatic changes, freedom of movement and the persistence of highly endemic infectious diseases in low-income countries. As a result of this fear and good will from the global community, more funds are being provided to help improve the health of the poor. Indeed current key concepts, such as "funding poverty-related diseases", "providing support towards neglected diseases" and "global health approach" are fast gaining momentum. Debt relief has been widely accepted as a strategy to allow better funding of health and education, and enhancing accountability and good governance by countries.

These are therefore promising moments and good opportunities for making populations healthier; however, as previous experiences have shown, the availability of a tool per se may not be sufficient to make a difference. The key is to ensure that endemic countries do own the means to solve their own problems and have the capacity to participate actively in global efforts targeting those who need them most. If the current funds do not flow to the targeted endemic countries to support capacity strengthening, there is great danger that health care systems will remain weak and endemic countries will continue to have weak research

capacities. It is indeed weak health care systems that prevent high vaccination coverage and the reduction of maternal mortality. Effective innovative skills are necessary to bring about the creation of health care systems that are closer and accessible to the client.

In addition, effective ways of disseminating knowledge for behavioural change requires research capacities for support. To accelerate the pace of current achievements, create greater certainty that new knowledge becomes a public good accessible to all, and ensure that new and improved tools are utilized effectively by those that need them most, we must encourage real partnership in the process of knowledge generation. This can be the case only if deliberate efforts are made to support research capacity development in disease-endemic countries.

Achieving the Millennium Development Goals should go hand in hand with developing capacities to sustain achievements and make even greater progress in future. Health and development are achievable. They must be linked to the capacity to generate and utilize effectively generated knowledge[9]. The role of research in being healthy is unquestionable. Hence, capacity for research and development is a prerequisite for empowering countries to participate actively in solving their priority problems, and contribute effectively to making a healthy global community. ❑

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The role of Knowledge Translation in bridging the "know-do gap"

Article by Ariel Pablos-Méndez (pictured) and Ramesh Shademani

During the 20th century, knowledge in all its forms contributed to unprecedented global health gains[2]. Yet ill-health and premature deaths from preventable causes persist, especially among poor children and women, in spite of available cost-effective interventions[2,3]. Studies show that more than half of the deaths to children under five years old can be prevented by the use of available interventions[2,3,4]. Such studies indicate that most of the burden of premature death and illness among the poor is due to problems for which solutions are known and prevention is possible. Even in war-ravaged countries, most deaths are from easily preventable and treatable illness rather than violence[5]. The achievement of the health Millennium Development Goals (MDGs) in many developing countries is questionable. The obvious "know-do gap" was recognized by the Mexico Ministerial Summit on Health Research in November 2004[6] and by the 58th World Health Assembly in May 2005 as a major obstacle to the attainment of the Millennium Development Goals.

Bridging the know-do gap is the foremost challenge and opportunity for public health in the 21st century. New initiatives and platforms to strengthen specific aspects of the health systems such as health information systems, human resources, and equitable access and coverage have emerged. Knowledge and its links to action is another platform for health system strengthening.

Evidence and knowledge for problem-solving

There is widespread agreement that policy and practice should be informed by the best available evidence that is applicable in a given setting. However, there is debate on what constitutes evidence and how to harness it in practice, and whether it is sufficient to bring about sustainable change in complex social settings. The goal of traditional researchers, conditioned by funding and tenure systems, is often to get published in a respected medical journal – assuming their findings will be translated into practice by somebody else at some point. In addition, learning about effective development projects taking place in poor countries is sometimes hindered by the lack of general knowledge of what works and how[8]. A shift from "moving" evidence to solving problems is overdue.

The contribution of knowledge to health gains has been dominated by consideration of benefits of science and technology, neglecting to exploit and use other valid sources of knowledge: knowledge from practice and the sharing and replication of people's experience. The tacit dimension of knowledge, the social context of knowledge, and the various knowledge-creating mechanisms in practice are gaining importance, paradoxically, following the ICT revolution which mainly handles increasing volumes of disembodied explicit (i.e. codified) information[9]. A strategic approach to creating and promoting evidence from practice in priority areas should contribute to bridging the know-do gap.

Knowledge has been recognized by economists as the most important factor of production in the new economy. A knowledge economy (including health sector) is "one in which the generation and exploitation of knowledge has come to play a predominant part in the creation of wealth. It is not simply about pushing back the frontiers of knowledge; it is also about the more effective use and exploitation of all types of knowledge"[10].

The golden era of modern research, which started after the Second World War, was a period in which research findings outside strategic government projects were published[11] and *passive diffusion* followed. The 1970s saw the birth of *evidence-based medicine* which took a push strategy with both active dissemination of practice guidelines and education for their local interpretation and adaptation; *technology assessment* also emerged at a time when private industry took over most *product* R&D. Conceptual frameworks derived from the social theory of *diffusion of innovation* at the time included *Research Transfer* and *Research Utilization*; the private sector developed *value chain models*, and *marketing strategies*. The success of evidence-based medicine, however, plateaued in the 1990s and the new millennium dawned with fresh thinking on this old frontier. In Canada, for example, institutions were reorganized or created, crafting the term *Knowledge Translation* and emphasizing *linkage and exchange models*[12].

Some plausible causes of the know-do gap	Some ongoing efforts to address the causes
Limited access to information, technology and medicines (digital divide, intellectual property rights, patents)	Medline, Health InterNetwork Access to Research Initiative (HINARI), Health information network (HifNet), Iowa University, Global Health Library, specialized libraries & portals (Maternal and Child Health (MCH), AIDS), Google scholar, virtual health libraries and other country initiatives, Digital Solidarity Fund
Ignorance of evidence-based problem-solving and learning approaches in health (including lack of learning from development projects due to structure of aid process)	International Network of Clinical Epidemiology (INCLEN), Cochrane collaboration, Cambell collaboration, UK NICE, guidelines and courses by professional associations, Health Evidence Network, EVIPNETs, etc.
Lack of need-driven research, particularly in developing countries	National Institutes of Health (country priorities), Council on Health Research for Development (COHRED), Global Forum for Health Research, WHO Special Programme on Research and Tropical Diseases (TDR), specialized initiatives, including new Public-Private Partnerships in Research & Development for diseases of poverty
Lack of ownership of knowledge by potential "users"/"adopters"	Successful immunization campaigns, tobacco-free inititatives, social entrepreneurship, knowledge brokering (Canada, Netherlands)
Lack of creation/exploitation of knowledge from practice (evaluation, continuous improvement)	Institute for Health Care Improvement (IHI), Bangladesh Rehabilitation Assistance Committee (BRAC), Management Sciences for Health (MSH), Tanzania Essential Health Interventions Project (TEHIP)
Slow diffusion of innovation or scale up	Strategic advocacy (Médecins Sans Frontières), social marketing (Greenstar-Pakistan-based social marketing organization), social entrepreneurship (BRAC, Ashoka Fellows)

Table 1: Some causes of the know-do gap and ongoing efforts to address them

Frequent sources of knowledge	Layers for knowledge-based activities in health	Select mechanisms or "schools" for KT
✣ Scientific and informal research (new or not) ✣ Surveillance systems ✣ Project monitoring and evaluation ✣ Practical experience ✣ Historical or news facts ✣ Others	✣ Policy work ✣ Institutional management ✣ Technology/R&D ✣ Clinical service provision ✣ Community enterprises ✣ Individual behaviour (healthy lifestyle, adherence) ✣ Others	✣ Utilization research ✣ Operational & action research ✣ Evidence-based guidelines ✣ Knowledge brokers, sages ✣ Implementation science ✣ Strategic planning & management ✣ Continuous improvement ✣ Social entrepreneurship

Table 2: Frequent sources and types of knowledge and select mechanisms for KT

Knowledge Translation

The importance of Knowledge Translation (KT) is its potential to bridge the know-do gap, the gap between what is known and what gets done in practice. This gap between knowledge and its application is not new, but today systematic approaches to address it are urgently needed[13].

KT is being developed at a time when unprecedented global investments in health research have generated a vast pool of knowledge that is underused and not translated rapidly enough into new or improved health policies, products, services and outcomes. KT comes at a time where the gap between what is known and what gets done (*the know-do gap*) is highlighted by shortfalls in equity (e.g. Millennium Development Goals) and quality (e.g. patient safety movement) in health services[14]. However, we witness a limited interpretation of KT as a linear transaction between research "producers" and "users" trading knowledge as a commodity. Knowledge can be created without science and KT *is not* research; it moves from responding to curiosity to focusing on purpose and problem-solving. It is defined as "the synthesis, exchange and application of knowledge by relevant stakeholders to accelerate the benefits of global and local innovation in strengthening health systems and improving people's health"[15]. More concretely, KT is about creating, transferring and transforming knowledge from one social or organizational unit to another in a value-creating chain – a complex interactive process that depends on human beings and their context.

Knowledge Translation is a cross-cutting, non-linear process that involves not only recent research findings but also knowledge that is created from the dynamic interaction of people who come together to solve public health problems, to learn and ultimately to drive productive change. Attention should be given to the knowledge itself, but even more so to the purpose, people and processes involved. The processes from knowledge generation to application are complex and influenced by factors including local context (where practice takes place), and the perceived relevance of knowledge that is enhanced when owned by relevant stakeholders.

Translating knowledge into new or improved health policies, services and outcomes requires a clear understanding of the characteristics of this process, the ways it can be used, the conditions governing it, and criteria to assess its impact.

When addressing issues related to KT, technical experts have the inclination to depend almost exclusively on encoded

knowledge – the "know what". The realm of biotechnology researchers and evidence-based medicine is dominated by the intensive use of encoded knowledge. By comparison, practitioners in the health professions, policy-makers and managers of health service organizations rely on the use of complementary types of knowledge in a context where encoded research knowledge does not usually dominate. We acknowledge that scientifically generated knowledge enjoys the highest degree of generalizability and potential for radical innovations[16], however, some phenomena do not lend themselves well to systematic research.

The lesson to derive from the examination of the types of knowledge is that sound decisions and sound professional practices must be based on multiple types and pieces of knowledge that bring complementary contributions to problem-solving in a progressive, Bayesian way[17]. Various sources of knowledge, besides that from research, are needed by various users who range from policy-makers, to practitioners, to managers and communities. The processes from generation to utilization of knowledge (value chains) is therefore dependent on the purpose and on who the stakeholders might be.

Different types of knowledge are especially important to perform a particular task and solve problems and manage change in unique, complex or uncertain circumstances.

Moving from KT conceptual framework to the knowledge value chain

Knowledge should be used as a resource adding value into the activities undertaken in the production and delivery processes of health service organizations. In the management literature, this idea of value creation is often approached through the concept of knowledge value chain (KVC) from strategic planning to implementation.

From an organizational perspective, the KVC is the set of knowledge creating activities to move from concept up to the production of new or improved products and services delivering added value for clients. While some variation is expected for different problems or settings, we propose that the knowledge value chain consists of five activities interrelated by multiple feedback loops from knowledge exploration to exploitation: acquisition, creation, sharing/dissemination, utilization/application, and performance assessment/innovations[18]. In turn, each activity is supported by specific tools and specific tactics. The mission, vision, goals and strategies of an organization or social enterprise drive the KVC. The higher the knowledge performance related to acquisition, creation, sharing, and use, the higher the value generated for key stakeholders along the value chain. Value is created by managing interactions between the strategic, operational and tactical levels of the KVC as well as between the different activities of the KVC. This dynamic process generates feedback loops that amplify or attenuate the knowledge conversion flows depending on key drivers (motivation and incentives) and local context and larger historical forces.

Value chains start and end with a purpose, to solve a problem and create value through the delivery of key services and products by orchestrating and navigating social and organizational processes involving motivation, strategy and incentives. The research to policy value chain (transfer-exchange-utilization) is complex but there is some experimentation. Diffusion of innovation in clinical practice is well established although there is room for improvement. The pharmaceutical R&D value chain is one of the most evolved and one to learn from. Community interventions, on the other hand, require major development. Paradoxically, this is the area where private sector has valuable experience in marketing a product or service. Nonprofit, social entrepreneurship thus has lots of potential where government services and market alone fall short.

Research needs

Knowledge Translation has the potential to bridge the know-do gap. The field is a growing one with scarce literature, although a new journal of implementation science has been launched recently. WHO, countries and the global community could be further engaged in efforts to address the know-do gap through research on KT. There is yet no agreed conceptual framework and a lack of a general learning platform to develop and spread good practices. Funding systems are not supportive and evaluation and accountability systems are not aligned.

The following are among the research topics/questions that will contribute to development of KT.

- Evidence on impact of evidence-based approaches.
- Evidence on impact of interactive approaches, including demand-driven models.
- Increase general knowledge of what works and how – what key factors contribute to success stories (a forthcoming issue of the Bulletin is devoted to KT and should contribute to this issue).
- Increase understanding of the processes, including diffusion of innovation from knowledge generation to its application-value chains.
- National and global assessments of the knowledge enterprise for health.

There is no clear picture of the knowledge systems in health in countries, and thus, a global assessment of knowledge for health is needed in order to landscape the state of KT in countries and the international space. Such assessment could highlight the importance of KT in countries, identify and engage new partners, identify needs and priorities for action in Member States, draw comparative lessons and derive best practices, and inform a baseline to monitor impact and progress over time. ❑

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Research resources

Research impact on equitable access in health: the Cuban experience

Article by Gustavo Kourí (pictured), María G Guzmán, José Luis Pelegrino, Alicia Reyes, Luis Estruch and Niviola Cabrera

Before 1959, medical sciences in Cuba[1,2] were weak, dispersed and with a low budget. However, even without official support some scientists were able to make important contributions of international relevance. In the 19th Century, Tomás Romay (1804), the father of Cuban vaccinology, introduced the smallpox vaccination and Carlos J Finlay (1879) described the transmission of Yellow Fever by the mosquito Aedes aegypti. Later, during the first half of the 20th Century, Juan Guiteras worked on the control of infectious diseases and Pedro Kourí the father of Cuban parasitology made original contributions in this field[3,4,5].

At the global level, Cuba was the first country that established a Ministry of Sanitation (1909)[6]. In spite of this, the health picture of the country before 1959 was characterized by high infant mortality (40 per 1000 live births)[7]. Life expectancy at birth was less than 60 years and the public health picture was characterized by tetanus, diphtheria, poliomyelitis, measles and tuberculosis, among other diseases. The issues of health and illiteracy were predominant in the 1950s. In this period, Cuba's health resources included only one medical school, two scientific institutes (the Institute of Hygiene and the Institute of Tropical Medicine), 6000 medical doctors distributed in the capital and the main cities, and very few public and some private hospitals.

A new social system was established in 1959, wherein health and education were considered human rights. In order to change the serious health picture, a new conception of the health system was developed, oriented to prevention and to an appropriate application of advances in science and technology on the basis of accessibility and universally free access for the whole population. Improvement of education at all levels (currently the lowest educational level is nine years) and scientific development are two fundamental and determinant factors for health development.

Scientific and technological development in the period 1959–2007

As early as 1960 human resources and scientific and professional development were recognized as a main priority. Under the umbrella of the Cuban Academy of Sciences, scientific organization started in 1962. Also in the 1960s, the first medical scientific institutions were founded in order to respond to the main health challenges. Eight research institutes, all under the Ministry of Health, commenced investigations in the fields of cardiology, oncology, gastroenterology, endocrinology, angiology, haematology, labour medicine and human nutrition. In 1965, the Centro Nacional de Investigaciones Cientificas (CNIC) was founded as part of Havana University and constituted the "mother institution" of most of the scientific centres in the fields of biomedicine and biotechnology.

The creation of the "*Frente Biologico*" early in the 1980s represented a further step in the development of Cuban biomedical sciences. This organization hosted the main scientific personalities and institutions, creating the basis for the development of the biotechnology and the pharmaceutical industries.

The "*Polo Científico*" or "Scientific Pole" was founded in 1991–1992 with the aim of coordinating integrated efforts for the overall scientific development of the country. Biomedical, veterinary, agropecuarian institutions, industry and the universities among others are part of the Scientific Pole that is coordinated and directed by the Office of the Secretary of the State Council. The Direction of Science and Technology at the Ministry of Health, created in the 1970s, maintains a very close interaction with the institutions of the Scientific Pole.

Supporting the organization and management of the scientific activities of the country, the Ministry of Science and Technology (CITMA) was created in 1994. Several national programmes were developed to respond to the main economic and social problems of the country.

Currently, Cuba hosts 57 scientific institutions dedicated to health research. The Scientific Pole of the State Council, CITMA, the Cuban Academy of Sciences and the Ministry of Health interact to solve the main health problems of the country through conducting national and ministerial programmes of investigation. Cuban science is characterized by collaboration and the integration of different scientific institutions, with some doing R&D activities and others applying results in a "closed cycle" strategy from research to post-marketing follow-up, where the integration and functioning of all scientific centres has as a main objective the application of scientific results to benefit the health of the Cuban population.

implemented on a small scale with substantial managerial and technical support, but may be less effective if implemented country-wide with relatively less support.

Combining systematic review evidence with other types of information – frequently policy-makers draw upon a range of different types of evidence. For example, a systematic review of effects might be complemented with cost-effectiveness analysis, or modelling data. Policy-makers will also wish to consider the political and social acceptability of the intervention or policy being considered, and probably also the equity implications. Questions such as these might require separate primary data collection research. In health technology assessment, evidence on the effectiveness of the technology is typically combined not only with cost-effectiveness analysis but also with consideration of legal, ethical, psychological and social implications[8]. Policy-makers need to consider carefully how best to combine these different forms of evidence.

Discussion and conclusions

Systematic reviews have great potential to play a key role in informing policy and decision-making regarding health systems. As systematic reviews have become the gold standard for clinical decision making, we should also strive to ensure that they are routinely used as an input into policy-making, acknowledging that other factors, including political issues, will also influence policy. In particular, systematic reviews can be helpful in identifying possible negative effects associated with a particular reform, so that such possible effects can be monitored.

The systematic reviews of health systems issues undertaken to-date are of considerable utility, but we need more impact evaluations to feed into reviews, more reviews, and more methodological development to make systematic reviews of even greater use to policy and decision-makers. In particular methodological development is needed to learn how best to synthesize research that explores the effects of complex packages of interventions, and to synthesize evidence regarding processes such as policy and implementation processes.

Given the complexity of health systems, considerable work is involved in assessing the relevance and applicability of international systematic reviews to policy questions being made in a particular setting. Moreover, systematic reviews themselves are often complex, and require some training in terms of how to assess and interpret them. In light of this it seems unrealistic that senior policy-makers will themselves employ systematic reviews directly in decision-making. Instead skilled knowledge brokers and analysts are needed who can help contextualize findings, and marry systematic review evidence with other types of evidence. To-date very limited attention has been paid to such functions within national health systems and much greater focus on these roles is needed.

Finally, systematic reviews are a useful reminder of how little we still know about effective health system strengthening interventions. When clear evidence regarding the effectiveness of a particular policy or intervention is lacking, it is important that policy change is accompanied by monitoring and evaluation both to avoid possible harms, but also to contribute to the knowledge base. Systematic reviews can also be extremely helpful in terms of providing guidance regarding appropriate study design for such primary research.

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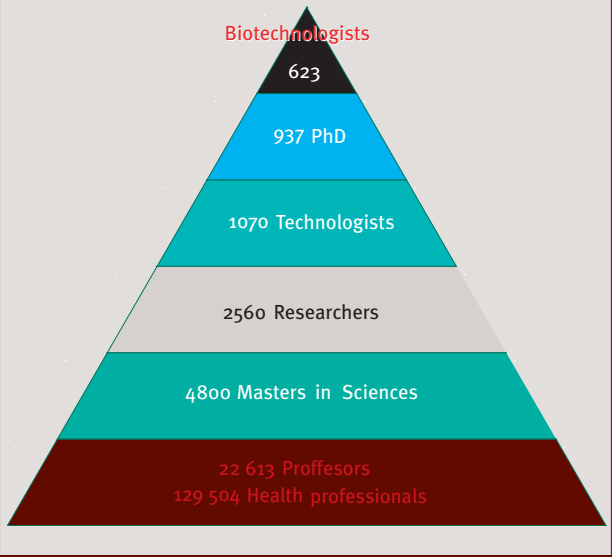


Figure 1: Health research workers

Since 1959, human capacity building was considered as the most relevant factor for the development of the country, with a direct impact on health development. The literacy campaign performed in 1961–1962 allowed the country to be declared free of illiteracy. The improvement in the educational level of the population in the following years and the high number of technicians, professionals and scientists are expression of this development. In this context, the number of medical doctors, scientists and technicians working in the biomedical branch is noteworthy (Figure 1).

At present, the country has four medical universities including 21 faculties of medicine, four of stomatology, four of nursing, four of health technology and one Latin-American Medicine School with 12 000 students from 28 countries of the world. In addition, Cuba has 248 hospitals, 498 policlinics and 14 078 medical posts. The medical and non-medical higher educational institutions are the main source of biomedical scientists. Pre-graduate students are selected and enrolled in scientific institutions providing an early association to research, with training and postgraduate studies in and outside of the country. In total, the scientific health human resource represents a high percentage of Cuban workers.

Another expression of Cuban biomedical development in the period of 1959–2007 is the number of patents and of scientific publications in high impact journals. A trend of increasing patent numbers has been observed, with 156 patents granted in Cuba and 66 abroad, and more than 650 patent applications in the biotechnological field alone.

Health research impact in the period 1959–2007

During this period of more than 40 years, the direct relationship between scientific development and improvement of the health system positively influenced the health indices of the population. In spite of being a poor country with a low Gross National Income per capita, Cuba shows health indices similar to those of developed countries[8,9].

Excluding influenza and pneumonia, infectious disease represents 1.1% of the total mortality. Infant mortality in 2006 was 5.3 per 1000 live births, showing an 11-fold reduction from the figure reported in 1959

For example, the first five main causes of death are similar to those of high-income countries: cardiovascular disorders, cancer, cerebrovascular illness, influenza and pneumonia and accidents. Excluding influenza and pneumonia, infectious disease represents 1.1% of the total mortality[8]. Infant mortality in 2006 was 5.3 per 1000 live births, showing an 11-fold reduction from the figure reported in 1959 (Figure 2). Life expectancy at birth increased from 60 years in 1959 to 77 years (75.1 for males and 78.97 for females) in 2006.

Cuba's immunization programme covers 13 diseases. Several infectious diseases such as poliomyelitis (1962)[10] and malaria (1967) were eradicated and tetanus neonatorum (1972), diphtheria (1979), measles (1993), rubella (1995) and mumps (1995) have been eliminated. Others such as tetanus, meningitis by *Haemophilus influenzae* type b, leprosy, meningococcal meningitis and hepatitis B, are no longer health problems. Table 1 shows the Cuban vaccination schedule.

With the main aim of solving domestic problems, but also to collaborate with other poor countries, biomedical and biotechnological research, which is fully supported by the government, is organized in programmes. At national level, 91 projects are included in the lines of vaccine, cancer and drug development. Currently, more than 1500 research projects are in progress at the ministerial level.

Some of the main scientific results with a crucial impact in health have been those related to the vaccine investigations. The Cuban vaccine against *meningococcus* B[11,12] (considered at global level the first effective vaccine against this microorganism), the recombinant hepatitis B vaccine produced in *Pichia pastoris*[13,14,15] and the *Haemophilus influenzae* type b vaccine[16,17,18] (the first one obtained by chemical synthesis) constitute good examples. These vaccines, already introduced in the Cuban immunization programme, have had a strong impact in the control and elimination of these three diseases as health problems in the country. Figures 3 and 4 show the reduction in the number of cases of hepatitis by hepatitis B and meningitis by *Haemophilus influenzae* type b.

In order to reduce the number of immunizations, a pentavalent vaccine (only produced in France and Cuba) combining diphtheria, tetanus, cellular pertussis, hepatitis B and *Haemophilus influenzae* type b vaccines was formulated and clinical trials were developed. This new combined vaccine was introduced in the national immunization programme in 2006. Table 2 shows the registered vaccines and those under development and research.

At advanced stages of research are the vaccines against cholera, HIV/AIDS, HCV and dengue. An attenuated vaccine against cholera, based on the deletion of the cassette of genes coding for the toxicity induced a low reactogenicity and high

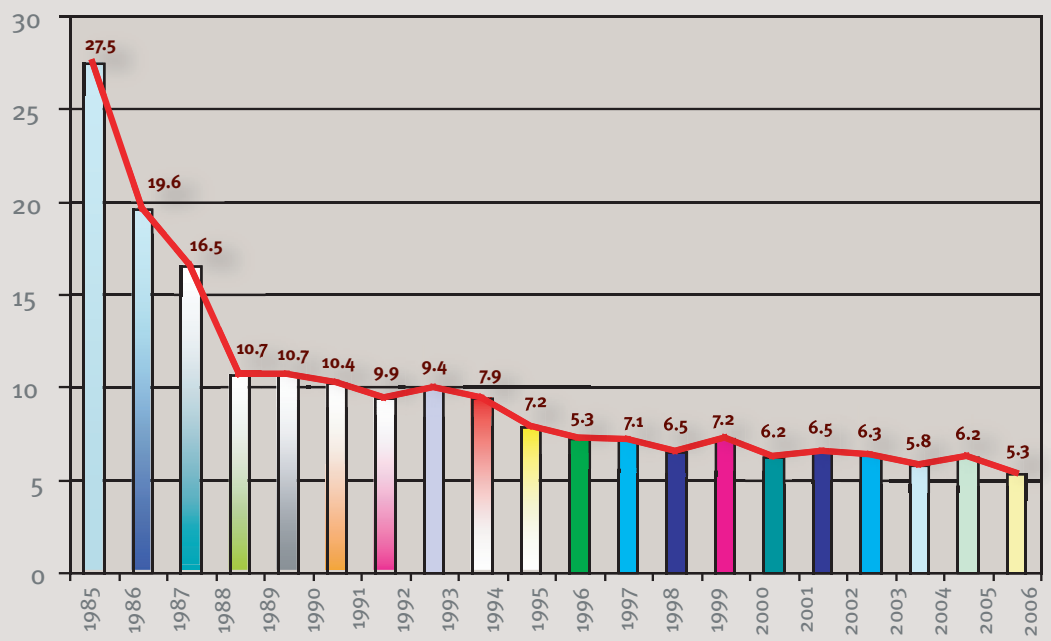


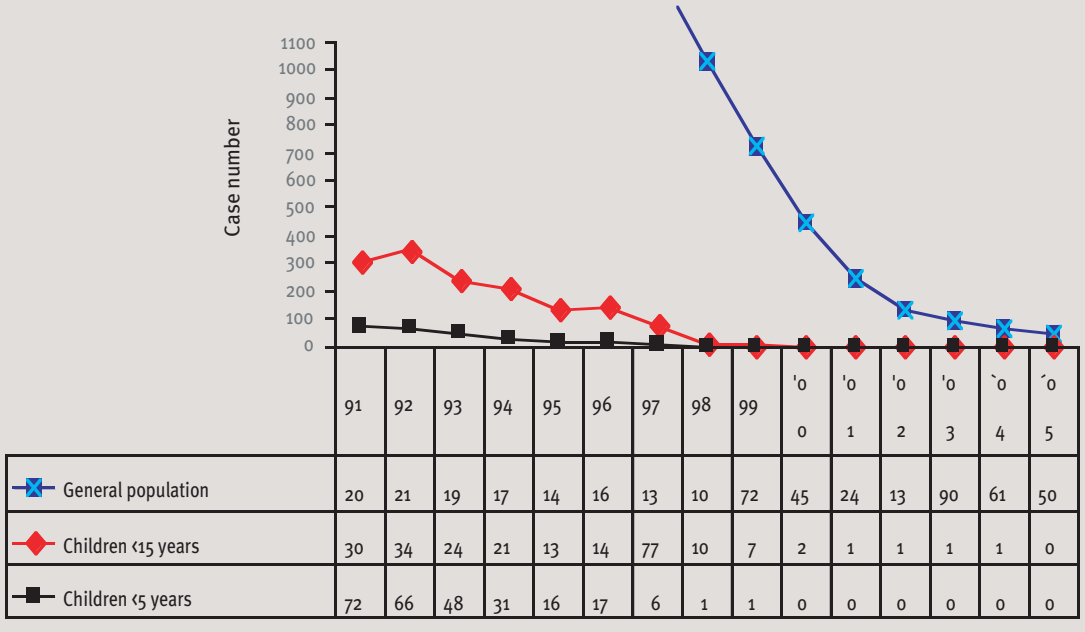
Figure 2: Infant mortality per 1000 live births, 1975–2006

immunogenicity in the Phase I trial. At present, this vaccine is in a Phase IV clinical trial in an African endemic country. The therapeutic vaccine for HIV/AIDS and the recombinant dengue vaccine, this last based on the domain III of the envelope of the virus, have shown good preliminary results in preclinical studies[19,20].

Research directed to drug development has been of great importance. Some of the most representative examples are the production of PPG (policosanol)[21], a product with an anticholesterol activity and recombinant streptokinase, which is useful in the early treatment of acute myocardial infarct (AMI). Since 1992 to 2003, more than 35 000 patients with AMI have been treated with recombinant streptokinase with a 28% reduction of mortality[22]. Citoprot-P is a novel drug for the treatment of the feet of diabetics, avoiding amputation.

Bioequivalence studies performed on Cuban generic antiretroviral drugs support the high quality of these products. The introduction of these drugs in the treatment of AIDS patients has positively impacted on their survival and life quality.[23]

Interferon – initially natural and later recombinant – applied to the treatment of viral and tumour diseases probably constituted the first products for human use produced by the incipient Cuban pharmaceutical industry during the 1980s.



	91	92	93	94	95	96	97	98	99	'00	'01	'02	'03	`04	´05
General population	20	21	19	17	14	16	13	10	72	45	24	13	90	61	50
Children <15 years	30	34	24	21	13	14	77	10	7	2	1	1	1	1	0
Children <5 years	72	66	48	31	16	17	6	1	1	0	0	0	0	0	0

Figure 3: Number of cases of hepatitis B in the period 1991–2005

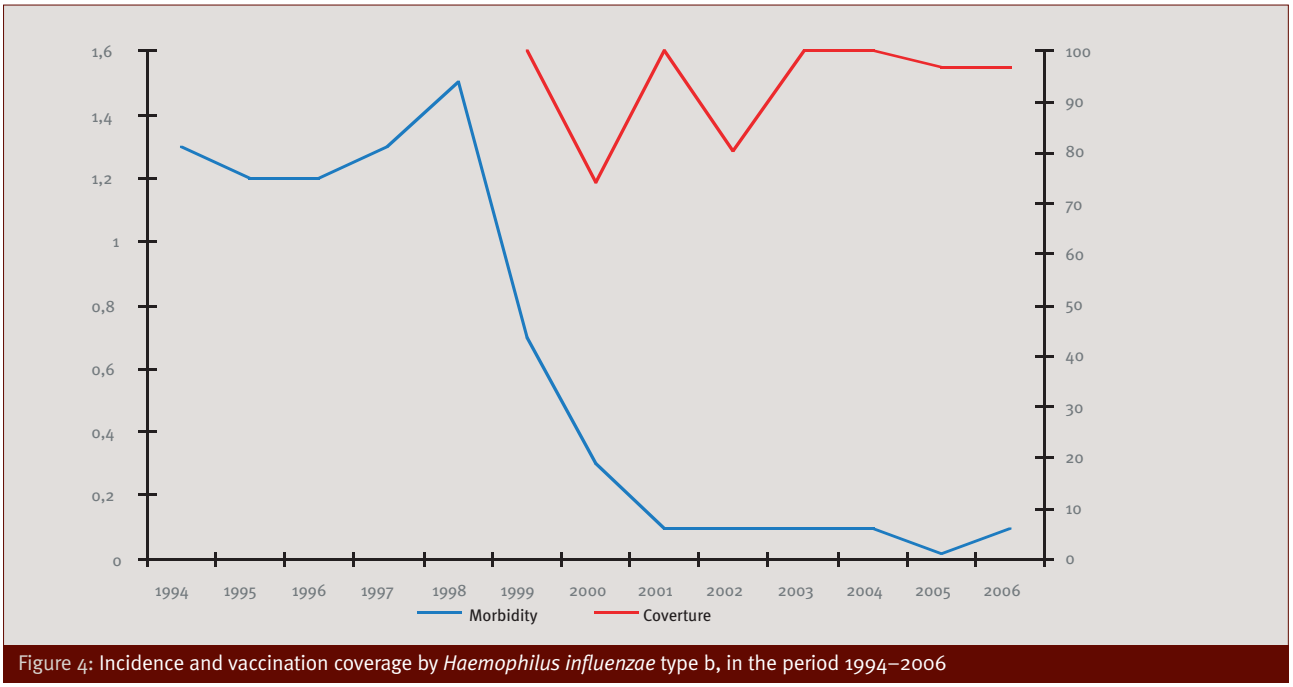


Figure 4: Incidence and vaccination coverage by *Haemophilus influenzae* type b, in the period 1994–2006

Scientific research in this field has enabled the country to become currently self-sufficient, with the production of 527 drugs including the antiretroviral, anticancer and immunosupressive drugs supporting the national programmes of HIV/AIDS, control of cancer and organ transplantation. Monoclonal antibodies, of wide application in nephrology and oncology, human transference factor and growth factor used in the treatment of cancer, proctitis and ulcers, and Surfacen for the treatment of respiratory distress of newborn are also included in the range of Cuban products.

UltramicroELISA, a Cuban diagnostic technology for neonatal and infectious disease screening, is widely used in the country, supporting the epidemiological surveillance of several infectious diseases such as dengue, HIV, HBV and HCV and the screening in all pregnant women of neonatal disorders such as congenital hypothyroidism, phenylketonuria, galactosemia and other malformations. In the period 1982 to 2006, more than 3 million pregnant women were screened and 6748 congenital malformations were detected[24]. Also, more than 2.7 million (100%) of newborns were studied, detecting 731 with congenital hypothyroidism. These children were treated early, avoiding cretinism. UltramicroELISA has also been fundamental for the blood certification programme.

A relatively recent national investigation allowed screening of all individuals with some disability. The physical and psychological characteristics of these persons and the contributing factors for intellectual or mental disability were determined. In the Medical Genetic services, extended to all provinces of the country as part of the National Programme of Attention to Persons with Some Disability and the programme of Medical Genetics, 29 genetic pathologies and more than 50 metabolic disorders are diagnosed. Several investigations relative to schizophrenia and Alzheimer disease, among others, are under way.

The development of advanced technology medical equipment, such as NEURONICA, MEDICID and EL AUDIX among others, supports the neurological services across the country and represents another line of health research. Of particular interest is the employment of EL AUDIX to the screening of hypoacusia in children and risk groups.

Investigations responding to global problems is also one of the priorities of Cuban biomedical science. Taking into account that Cuba was the first country to eradicate

BCG	Newborn
HB	Newborn
DTwP - HB + Hib	2, 4 & 6 months
AM-BC	3 & 5 month
MMR	1 & 6 years
DTwP	18 months
Hib	18 months
DT	6 years
AT(Vi)	10, 13 & 16 years
TT	14 years
OPV (campaign)	<1, 1, 2 & 9 years

Table 1: Cuban immunization programme

RESEARCH (22)	DEVELOPMENT (13)	PRODUCTION (11)
Cholera	Cholera attenuated	VA-MENGOC- BC
Tuberculosis	DT, dT y t	vax-TET
Adjuvant	(reduced doses)	vax-TyVi
N. meningitides B	Poli ACYW135	vax-SPIRAL
Malaria	Poli AC	DTP
Leishmania	dT - Poli Vi	DT
Shiguella-Salmonella	BCG intra vesical	IFAs
Leptospira	VA-MENGOC- BC®	HB preventive
Pertussis acellular	reduced aluminum	recombinant
Pseudomonas	VME as product	Hib
Animal models	Cholera inactivated	TRIVAC DPT + HB
Monoclonal antibodies	Adjuvant Cocleato	Pentavalent DPT + HB + Hib
HIV/AIDS	Neumococo	
Dengue	HC therapeutic	
8 Cancer vaccines	HB therapeutic	

Table 2: Registered vaccines, in development, in research and in clinical trials

poliomyelitis and given the particular success of the Cuban vaccination strategy, several investigations supporting global polio eradication have been conducted in our country at the request of the World Health Organization (WHO) and the Pan American Health Organization (PAHO), allowing demonstration of the circulation-time of the vaccine viruses in the environment after the oral vaccination and the immunity of the inactivated vaccine. This new knowledge and the investigations in course will allow improved definition of the strategy for global polio vaccination after eradication[25]. New findings of global impact related to dengue hemorrhagic fever (DHF), have been reported by Cuban scientists. The confirmation of secondary infection as a risk factor for DHF, the influence of the interval between infections and the role of ethnicity and chronic diseases are only some examples[20].

Flexibility also characterizes Cuban science, allowing incorporation of new topics in the research agenda depending on the epidemiological national and international situation. The preparation of the country in terms of surveillance, diagnosis and research to face new global epidemics such as West Nile Fever, SARS and Avian Flu are recent examples.

Current research needs and agenda

At present, the Cuban population shows a very high health level with the Millennium Development Goals already accomplished[26,27,28]. However, the country is working to reach new goals, with an infant mortality ratio of less than five deaths per 1000 live births, life expectancy at birth of 80 years and quality of life improvement being the most important new targets. At this new stage, research occupies a leading place due to its direct impact on health development. To achieve these new goals, different investigations are under development, notable ones being active screening of risk groups and of the open population for diseases that are the major causes of mortality. These investigations will allow early detection of the illness in order to apply the appropriate treatment and management of patients, avoiding disability and death. Supporting this new strategy, the accessibility of the health system has increased by the introduction of advanced technology at the primary heath care level.

A totally different health picture is observed in many other poor countries. According to WHO, and as an example, Africa shows an infant mortality per 1000 live births of 100, a life expectancy at birth of 47 years for males and 49 for females, and HIV/AIDS and TB constitute major causes of mortality[29,30,31]. Due to this serious situation, a new agenda for research and the implementation of research findings is needed at the global level. In this sense, Cuba is developing a new model of regional and international cooperation in health, education and science. Currently, the country hosts 22 000 students from developing countries in its medical schools and more than 32 000 Cuban collaborators labour in more than 80 countries. From the 1960s, more than 132 000 health workers collaborated in 102 countries of the developing world. This model of collaboration is having a direct impact on strengthening human capacities, the development of scientific research and public health. ❑

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Nursing research: meeting today's health challenges – perspectives from the International Council of Nurses

Article by Judith A Oulton (pictured) and Patricia Caldwell

Today's health systems face an ever burgeoning number of challenges, ranging from health care reform to the demands of shifting demographics; the growing burden of chronic, noncommunicable diseases; emerging and re-emerging health problems; shrinking resources; and health workforce shortages. The quest for quality and cost-effective health care has brought evidence-based practice and nursing research to the forefront.

This article begins by briefly exploring nursing's contribution to health research. It highlights nursing research priorities and concludes with an overview on strengthening nursing's contribution to research and offering suggestions on the way forward from an international perspective.

Nursing's contribution to health research

Nursing research plays a major role in optimizing the health and welfare of individuals, families, communities and populations, and in reducing inequalities in health. Nursing research encompasses inquiry into all aspects, components, activities and phenomenon relating to health and of interest to nurses[1]. It covers all facets of health and disease, spanning from health promotion and illness prevention, to curative, rehabilitative and supportive care[2]. Nursing research examines the provision of care across all health settings including hospitals, long-term care facilities, workplaces, schools, community health centres, clinics, rehabilitation centres and homes[3]. The knowledge generated through nursing research provides the scientific basis and evidence that help shape nursing practice, enhance delivery models and systems, guide health service planning and policy, inform education and, most importantly, improve patient safety and quality of care.

Nurses are active in various aspects of research. They serve as principal investigators, project directors and co-principal investigators. As well they participate as advisory board and committee members on research projects and function as data collectors. Nurses may work independently, together with other nurses or in multidisciplinary research teams alongside other disciplines such as medicine and pharmacy. Increasingly, nurses are employed by the pharmaceutical industry to coordinate clinical trials evaluating new medications.

Box 1 provides a number of examples illustrating the varied expertise and contribution nurse researchers are making to nursing, health and health systems research.

Indeed, the past decade has witnessed an exponential growth in both the quantity and quality of nursing research. Its development has been influenced in part by the recognition of the importance of research to the profession and an expansion in the number of graduate and doctoral programmes available to nurses. A rise in the number of institutions funding, supporting and conducting nursing research has also been a good indicator of its growth and development. Examples of such organizations include the United States National Institute of Nursing Research; the International Center for HIV/AIDS Research and Clinical Training in Nursing; the Research Centre for Nursing and Midwifery Practice in Australia; the Canadian Health Services Research Foundation; the World Health Organization Collaborating Centres for Nursing Research and Development; and the Working Group of European Nurse Researchers. Also noteworthy is a steady increase in the number of high-quality journals and text books devoted to nursing research and the growth in scientific events at national, regional and international levels. In addition, more countries have begun developing and adopting national research plans for nursing, such is the case in Ireland and Denmark[14,15].

Nursing research priorities

The International Council of Nurses' (ICN) position with respect to nursing research is embodied in the 1987 statement on the organization's role in research and considered equally relevant today:

"ICN is convinced of the importance of nursing research as a major contribution to meeting the health and welfare needs of people. The continuous and rapid scientific developments in a changing world highlight the need for research as a means of identifying new knowledge, improving professional education and practice, and effectively utilizing resources [….] ICN believes that nursing research should be socially relevant. It should look to the future while drawing on the

- A group of nurse researchers in southern Africa have begun a five-year, multi-national study on HIV/AIDS and stigma. Stigma related to HIV/AIDS continues to have a significant impact on people living with and affected by the disease, as well as on their health-care providers[4].
- Nurse scientists report success of a culturally-specific HIV risk reduction programme aimed at reducing risky sexual behaviour among Hispanic youths[5].
- Nurse researchers in the United Kingdom have uncovered hidden early symptoms of lung cancer. The research is contributing to early detection and management of the disease.
- Nurse anaesthetists have recently discovered a faster way to treat Malignant Hyperthermia, a deadly metabolic muscle disorder[7].
- A team of nurse scientists from Canada are leading a government funded study on near misses and nursing's contribution to patient safety.
- Nurse researchers in Botswana are examining the extent of nurse migration and its impact on health services and the nursing profession. The outcomes will be used to develop recommendations and strategies to inform policy-making[8].
- Nurse researcher Dr Kate Lorig and her team have been instrumental in developing and testing a model of chronic disease self-management which has been adopted by a number of countries throughout the world[9].
- Nurse-led research out of the United Kingdom has found that interventions undertaken by a diabetes nurse specialist result in fewer prescribing errors and reduced length of stay for hospital patients with diabetes[10].
- Interdisciplinary teams involving nurse scholars and researchers from other disciplines are investigating the link between nurses' contributions and the safety and quality of patient care as part of the Interdisciplinary Nursing Quality Research Initiative[11].
- Dr Linda Aiken and colleagues published a landmark study linking higher nurse staffing levels to lower patient mortality and increased patient satisfaction. The results are being used internationally to advocate for safe nurse staffing levels and patient safety[12].
- A nurse researcher has developed an instrument (the Braden Scale) to aid health care workers in assessing patient risk for pressure sores. The tool is widely used in health facilities throughout the world[13].

Box 1: Examples of contributions by nurse researchers to nursing, health and health systems research

past and being concerned with the present [...] Research should comply with accepted ethical standards".

ICN has identified nursing research priorities in two broad areas: (1) health and illness and, (2) delivery of care services[17]. The Council views gender equality and poverty as important cross-cutting issues.

Health and illness

Nursing research in health and illness focuses on a number of areas including health promotion, prevention of illness, control of symptoms, living with chronic conditions and enhancing quality of life; caring for patients experiencing changes in their health and illness; assessing and monitoring patient problems; providing and testing nursing care interventions and measuring the outcomes of care. The recommended nursing research priorities relating to health and illness include issues such as HIV/AIDS and other sexually transmitted infections, chronic illness, infection control, women's health and mental health[18].

Delivery of care services

Nursing research priorities in this area focus on quality and cost effectiveness of care, community-based care, nursing workforce and health care reform. Areas for nursing research include the impact of nursing interventions on patient outcomes, evidence-based nursing practice, primary health care, home-based care, quality of nurses' work life, retention, satisfaction with work, impact of reform on health policy, programme planning and evaluation, impact upon equity and access to nursing care and its effects on nursing, and the financing of health care[19].

The global emphasis on the United Nations Millennium Development Goals, international calls for health systems strengthening, the renewed focus on primary health and community-based care and mounting concerns about obesity and chronic, noncommunicable diseases all present important opportunities for the nursing research community in both industrialized and developing countries. Also significant to nursing are health policy and systems research and the testing of new models of care delivery, especially as governments and employers struggle with rising demand for services, issues of cost containment and the realities of rapidly shrinking pools of skilled health care workers[20]. Particular attention to innovative research in evolving areas of need such as chronic disease management, care of vulnerable groups, primary prevention, aged care and disaster preparedness is needed. These are all areas where the need for scientific knowledge is great and where nursing excels.

Strengthening nursing's contribution to health research

Nursing research has evolved significantly over the past decade and is now well established in most industrialized countries. However, its development lags behind in many developing countries. Nursing research in developing countries is largely underfunded and capacity for research is often weakened by a limited cadre of trained and skilled researchers, poor infrastructure and support, little or no access to basic technologies, inadequate opportunities for continuing education and training and few mentorship opportunities for new nurse researchers. Further, owing to limited financial resources, researchers have few opportunities to present and discuss their findings at national, regional and international levels.

Dissemination and utilization of research findings are also equally important challenges which resonate globally. Too frequently new knowledge and evidence lie unused. The need for effective strategies for research dissemination and

utilization are paramount to good decision-making at both the policy and practice level. Databases, marketing and networks are three such strategies. Increased access to the Internet, particularly in developing countries, will allow better sharing of information – both published and that underway. Marketing results in simple, easy to read and easy to apply packaging is also another means of advancing dissemination and uptake of findings[21]. For example, the ICN is launching a series of Fact Sheets that focus on Innovation, Evidence and Effectiveness which aim to inform the profession, public, politicians, policy-makers and others about nursing roles and outcomes. Networks linking nurse researchers and those interested in nursing research (e.g. the ICN Research Network and the Working Group of European Nurse Researchers) are also helping to bring synergy and stewardship to the profession's efforts.

There is a need for more national level structures that support/promote nursing research as an element of essential national research. Ensuring that reliable, sustainable funding is available and aligning research programmes with national health priorities are paramount. Stronger linkages among government, policy-makers, researchers, practitioners, employers, educational institutions and funding agencies are critical, as is the inclusion of nursing in broader policy level discussions and decisions about health-related research programmes.

The International Council of Nurses has long recognized research-based practice as a hallmark of professional nursing and maintains an ongoing commitment to supporting advancements in this area[22]. The Council works with the World Health Organization, nongovernmental organizations and others to ensure that the international nursing research agenda is visible and included in priority statements.

ICN works to enhance nursing research and research-based practice by:

- Facilitating and promoting the conduct, dissemination and utilization of research related to nursing, health and health care systems.
- Collaborating with national and international organizations to enhance nurses' contributions to nursing, health and health systems research.
- Promoting opportunities for nurses to disseminate research and publish in international journals such as the *International Nursing Review*.
- Supporting networks that link nurse researchers (e.g. the ICN Research Network http://www.icn.ch/resnet.htm).
- Providing opportunities for nurses from around the globe to exchange experiences and views on current issues and trends in nursing research (e.g. ICN Research Network meetings at ICN congresses and conferences).
- Encouraging member national nurses associations in their research-related capacity building.
- Promoting research in areas which have practical implications and improved outcomes for patients, and which are meaningful to nurses' daily practice.
- Providing global leadership in establishing ethical guidelines for nurses in the conduct, dissemination and utilization of research.
- Publishing comprehensive guidance (e.g. ICN Practical Guide for Nursing Research and Ethical Guidelines for Nursing Research).
- Maintaining position statements on nursing research and fact sheets.
- Lobbying for the inclusion of nurse researchers on appropriate research boards, and health-related international research bodies.

ICN is also supporting its member associations in their efforts to enhance nursing research, particularly through:

- Improving access to education which prepares nurses to conduct research, critically evaluate research outcomes, and promoting appropriate application of research findings to nursing practice.
- Lobbying for nursing research funding from public and private sources.

Concluding remarks

Globally, nurses are discovering new and improved ways of delivering care that are grounded in new knowledge and evidence derived through research[23]. Today nursing research is increasingly part of the curriculum of basic nursing education and students and staff are expected to incorporate research findings in their daily practice. Investing in nursing research and health research more generally makes good economic and social sense. The knowledge acquired through research is a public health good that helps find better ways of health promotion, disease prevention, treatment and rehabilitation as well as improved systems design, financing and functions[24]. This is assuredly the case with nursing research. ❑

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The need to develop research capacity

Article by Mary Ann D Lansang (pictured) and Rodolfo J Dennis

The need for health research capacity strengthening (RCS) is widely recognized as a major unmet need, particularly in low- and middle-income countries (LMICs)[1,2,3,4]. Despite revolutionary advances in health research, science and technology, health gains among the poor continue to lag far behind the pace of health improvement among the wealthy. RCS efforts, which have been largely uncoordinated and inadequately funded, have yet to make a significant impact on addressing the widening inequities in health and health human resources.

Recent global, regional and national developments have made the agenda of RCS all the more important and urgent. Moreover, new challenges for RCS have emerged as a result of these developments. In response, three international bodies – the Council on Health Research for Development (COHRED), the Global Forum for Health Research, and the Special Programme for Research and Training in Tropical Diseases (TDR) – agreed to collaborate, in order to support and to improve the performance of national health research systems, particularly in LMICs[5]. In this paper, we review recent developments and discuss the implications and opportunities for strategic action for strengthening research capacity.

Recent trends influencing health RCS

To determine the opportunities and strategies for RCS in the future, it is necessary to track new developments that are likely to affect RCS initiatives. Key developments have been selected from the following spheres of influence: the policy environment, the different research actors, major health problems, and the tools and competencies for health research.

Global health policy environment

There is strong convergence in the international community on the importance of strong health systems in achieving the goals of improved health and alleviating poverty. Likewise, the WHO Commission on Macroeconomics and Health, the countries resolving to achieve the UN Millennium Development Goals (MDGs), and the Global Fund to fight AIDS, Tuberculosis and Malaria have underscored the need for health research to support the goals of health and development. This was reiterated in November 2004 by delegates at the Ministerial Summit on Health Research and Forum 8 in Mexico City, even as they recognized the limited capacity in LMICs to tackle the research agenda for development[3,4].

Funds for health research

Resource flows for health research significantly increased from US$ 84.9 billion in 1998 to US$ 125.8 in 2003. However, it has been difficult to track how much of the global health research funds go to RCS. International health research (IHR) has been used as a proxy for RCS. This consists largely of official development assistance (ODA) to build and strengthen "health research for development" and has seen a moderate increase in funding from 1998 to 2001, with further increases projected until 2006, notably from the USA, UK, France, Italy and Germany[6].

In 2003, a notable research programme with a sizeable RCS component was launched by the European Commission: the European & Developing Countries Clinical Trials Partnership (EDCTP). This long-term programme has initially obligated a total of €600 million for 2003–2007 to develop new interventions against HIV/AIDS, malaria and TB, with the collaboration of European and African scientists. In recent years, the private not-for-profit sector, led by the Bill & Melinda Gates Foundation, has also increasingly caught the attention and imagination of health researchers with its targeted and high-stakes approach to selected IHR initiatives such as the Grand Challenges in Global Health and the Global HIV/AIDS Vaccine Enterprise.

The steady increases in funds for IHR are potential opportunities for RCS. However, since the bulk of the huge IHR grants are coursed through scientists and institutions from High-income countries (HICs), national health research systems and researchers in LMICs need to be strengthened to negotiate fairly and squarely throughout the research process.

Emerging public health problems

Infectious diseases, nutrition and child and maternal health continue to be major public health concerns in LMICs and among the poor in HICs. But epidemiological trends in LMICs warn against equally disastrous consequences in morbidity and mortality from cardiovascular diseases, diabetes mellitus and other chronic diseases.

The threat of pandemics from new and emerging diseases such as the severe acute respiratory syndrome (SARS) and avian influenza (AI), as well as widespread natural disasters has demanded the rapid development of global alert and response systems as well as basic and clinical research right at the core of these affected countries. Bioterrorism also has the potential to modify a country's research priorities and resources. Situations such as milk supplies and botulinum toxin, smallpox and self-infected terrorists, and release of aerosolized microbes in closed environments are new problems that need previously untaught tools and skills.

The growing burden of disease from injuries and violence as well as mental and neurological diseases must also be recognized. Likewise, cross-cutting issues of equity, particularly gender-related issues, and intersectoral concerns like environmental health and global warming, have grown in importance through the years.

All of the above developments require RCS, where scientists and public health officers will be asked to lead needs assessments, develop new tools and interventions and work with policy-makers. Without coordinated research and programmatic action, health systems and the health of the people in many LMICs are bound to deteriorate even further.

Brain drain

In 2005, the Joint Learning Initiative, a group of more than 100 scientists, called the world's attention to the dire crisis in the health workforce, especially in LMICs. The *World Health Report 2006: Working together for Health* also focused on the global human resources for health and proposed a 10-year action plan for addressing this challenge, both in the public and private sectors. Far less aired but also a significant problem is the chronic lack of skilled health researchers in many LMICs due to intra- and international migration.

Many of the root causes are similar to those of the general health workforce, such as the quest for state-of-the-art technologies, better socio-political conditions, and improved revenue and quality of life. Among researchers, the situation is compounded by the lack of a nationally coordinated career path for researchers and an enabling research environment.

It is critical for LMICs to achieve and sustain the minimum knowledge-based mass needed for creativity, credibility and innovation in health and development. The vigorous call to action for building and retaining the health workforce in LMICs must also include strategic action for RCS.

Recent research developments

New research streams and technologies require constant sharpening of research skills or developing new cadres of scientists, refining old methods or developing new research approaches, and arranging innovative partnerships. There are tremendous research challenges related to the attainment of the MDGs, the reduction of poverty, inequities and other social determinants of ill health, but insufficient numbers of trained professionals to carry out health policy and systems as well as health social science research. The attention to the "know – do" gap in recent years underscores the importance of considering other stakeholders as essential players in research formulation, implementation and translation to policy and action.

Without coordinated research and programmatic action, health systems and the health of the people in many LMICs are bound to deteriorate even further

The revolutions in science and technology – from information and communication technology, to genomics, proteomics and nanotechnology – present new opportunities for North–South and South–South research partnerships for improving access to much-needed drugs and tools. On the other hand, they pose dilemmas in the realm of research ethics, intellectual property and equity – all of which national health research systems must be prepared to confront.

The growing emphasis on performance-based funding, the need to track progress towards the MDGs and the complexities of decentralized reporting in devolved health systems agencies have necessitated a fresh look at health information systems and strengthened competencies at country levels to generate reliable and accurate health statistics. The explosion of information and knowledge has also generated global interest in knowledge management and the synthesis, dissemination and translation of the best available evidence for health policy and practice.

Globalization

This phenomenon is not new, but the rapid changes in science, communication and technology frontiers, new international trade and market regulations, macroeconomics and the environment have heightened the impact of globalization more than ever before. Overall, it has had a deleterious effect on health care systems in developing countries, affecting not only the migration of health human resources, but also the capacity to deal with emerging diseases, bioterrorism and biased health sector markets. LMICs need to build their capacity to define and pursue globalization-related research that can reduce inequities in health and knowledge capacities and that can strengthen regulatory policies. Only then can national health research systems derive maximum gain from the opportunities and threats from globalization[19,20].

Recent trends in RCS

The urgent and enormous need for research capacity to address the problems of LMICs and the poor has not gone unheeded. In addition to a number of existing and recently established initiatives that have RCS as a major strategic objective, there are numerous research initiatives that have RCS streams integrated into their respective activities. A panoramic view of capacity strengthening efforts and issues was recently published by the Global Forum for Health Research according to the following parameters:

- RCS levels: individual training, institutional development, organizational development, national health research systems, supranational health research bodies;

- Health research system functions: stewardship, financing, resource generation, production and utilization of research;
- Research process: managing the research agenda, producing evidence, promoting the use of evidence, utilizing evidence in policy, practice and action.

More recently, Nuyens made a review of useful and accessible resources on RCS, ranging from analytical documents, RCS tools, programmes and grants[22].

Of the above efforts, we highlight some recent RCS examples that specifically address developments described in the previous section. In line with developments in the global health policy environment, there have been three notable developments:

- The Global Forum for Health Research and TDR initiated collaboration in 2005 on RCS efforts that would improve the performance of national health research systems, especially in LMICs[5].
- The 60th World Health Assembly adopted a resolution on 23 May 2007 – WHO's roles and responsibilities in health research, including a major role in RCS[23].
- Strengthening of national health research systems: national efforts to consolidate research within countries and develop and implement strategic plans for NHRS. Some developing country efforts have been described in Forums 6–9, www.globalforumhealth.org and also at the COHRED website, www.cohred.org.

New RCS activities have been associated with recent mega-infusions of funds for health and health research. For example, the EDCTP has a substantial portfolio for capacity building in the areas of project management, clinical trials methodology, research ethics, and support for libraries, laboratories and information technology. These RCS activities, however, are focused on Africa in partnership with European institutions. Also worth mentioning is the Systemwide Effects of the Fund Research Network (SWEF). This is a collaborative research network of research organizations in the South and in the North that conducts country case studies to understand how the Global Fund grants and similarly large funds affect the broader health care systems of recipient countries[24]. Although the RCS thrust is not explicit, the implications of the SWEF studies are important for health systems strengthening of recipient countries, while harnessing skills for health systems research through learning in the context of these large and complex public health interventions.

Spurred by the unprecedented scale of philanthropies as well as the huge unmet needs for new drugs and tools and their cost-effective delivery to the poor, 80 or so public-private partnerships (PPPs) for health and health research have emerged over the years. With this changing landscape, the RCS response has also become increasingly collaborative and more focused on networks and partnerships, both North–South and South–South. The approach to RCS within these networks and PPPs has been largely pragmatic, i.e., on-the-job training, short courses and workshops, or fellowship and graduate degree programmes built into the research programmes. Many of these have focused on capacity for specific fields of interest like demographic health surveillance, health information systems, knowledge repositories, clinical trials of interventions for neglected diseases, basic and applied research on emerging infections, research ethics, research synthesis, health policy and systems research, equity research, product development and innovation, and leadership and management.

The vast opportunities for strengthening capacity through ICT have certainly been recognized in the health research field, although there is much room for growth. Internet communications and open access to research and evidence have been a big boon to researchers in LMICs despite the persistent digital divide. The Health InterNetwork Access to Research (HINARI), launched in 2000 by the United Nations and coordinated by WHO, has been a landmark undertaking now serving more than 1800 institutions in 113 eligible developing countries. There are other free or highly discounted initiatives for journal access such as the Programme for Enhancement of Research Information, Electronic Information for Libraries and the Ptolemy Project[25]. A related innovation for increased access to the scientific literature is Biomed Central, where original, peer-reviewed research articles are published online and are freely, immediately and permanently accessible[26]. The "next generation" Internet is seeing a growing number of middle-income countries joining Internet2, a consortium of academic partners, the technology industry and government, which enables high speed applications in various fields including the health sciences[27].

South-based virtual campuses for health education and research, such as the Virtual Campus for Public Health launched by PAHO/WHO and the University of Zimbabwe master's degree programme in clinical epidemiology offered to the African region, may be one answer to the rising need for expanding the health research human resources in LMICs. But large challenges remain. In addition to the digital divide, there are issues to resolve regarding adaptations to the virtual environment, language of instruction, cultural appropriateness, student motivation, faculty resources, and quality assessment and evaluation[28,29].

In terms of the long-haul process of institution building, much can be learned from the more systemic approaches to capacity building for science and technology. The Academy of Sciences for the Developing World (TWAS), the Millennium Science Initiative (MSI) and the InterAcademy Council (IAC) have all emphasized the role of universities and institutions in building scientific capacity for sustainable development[30,31,32]. Centres of excellence, as well as virtual networks of excellence, which are aligned to nationally determined S&T priorities, have been proposed and are being established in several LMICs. Interestingly, the MSI projects planned in Uganda, Cameroon, Botswana and Namibia include a biotechnology component for drugs and vaccines, while that in Tanzania focuses on instrumentation and ICT for its scientists.

Challenges for RCS

RCS needs have been laid out and discussed in previous

Changing environment	Examples of RSC needs
Global health policy environment	✣ Health policy and systems research ✣ Knowledge management systems
Emphasis on development of tools and interventions for high-burden diseases	✣ Surveillance and information management systems ✣ Product discovery and development ✣ Clinical and field trial design and methodology ✣ Economic analyses
Emerging public health problems and recent research developments	✣ Surveillance and global alert systems ✣ Research training on priority health problems identified by countries/regions ✣ Equity research ✣ Health policy and systems research ✣ Interdisciplinary research
Brain drain, globalization	✣ Centres of excellence and/or virtual centers of excellence ✣ Research financing and incentive systems ✣ Knowledge of regulatory issues and intellectual property rights
Others (cross-cutting)	✣ Leadership and management: e.g., priority setting, strategic planning, partnership development, community involvement, monitoring and evaluation ✣ ICT: equipment, access and know-how ✣ Research ethics ✣ Research synthesis ✣ Knowledge translation

Table 1: Specific RCS needs related to recent global health developments

publications[17, 21, 33] as well as in the annual fora of the Global Forum for Health Research. Broadly speaking, these relate to training and retention of human resources, the research environment, translation of evidence to policy and practice, and the management of the health research system. In relation to recent trends in the global health landscape, Table 1 outlines some specific RCS needs to be able to respond to these developments, ranging from training in strategic and implementation research to leadership and management skills. The needs have been so overwhelming that the research response has tended to be diffuse and patchy. The tipping point for RCS is unlikely to be reached without a consolidated strategy. This very much depends on the responsiveness of the health research systems in LMICs.

A number of countries have begun the process of re-engineering their health research systems. And yet, in spite of the clear evidence on the link of health research to development, strengthening of the NHRS has failed to figure strongly in national development plans and support from overseas development agencies. While the need for health systems research has been articulated strongly in connection with the MDGs, the very system that underpins the generation of sustainable research resources has failed to garner the same attention. The debates on RCS for basic vs. applied research, health systems research vs. innovation, SARS/AI/HIV/TB/malaria vs. non communicable diseases are all symptomatic of the "silo syndrome" in health research, aggravated by the "Willy Sutton Law"[34].

Reference has been made to the UNAIDS "three ones" principle of "one action framework, one coordinating authority and one monitoring and evaluation system" as a model for effective RCS at the national level[21]. More specifically, a unified framework and strategy for health research for national development, in response to the changing landscape at the national, regional and global levels, needs to be carved out, advocated and vigorously implemented by each country.

At the global level, recent moves to consolidate and innovate on RCS efforts to strengthen NHRSs are encouraging. However, if this collaborative enterprise is to have a significant impact on health research systems for development, it is equally essential to have wide, deep and long-term political and financial commitments from national and international stakeholders towards a common vision and strategic plan for "research for development". ❑

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Partnerships offer promise in developing systemic methods of male fertility regulation

Article by Kirsten M Vogelsong (pictured), Henry L Gabelnick and Eberhard Nieschlag

In response to the Programme of Action approved by 179 countries at the International Conference on Population and Development (ICPD) held in Cairo in 1994, an increasing emphasis is being placed on free reproductive choice, gender equity and greater male participation in sexual and reproductive health and family planning programmes worldwide. One means by which to promote partnerships with men in family planning is through increasing options by the development of safe, effective and acceptable methods of contraception for men to use.

Men around the world, in a variety of countries and settings, are aware of the existence and use of methods of family planning; many support their sexual partners in using the family planning methods of their choice. On a global level, of the more than one billion married women of reproductive age, approximately 60% are using any method of family planning. Most of these women report using methods that they themselves initiate, with fewer couples relying on the use of condoms (about 5%) or vasectomy (about 3.5%) to plan whether and when to have children. However, these numbers present a limited view of male participation in contraceptive behaviour, since traditional methods like rhythm and withdrawal (each relied upon by approximately 3% of married women of reproductive age) also require the male partner's cooperation. Significant country and regional differences in the rates of use of these methods do exist, with vasectomy, condoms and withdrawal all used by a higher proportion of couples in more developed regions of the world[1].

At least 120 million couples around the world do not use any method of family planning, despite a desire to avoid a pregnancy. This unmet need for family planning is especially apparent in the developing world and is probably symptomatic of a variety of shortcomings in the available health care systems (lack of knowledge about contraception, lack of services or trained medical personnel, limited supplies) as well as the limitations of the methods themselves including real or perceived health effects, and personal and cultural objections to the use of existing contraceptive technologies.

In early 2007, the All Party Parliamentary Group on Population, Development and Reproductive Health of the United Kingdom launched its report *Return of the Population Growth Factor – Its Impact Upon the Millennium Development Goals*. The evidence gathered and reported by this group demonstrates that it is essential to address and meet the increasing needs for family planning worldwide, in order to achieve these international goals. The recommendations include promotion of gender equality and sustained provision of contraceptive commodities[2].

The World Bank, too, has recently presented updated evidence linking population and development and has again committed to working with government, country and United Nations partners to address family planning issues at the highest levels of country policy-setting[3].

Traditionally, women have assumed the responsibility for family planning. However, many women do not have access to the most effective methods, find their side-effects intolerable, or would simply prefer to share this role with a partner. For their part, a significant proportion of men report a willingness to use a method to regulate their own fertility in repeated surveys in various countries and settings, with the most recent research conducted in Europe, the USA, Latin America and Indonesia[4] and the UK, China and South Africa[5]. The Programme of Action from the ICPD calls for increased research to develop male methods, in order to better meet individuals' needs and rights in reproductive health[6].

For more than three decades, the public sector has been working in collaboration with major pharmaceutical companies, small independently-owned companies, not-for-profit organizations and academic scientists on a research agenda geared towards the development of safe, effective and acceptable methods to regulate male fertility. Since family planning programmes that offer a wider variety of methods are more successful in meeting the contraceptive needs of couples, making a method available for men to use could address the needs of a significant number of couples who are not using any method, or who are unsatisfied with the methods available.

Successfully regulating male fertility can be achieved by exploiting one or more of several aspects of male reproduction, as long as sperm are prevented from reaching an egg in a woman's reproductive tract. Following the resurgence in condom promotion associated with the public health emergency of the HIV/AIDS pandemic, improved condoms have been developed, using innovative designs and alternative materials, with the goal of increasing acceptability and, therefore, use[7,8].

In addition, researchers and small companies have

investigated the vas deferens as a site of male contraception, particularly to develop alternative approaches to male sterilization[9]. The goal of this line of research is to make available, effective methods associated with less tissue trauma, faster recovery, and fewer side-effects with, in some cases, improved probability of reversal. The VasClip® was approved for marketing in the USA in 2002, but is not widely available in that country and not available at all outside of the USA. Research on vasectomy techniques has provided information on the most successful surgical approaches[10] and studies on other physical or chemical devices to block the vas are ongoing. To date, no method is more effective, safer or more acceptable than the no-scalpel vasectomy technique, developed in China in 1974 and introduced outside of China in the mid-1980s.

A novel approach to male contraception is through hormonal manipulation of the process of sperm production. Data collected over the last 20 years have demonstrated the proof of the concept of using steroid hormones to disrupt sperm production in men. Exogenous androgens were initially used to suppress the hypothalamic engine of spermatogenesis[11,12]. Long-acting androgens offer a viable method of male fertility regulation in Chinese populations[13]; a regimen of monthly injections of testosterone undecanoate is currently being evaluated in a Phase III safety and efficacy trial in 10 centres in China, supported by the World Health Organization, the Chinese Government and the drug manufacturer. Combined progestin and androgen regimens have been investigated as being more effective, and possibly safer, for a global audience[14] and may very well offer the best opportunity for a marketable male contraceptive product in the medium-term future[15].

The World Health Organization, in partnership with the USA-based CONRAD program, is currently working to initiate an international, multicentre Phase II clinical trial of the safety and contraceptive efficacy of one such combined hormonal regimen. In small preliminary studies, injections of the progestin norethisterone enanthate, when given together with injections of the long-acting androgen testosterone undecanoate (both provided by Schering AG, now Bayer Schering Pharma), produced profound decreases in sperm output in men with no serious side effects[16,17,18]. The planned study will enroll 400 couples in eight countries to test the efficacy of the regimen when administered every eight weeks; we expect the pregnancy rate to be no greater than the failure rate of combined oral contraceptives. Because each of the compounds is widely marketed, we do not anticipate any serious risks or side-effects. If enrolment can begin before the end of 2007, as planned, final study results should be available in 2011. Keeping in mind the service delivery aspect of product development, if the results of the planned study are promising, the study sponsors are interested to develop a combined, single injection for delivering the steroid hormones and will test a novel formulation in a follow-on clinical trial, if funds can be raised.

Only a handful of pharmaceutical companies have been actively engaged in contraceptive research and development; even fewer have supported research on methods to regulate male fertility. In 1997, investigators researching hormonal regimens of contraception for men urged the pharmaceutical industry to become actively involved in this exciting and promising field of work[19]. Around this time, the large European companies Organon (Oss, the Netherlands) and Schering AG (Berlin, Germany) initiated clinical research on hormonally-based methods of fertility regulation for men and, in 2002, the two companies launched a collaborative initiative to conduct a clinical trial to explore the safety and efficacy of a combined hormonal method of male contraception. Each company also planned to pursue independent avenues of research related to male fertility regulation, as did Wyeth (Madison, New Jersey, USA).

Schering's not-for-profit arm, the Ernst Schering Foundation, in collaboration with the Rockefeller Foundation, had already made substantial investments in basic science research related to regulation of the male reproductive system, in particular post-testicular activity. The AMPPA (application of molecular pharmacology for post-testicular activity) network, established in 1997, proved so successful in identifying new targets suitable for drug discovery in male contraception that the project was renewed in 2002, with CONRAD replacing the Rockefeller Foundation as funding partner for the AMPPA-II (application of molecular pharmacology for post-meiotic activity) network. AMPPA-II supported work in identifying novel epididymal and testicular targets that could be exploited in the development of male contraceptives; several approaches were selected for continued support to evaluate target validation.

The significant corporate commitment to research and development of a method for male use in contraception was a signal of confidence in the potential market for such a product. In a collaborative process, pharmaceutical companies, investigators and donors have proposed recommendations for regulatory review and approval of a potential method of male fertility regulation[20].

Despite their combined efforts and achievements, however, the collaboration between Schering and Organon came to a close following completion of the clinical trial in 2006, and all the large companies and their subsidiaries have phased out their programmes of research and development on male fertility regulation, for various reasons. Both Schering and Organon were bought by larger pharmaceutical companies that re-aligned their respective research portfolios. Even the AMPPA-II network has been terminated, due to lack of funding and the change in corporate ownership at Schering. This puzzling transformation of research priorities in the private sector has made the efforts of the public sector and research institutions paramount in the search for new methods of family planning to meet couples' needs.

The United States National Institute of Child Health and Human Development, part of the National Institutes of Health, has established a Cooperative Research Program on Male Fertility Regulation, which supports basic, applied and clinical research. The Institute funds research on topics that are relevant to both short-term and long-term product development. This research initiative may very well lead to the development of a non-hormonal method of male fertility regulation, with targeted action and few side-effects, which will be an essential component of the range of methods required to meet the contraceptive needs of the next generation of young people entering their reproductive years.

We encourage other national governments to follow this lead and fund a broad portfolio of research in this area. Some countries are already supporting their scientists to research the male reproductive system and develop methods to regulate male fertility, but governments need to do more in terms of funding, networking, partnering and political support. It is now clearly apparent that only through the combined efforts of scientists, not-for-profit research organizations, governments and international organizations will the hope of greater access to family planning through delivery of methods for men to use be realized. We are strongly committed to this goal and encourage greater public-sector involvement and investment in this important area of research. ❑

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A new landscape of partnerships

Article by Stefanie Meredith (pictured) and Elizabeth Ziemba

Over the last few years, partnerships between public and private sector organizations have become a growing phenomenon. These partnerships grew out of a need to fill gaps in the health systems of developing countries and have become an increasingly common mechanism to address some of the diseases of the poor in developing countries.

The ultimate goal of most of these partnerships is to improve and increase access to treatment, particularly for the "neglected diseases", and many also express the goal of contributing to the alleviation of poverty.

The need for such partnerships is explained by a failure of the public health system – the inability of the public sector to provide the public goods entirely on its own due to lack of resources; competing priorities for the limited resources available; management issues; conflict and post-conflict situations, etc. There is also a failure on the part of the private sector when there is little or no commercial incentive for the development of diagnostics and medicines for most of the diseases endemic in developing countries and affecting mainly the very poor.

Introduction

Every year, approximately US$ 70 billion is spent in health research but only about 10% of funding is targeted to the diseases that account for 90% of the global disease burden. The unavailability of medicines to people in developing countries results in enormous human and economic costs[1].

During the past ten years, the global health community has identified gaps in research and development of medicines to prevent or cure diseases that are primarily associated with extreme poverty and its attendant lack of access to clean water, adequate nutrition, and basic sanitation[2]. While diseases such as malaria, tuberculosis and others that are even less well known are rampant in developing countries; they are of lesser or no consequence in developed countries[3,4,5,6].

There is little or no economic incentive to develop pharmaceutical products[7,8] for these diseases as well as other issues including: "distribution challenges in countries with poor infrastructures and lack of awareness about these diseases in more developed countries"[3], "liability considerations, inadequate science base, and underestimation of the disease burden"[9]. As a consequence, compared with other diseases, minimal research on diseases affecting the poor has been conducted. To address this enormous and widening gap in availability of medicines, the innovative approach to address this problem has been the formation of Public-Private Partnerships (PPPs)[10].

The PPPs bring together skills, knowledge, and resources from a variety of sectors including academia, non-governmental organizations, philanthropists, not-for-profit organizations, government and intergovernmental agencies, as well as members of the for-profit private sector such as pharmaceutical and biotech companies to create a unique approach to solving a global health issue. From 1986 when the first such PPP for health was created until the end of 2003, 91 such partnerships have been instituted, 78 of which are still in existence[11]. Each partnership has its own separate legal status, broad range of goals, combinations of partners from the public and private sectors, management structures, and strategies[11].

Many partnerships reflect a mix of representatives from the public and private sectors on their boards of directors, some of whom represent a particular institution while others sit in an individual capacity; however, it remains unclear which model is optimum for ensuring success.

The nature, variety, and individuality of public-private partnerships make definition difficult[12,13,14]. For a working definition, Public-Private Partnerships for health can be defined as "arrangements that innovatively combine different skills and resources from institutions in the public and private sectors to address persistent global health problems"[15].

Although the philosophy behind PPPs includes shared risk, using complimentary skills and expertise from each partner organization and equal input from public and private organizations, the reality is that many of these so-called PPPs would be better described more classically as partnerships or even collaborations due to the traditional division of financial and technical roles of the organizations.

Global health partnerships frequently use the term "neglected diseases" when referring to a group of diseases affecting developing countries. According to the Drugs for Neglected Diseases Initiative (DNDi)[16], "neglected diseases" can be characterized as diseases that:

- kill millions each year, primarily in the poorest areas of

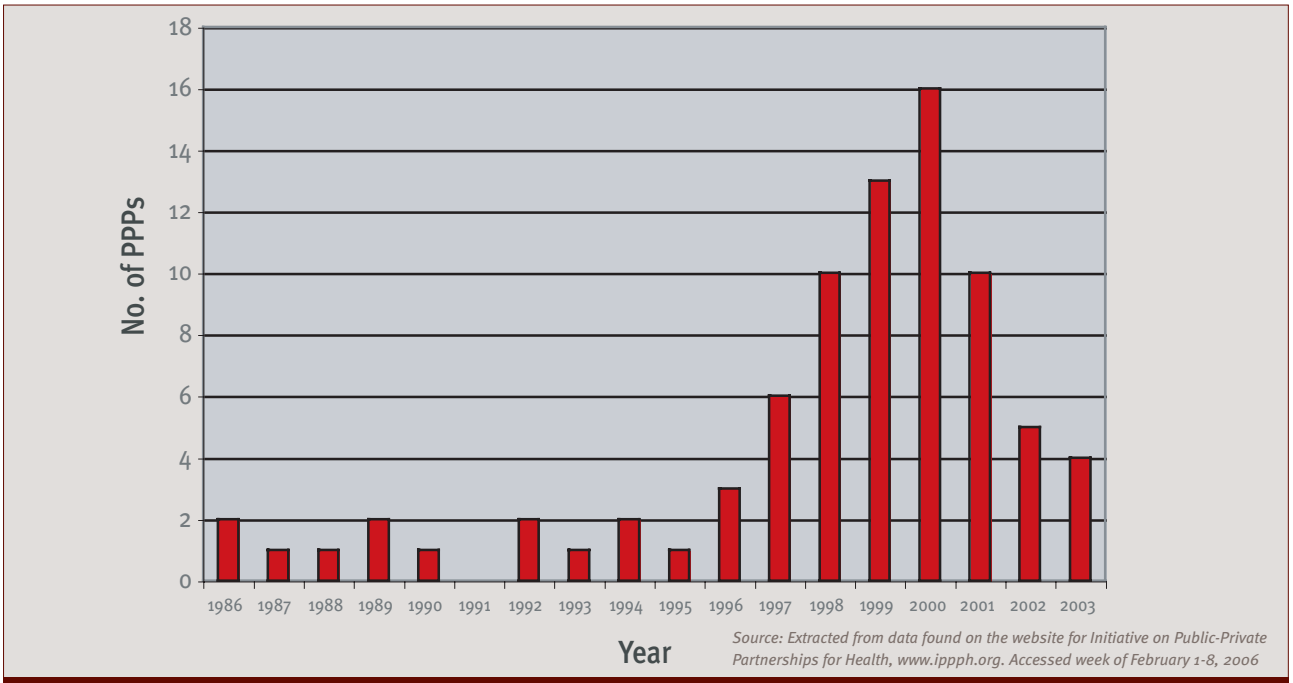


Figure 1: Number of Public-Private Partnerships created between 1986 and 2003

the developing world, such as malaria and tuberculosis;
- are seriously disabling or life threatening, for which treatment options are inadequate or do not exist such as leishmaniasis and Chagas' disease;
- could be cured or prevented with the currently available science and technology, but for which research and development has ground to a standstill;
- do not constitute a valuable enough market to stimulate adequate research and development of new medicines;
- governments have failed to redress market failure.

To redress the imbalance in availability of medicines to developing countries, PPPs are used as a means to gather resources and funding to be applied to solving this problem, as by the 1990s, both the private and public sectors acknowledged that "a pure market mechanism generally does not work"[12] where medicines are involved and new approaches needed to be developed.

Millions of people globally die or become disabled from diseases for which there are inadequate or no medicines and the free market had no incentive to develop such medicines. From 1975 to 2004 only 1.3% of the 1556 new chemical entities marketed were registered for tropical diseases and tuberculosis despite the fact that these diseases account for 12% of the global disease burden[17]. Partnerships and more specifically, PPPs were created to fill this void.

Barriers to access to products and treatments for diseases of the poor

The barriers to access to products and treatment for diseases of the poor that these partnerships have been created to address can be classified under the following six groupings.

1. Lack of affordable, effective safe diagnostics, medicines, or vaccines.
2. The cost of the products, medicines, and vaccines (to both the National Health Service and to individuals).
3. Lack of a reliable supply of products, medicines, or vaccines.
4. Weak/fractured health systems.
5. Cultural perceptions and beliefs.
6. Political will.

The majority of PPPs were formed in the past seven years as illustrated in Figure 1, corresponding to interest and energy from private foundations, particularly the Rockefeller Foundation and the Bill & Melinda Gates Foundation.

Kinds of partnerships

In general, public-private partnerships can be broadly categorized into the following areas: (1) product distribution or disease control programmes; (2) product development; and (3) policy, advocacy, or health systems issues[18].

1. **Disease control programmes/product distribution.** Certain PPPs are designed to improve access to treatment in developing countries by improving distribution of medicines or medical products to prevent or treat specific diseases. The disease control programmes are mainly through drug donations; there are now four major drug donations for annual mass treatment: Ivermectin, MSD, for onchocerciasis (Merck & Co. Inc.); azythromicin for Trachoma (Pfizer); Albendazole and Ivermectin for lymphatic filariasis (Glaxo Smith-Kline, Merck & Co. Inc.), mebendazole for soil transmitted helminthes in children (Johnson and Johnson) and two for individual treatment; leprosy (Novartis) and sleeping sickness (Aventis, Bristol-Myers Squibb).
2. **Product development.** The majority of partnerships focus on the development of medicines, vaccines, or products for use in the treatment or prevention of neglected diseases[19] such as the Medicines for Malaria Venture (MMV), The International AIDS Vaccine Initiative (IAVI) and the Global Alliance for Vaccines and Immunization (GAVI Alliance).

13 + 1*-	HIV/AIDS (see Global Fund below)
12 + 1*-	Malaria (see Global Fund below)
8	Health policies and systems
7	Chagas', leishmaniasis, trypanosomiasis, lymphatic filariasis – individually or in combination with each other
6	Microbicides
5 + 1*	Tuberculosis (see Global Fund below)
5	Vaccines of the poor
4	Onchocerciasis and/or trachoma
3	Micronutrients/Vitamin A
3	Reproductive health
2	Dengue
1	Communicable diseases – prevention through hand washing with soap
1*	The Global Fund to Fight AIDS, Tuberculosis and Malaria
1	Guinea worm
1	Hookworm
1	Lassa fever
1	Leprosy
1	Meningitis
1	Polio
1	Schistosomiasis
1	Tetanus

Source: Extracted from data found on the website for Initiative on Public Private Partnerships for Health, www.ippph.org, accessed 1-8 February 2006.

Table 1: Number of partnerships with associated disease or issue

3. **Advocacy and policy.** The third type of PPP concentrates on health policies and systems and advocacy. Most of the partnerships that fall in this advocacy and policy category however, also have some technical, access, or product development component as well for example, GAVI, Drugs and Neglected Diseases inititative (DNDi), Global Alliance for Improved Nutrition (GAIN), SIGN.

Of the 78 active partnerships, the number of partnerships that focus on certain diseases or health policy issues is set out in Table 1. Categorization is not an exact science as partnerships may deal in any combination with product distribution, product development, and/or policy and health systems issues between or among various diseases.

Twenty-four public-private partnerships devote the majority of their efforts to developing medicines, vaccines, or diagnostics for diseases of developing countries including malaria, tuberculosis, HIV, leishmaniasis, and others collectively referred to as "neglected diseases" (see Figure 2).

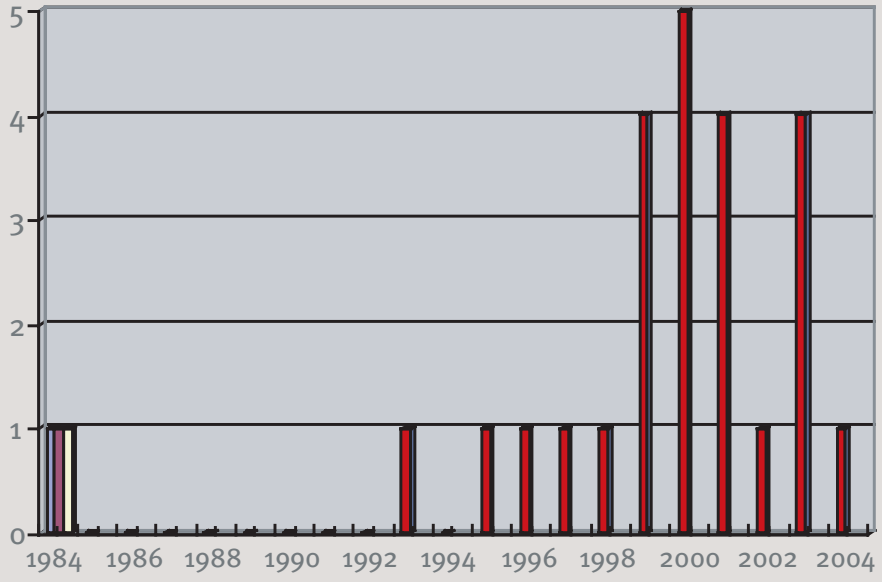
Of the 24 PPPs for Product Development, 9 are devoted to developing medicines and/or microbicides, 11 are committed to vaccine development, one is focused on diagnostic products, and three are involved with the development of a combination of medicines, vaccines and/or diagnostics. Five partnerships focus exclusively on reproductive health issues, four focus on malaria and two are committed to tuberculosis and HIV/AIDS respectively.

Current situation with regard to PPPs for health

There were early perceptions and criticism that these partnerships would lead to distortion of national policies and public health funding, parallel systems of drugs supply etc. However these have been largely dispelled through programme evaluation and assessments which have shown a positive impact – although it is true to say that many of the partnerships are still too young to measure real impact.

The raised awareness and stimulation of research and development on drugs/prevention for neglected diseases has certainly changed the field over the last seven years. There is now a very crowded landscape of PPPs, particularly in a few sectors as illustrated by Figure 3, which has changed considerably since the early partnerships were formed. Most of the neglected diseases are addressed by at least one PPP providing research and development, drugs and technical support and/or some funding.

The recent analysis of drug development for neglected



Extracted from partnership database found on website for Initiative on Public-Private Partnerships for Health, www.ippph.org, accessed various times December 2004.

Figure 2: Number of Public-Private Partnerships for Product Development created by year from 1984 to 2004

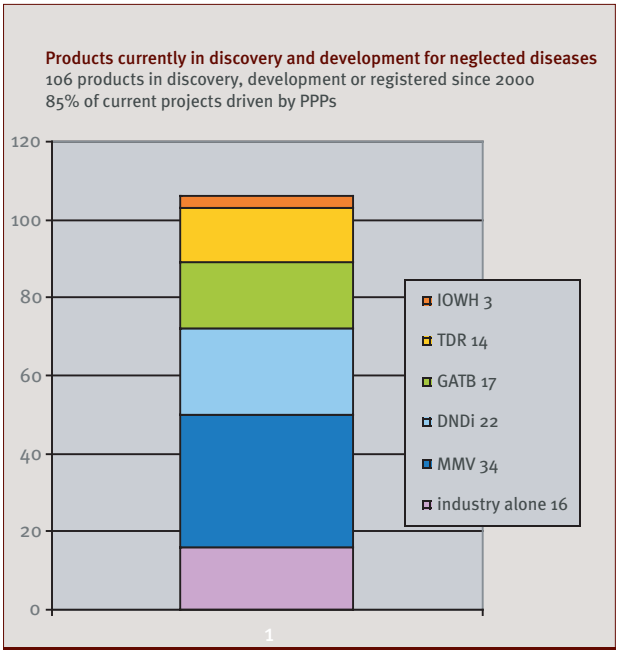


Figure 3: Products currently in discovery and development

diseases has shown that many of the long-held beliefs on the activity of development of drugs for neglected diseases are no longer valid or accurate and product development since 2000 has increased substantially (Figure 3). However, despite the public-private label, 80% of the drug development is through private philanthropy and the industry institutions are largely self-funding. Moran et al point out that although the product development PPPs have proved to be a good conduit for directing public funding to industry and academia, they could collapse if there is not more public support.

The access partnerships and drug donation programmes have raised the profile of the diseases involved, kick-started national disease control programmes and improved delivery systems to those at "the end of the road".

However, there remain many gaps that the partnerships have not been able to address which raise the concern of sustainability – systemic problems in health systems and infrastructure, capacity and human resources, long-term operational funding. The clinical trial capacity is limited and under-funded at present and mechanisms for "after research and development" are not being addressed – i.e. how to get the products to the people that need them.

Overall, a better coordination between the partnerships is needed, and integrated approaches to addressing the neglected diseases which would maximize efficient use of resources.

The research needs in this area include: operational research on sustainable delivery methods; implementation practices/opportunities for collaboration across disease programmes; bringing new products to markets and target communities and finally, how to "harmonize the partnerships with health systems".

Conclusion

Public-private partnerships have changed the landscape of drug development for medicines for neglected diseases and the delivery of medicines for some neglected diseases in the developing world. Stemming from market and government failures as well as ineffective legislative incentives, PPPs have brought together participants from all sectors in an attempt to maximize the skills and resources of those participants to tackle complex issues of drug development and distribution.

Whilst the product distribution and disease control programmes are filling a gap and improving access to treatment for specific diseases, many issues concerning long-term sustainability remain.

The product-development PPPs are relatively new entities and have not yet brought a product to market so it remains to be seen if this innovative approach to drug development will really succeed. They have introduced innovative and creative systems and processes for drug development outside the traditional for-profit pharmaceutical model. PPPs are challenging governments, industry, academia, and non-profit organizations to face urgent public health issues.

Product-development PPPs face the challenges presented by the risks inherent in the costly and time-consuming process of drug development especially for diseases where basic science and research has been dormant for decades. The cost of drug development is high and PPPs are optimistic that sufficient funding will be available as drug candidates move through each stage of the development process. It remains to be seen if the optimism is justified.

As yet, most of those affected by the diseases that these partnerships were developed for are not yet benefiting. ❑

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Capacity strengthening for global health research

Article by Gunvanti Goding (pictured), Michael Chew and Jimmy Whitworth

Disparities around the globe in life expectancy, child survival, maternal mortality and health expenditure all highlight the gross inequity of health and welfare in the world today. Several of the Millennium Development Goals focus on health. The goals of reducing child mortality, improving maternal health, and combating HIV and AIDS, malaria and other diseases all require major improvements in delivery and uptake of health services. We need both new interventions and better application of existing proven interventions. A concerted response is urgently required to ensure the generation of new knowledge for effective disease prevention, development of affordable diagnostics and therapeutics, efficient delivery of cost-effective interventions, and health promotion. Central to this response is the need for research and increased uptake of research outcomes.

The developing world faces many challenges in relation to health research: lack of funds; poor institutional infrastructure; a lack of appropriately trained personnel; huge health burdens of both communicable and non-communicable diseases; and a lack of cohesive political advocacy.

Since its establishment in 1936, the Wellcome Trust has played a significant role in promoting global health. The Wellcome Trust's mission is to foster and promote research with the aim of improving human and animal health. With annual grant support of over £500 million, a significant proportion is devoted to fund global health research. For example, in 2006, we spent £73 million on health research in low- and middle-income countries.

Strengthening research capacity in biomedical science and public health constitutes a major component of the Wellcome Trust's international funding strategy. We aim to build a critical mass of sustainable research capacity in developing countries. In doing so, we support researchers to tackle the most pressing local health problems and to deliver health benefits for people and their livestock.

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Personal support

Building capacity locally includes encouraging excellent researchers to develop their careers in their home countries or regions (see Example 1). Support needs to be long-term to nurture the organic development of teams, centres and networks. A good example of this working successfully is our relationship with research teams in Kenya which has flourished over the past 50 years. The Trust's current programme, led by Dr Norbert Peshu and Professor Kevin Marsh, undertakes laboratory, clinical, field and policy research on issues of public health importance to Kenya and the region. There are strong links with the Kenyan Ministry of Health through the Kenya Medical Research Institute (KEMRI), which ensure that important research findings make their way into policy and make a difference to medical care (see Example 2). This programme has influence across Sub-Saharan Africa and is attracting research workers from many parts of Africa and beyond.

We provide flexible training and career progression opportunities for the best people at all stages in their careers to work on diseases of importance in a developing country setting. We have recently established a range of fellowship awards for applicants from Africa, Asia and South America wishing to carry out public health and tropical medicine research. Awards are available from junior fellowships for Masters students to senior fellowships for outstanding individuals wishing to establish themselves as research leaders.

Institutional support

Crucial to boosting research capacity is the need to ensure that the research that we support helps to consolidate local infrastructures and national institutions, and is geared to national priorities. To this end, the Trust has committed £10 million over 5 years to a partnership with the UK Department for International Development, and the International Development Research Centre, Canada, which aims to strengthen health research capacity in Kenya and Malawi. The partnership aims, through working with local ministries of health and key national institutions, to strengthen the generation and use of health research at a national and

international level. Key components of this initiative include:

- supporting and training promising individual scientists;
- strengthening key academic research and policy-making institutions;
- facilitating collaborative engagement of national representatives;
- improving regulation and co-ordination of the national research environment.

There are significant difficulties with building research capacity in developing countries. Funding opportunities for individuals are often fragmented and difficult to access. The pipeline of young school leavers and graduates needed to embark on scientific careers is thin and unreliable. There is a lack of credible career pathways and few role models of successful research leaders. Research infrastructure is often inadequate and there is a lack of connectivity between teaching in universities and the institutes in which research is conducted. Over time we aim to help support the development of a critical mass of skilled and adequately remunerated academic and technical staff working in a vibrant academic environment with strong national and international links with research partners and networks. This requires strong national political advocacy for science and research and development of national strategies for research priorities. This will involve not only the scientific perspective of what will work but also the social viewpoint of health delivery to those in most need.

Challenges

Looking to the future we need to think about how we can use our funding schemes and other mechanisms as drivers of change. We need to encourage more partnerships and networks between institutions in developing countries and also to encourage more equitable partnerships between northern institutions and those in developing countries (see Example 3). The issues of attrition and brain drain need to be addressed. This requires not only sensitive policies in developed countries to avoid pulling skilled scientists away from their home countries, but also local Government and international support for developing mechanisms for the retention of high quality trained professionals.

We all need to be advocates for science and technology, and to support the skilled individuals who are essential to enhance the health, lives and livelihoods of those in the poorest countries of the world. ❑

Example 1

In 2002 Dr Mayfong Mayxay received a Wellcome Trust Research Training Fellowship for a clinical and laboratory assessment of antimalarial drug efficacy in the Lao People's Democratic Republic (Lao PDR or Laos). His research involved spending long periods in rural Lao studying how best to treat malaria patients in one of the poorest countries in the world, living and working in villages where initially there were no modern utilities like piped water and grid electricity, let alone telephones, televisions and the Internet.

When Mayfong obtained a scholarship under a SEAMEO-TROPMED programme he contacted Mahidol University Professors Sasithon Pukrittayakamee and Nick White, who took him under their wing. Mayfong completed a PhD, succeeded in obtaining a competitive Trust fellowship, and is now a critical member of the Lao Project funded by the Trust as a part of its Major Overseas Programme in South-East Asia. Since 2001 Mayfong, in collaboration with his mainly Lao and British colleagues, has published nearly 30 papers in international peer-reviewed journals, many having real impact in directing health policies and practice in Laos. His clinical trials on artemisinin-based combination therapies (ACT) provided key evidence for the Lao Government to change its national malaria treatment policy to ACT. He has also been investigating the causes of fever in rural Laos and made key contributions to the first post-colonial medical journal in Laos which describes the Project's infectious disease research in English and Lao languages.

In July 2007, Mayfong published a paper, in collaboration with his colleagues in the Lao Project, the Lao Government and the USA, in the prestigious *American Journal of Tropical Medicine and Hygiene*, reporting a sophisticated study on population genetic markers in malaria parasites. This paper suggested that the previous national antimalarial treatment policy of chloroquine would not be efficacious in any parts of Laos and that ACT would be superior over the whole country and not just where clinical trials had been conducted. It exemplifies the nature of the research emanating from the Trust's Major Overseas Programme in South-East Asia which includes work in Laos. Under the overall direction of Professor Nick White, University of Oxford, the South-East Asia Programme, which includes developing the research site in Laos, has its major base at Mahidol University, Bangkok, Thailand. Professor White's interest in the pharmacology of antimalarial drugs and the studies on artemisinin derivatives has provided the basis for treatment trials for malaria on a large scale in Thailand and Viet Nam, and subsequent recommendation by WHO as the treatment of choice for malaria in many countries.

Example 2

Dr Michael English is a Wellcome Trust Clinical Senior Fellow based at the Kenya Medical Research Institute/Wellcome Trust programme in Nairobi, Kenya. His previous research funded through the Trust's Research Career Development Fellowship, also based in Kenya, has demonstrated that health workers are unaware of the evidence defining appropriate hospital treatment of children with severe diseases including malaria, anaemia, pneumonia, diarrhoea/dehydration, severe malnutrition and simple neonatal disorders. Treatment is therefore commonly inappropriate, inadequate or occasionally, even actually dangerous. Such

treatment is provided to hundreds of thousands of children annually in Kenya and, almost certainly, to millions of children throughout Africa. Major gains in child survival can only be made if improved preventive and primary care are combined with the right treatment at the right time for those that present with severe disease. In Kenya, the majority of the first-line resources needed to support care of the severely ill child are available. The challenge then is to determine how the care provided can be optimized to suit the context, in line with the best available evidence. Research addressing this issue has very rarely been attempted in rigorously designed studies in developing country settings and never as part of an integrated approach to inpatient paediatric care.

The aim of Dr English's current research project is primarily to conduct a public health efficacy study of an intervention to improve care for children in hospitals in Kenya. The intervention, based on the referral care component of the Integrated Management of Childhood Illness (IMCI) strategy, with Kenya's Ministry of Health comprises training, guidelines, job aides, supervision and quality improvement activities delivered over 18 months to a number of hospitals in the country. Results will critically inform the debate on scaling-up and improving new integrated health systems in Kenya.

Example 3

International Partnerships for Capacity Development

✣ International Collaborative Research Grants scheme

This £12 million initiative is a partnership between the Wellcome Trust, the National Health & Medical Research Council of Australia and the Health Research Council of New Zealand and is designed to foster collaborations between the researchers in low- and middle-income countries (LMICs) in South and Southeast Asia and the Pacific Islands with the investigators based in Australia and New Zealand. Eleven research programmes were awarded which focus on major health issues of the LMICs of the region and develop research capacity in the region.

✣ Wellcome Trust – Burroughs Wellcome Infectious Disease Initiative

This £18 million partnership initiative supported 13 trilateral international collaborations between the UK, USA or Canada and LMICs anywhere in the world. The aim of the partnership initiative was to advance understanding of infectious diseases which affect developing countries and to increase research capacity in the LMICs through training and technology transfer.

✣ The Health Research Capacity Strengthening (HRCS) initiative

The HRCS initiative is a partnership between the Wellcome Trust and the UK's Department for International Development (DFID) who agreed to commit £10 million each towards a joint programme of health research capacity strengthening in Africa as part of the UK Government 2004 Spending Review. The International Development Research Centre (IDRC), Canada has joined the initiative, both as an implementing partner with experience in health research programmes in East Africa, and as a co-funder. The partnership aims to strengthen the capacity for the generation of new health research knowledge within Kenya and Malawi, and improve its use in evidence-based decision-making, policy formulation and implementation.

Gunvanti Goding *is a science programme officer at the Wellcome Trust in the Populations and Public Health Section, which manages research grants, fellowships and partnership programmes based in the UK and the low- and middle-income countries of the world. She obtained a doctorate from her research on gene regulation at Cancer Research, UK and has carried out a number of research projects in virology and molecular biology.*

Michael Chew *is a science programme officer at the Wellcome Trust and works for the Tropical and Clinical Immunology and Infectious Disease Section, which manages many of the research grants based in low- and middle-income countries. Before joining the Trust, he undertook research for a PhD in parasitology at Imperial College London, and worked as a scientist at the Institute of Child Health, London, and Imperial College for 16 years.*

Jimmy Whitworth *is head of International Activates at the Wellcome Trust, where he oversees strategy and policy for research in developing and restructuring countries of the world, including fellowships, project and programme grants, networks and partnerships. Previously he was Professor of International Public Health at the London School of Hygiene and Tropical Medicine, and has spent most of the past 25 years working on medical research topics in Africa.*

Partnership dynamics, issues and challenges

Article by Mary Moran (pictured), Anne-Laure Ropars and Javier Guzman

One of the biggest issues for Public-Private Partnerships (PPPs) is that the term itself is a misleading representation of what many PPPs actually are and do – a factor possibly contributing to government confusion and hesitancy over the legitimacy of PPPs.

The first area of confusion is the failure to distinguish between public-private partnering as an activity (a functional definition) and Public-Private Partnerships as an organization (a structural definition).

The functional definition encompasses many activities ranging from drug donations (e.g. the Malarone donation programme for malaria), through to partnerships that involve existing public and private organizations working together on joint product development projects (e.g. the moxidectin anti-onchocerciasis drug project between Wyeth and the Special Programme for Research and Training in Tropical Diseases (TDR). In most cases, these activities are carried out as new or additional projects within existing organizations, and often from within existing resources.

The structural definition refers to formal organizations, including the relatively small number of Product Development Public-Private Partnerships (PDPPPs) specifically set up to develop neglected disease products. Although these PPPs may contract with multiple partners for multiple projects that change over time (i.e. a range of partnering *activities*), the PPP itself is a single organization that encompasses these many deals. Although each of these individual deals could be counted as partnerships under the first definition (and sometimes are), they do not constitute new PPP organizations. Using this structural criterion, there are far fewer PPPs. Indeed, in the neglected disease drug development field there are only four, the last two of whom would perhaps argue that they are not strictly PPPs.

1. Partnerships for disease control–product development
2. Partnerships for disease control–product distribution
3. Partnerships for strengthening health services
4. Partnerships to commercialize traditional medicines
5. Partnerships for health programme coordination
6. Other international health partnerships
7. Country level partnerships
8. Private sector coalitions for health
9. Partnerships for product donations
10. Partnerships for health service delivery

Table 1: Categories of Public-Private Partnerships for Health[1]

- The TB Alliance, which develops TB drugs;
- Medicines for Malaria Venture (MMV), which develops anti-malarials;
- Institute for One World Health (iOWH), which covers a range of technologies and diseases from malaria to diarrhoea;
- Drugs for Neglected Disease Initiative (DNDi), which has a first focus on the kinetoplastid diseases (sleeping sickness, leishmaniasis, Chagas' disease).

Collectively, these PPPs are now responsible for around three quarters of all neglected disease drug development projects, including with both small and large industry partners; and have been the driving force behind the post 2000 increase in neglected disease R&D (see Figure 1).

The second key area of confusion revolves around a misunderstanding of how PPPs operate. The classical understanding of PPPs, under both the structural and functional definition, is based on the notion of public and private groups working collaboratively on a project with joint decision-making. This partnership dynamic is often seen as chiefly involving public contribution of funding and private contribution of expertise, effort or products (often as in-kind donations). The Lapdap® anti-malarial drug project is an example of this classical model, with the UK's Department for International Development (DFID); TDR providing staff resources but limited funding, and GSK conducting the R&D on a partially in-kind basis.

However, many of the new PPP organizations – and the "partnered" activities they conduct – simply do not match the classical understanding of what a PPP means or of how they are thought to operate. Indeed, if we examine the four PPP organizations who conduct neglected disease drug development, we find that both the organizations themselves and the projects they conduct often diverge significantly from this classical partnership model.

Dynamics

Rather than struggling with the many anomalies between PDPPPs and the classical definition, it is easier and more productive to look at what PDPPPs actually do and how they operate, i.e. their dynamics. (From here on in, the term "PPP" will be used to signify these PDPPP organizations, and inparticular drug development PDPPPs, which we have

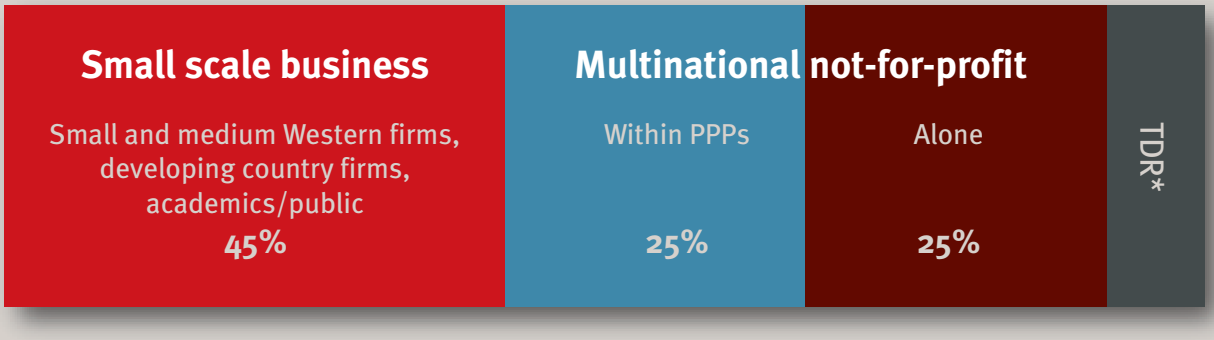

Figure 1: The drug R&D landscape for neglected diseases (Dec 2004): 63 active drug development projects

studied most closely.)

The organizations themselves are private groups not public-private partnerings and are majority funded from private philanthropy

Although they are entirely focused on forwarding the public interest in promoting developing country health, as opposed to a private interest in generating profit, and though they include extensive public health expertise on their Boards, Steering Committees and staff, these PPPs are nevertheless not public entities but are independent private not-for-profit groups with a public health focus.

By accident, rather than design, they are also predominantly funded from private philanthropic sources (see Figure 2).

The failure of government donors to step up to the table means that private groups such as The Bill & Melinda Gates Foundation and Médecins Sans Frontières continue to provide the bulk of funding for these PPPs and their activities, and to be the main auditors of their performance and outputs.

The unintended outcome of this situation – and we note that most of these PPPs had hoped for, and sometimes planned on, having far more substantial government funding – is that, in practice, they are more "private" than "public" in both their funding, auditing and accountability. This situation has led to oft-voiced concerns that "Bill Gates is running world health", however both private donors and PPPs themselves would strongly prefer a healthier public-private funding mix, and the greater public responsibility this would bring. Nevertheless, until this happens, these PPPs will continue to be predominantly privately-funded private organizations – they do not stand-in for public participation in the neglected disease field.

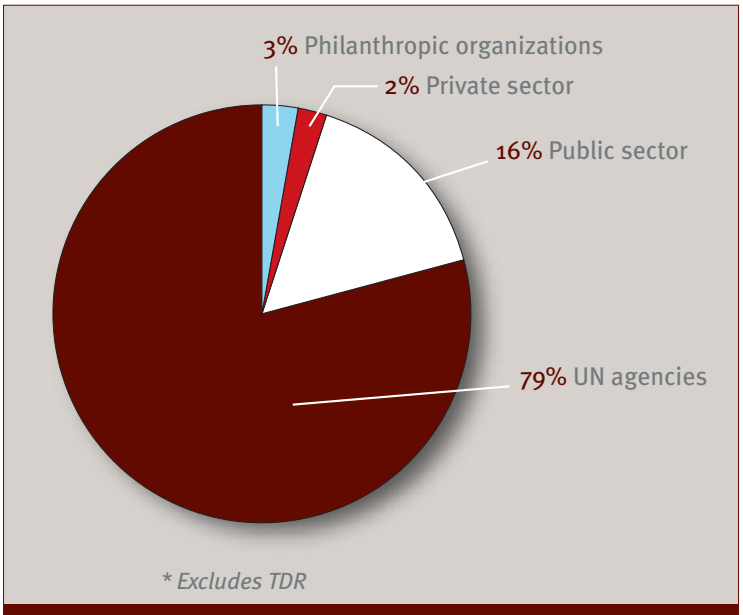

Figure 2: Total cumulative PPP funding by type of funder (as of April 2005, including forward funding committed by that date)*

PPPs fund academic and developing country R&D activity as well as private industry R&D

These PPPs do not primarily channel public funds to private industry activity (often multinational companies), as the broad brush classical model would suggest. It is not only that PPP funds largely come from private philanthropic groups, as seen above, but that these funds are distributed to optimal R&D partners in both the public and private sectors and in both the developed and the developing world.

In practice, around one third of PPP R&D grants go to public sector groups (academic drug development); around one third to private or not-for-profit companies, including companies in the developing world and small- to medium-sized drug firms; and one third to multinational drug companies (see Figure 3).

This funding distribution reflects the fact that these PPPs not only develop promising industry leads but also work to actively generate new leads, many of these from the public academic sector. The role this plays in translating basic academic research into applied research that results in new neglected disease compounds is often overlooked.

PPPs are not simply funders. They play a central management role in the R&D process, closely akin to the role played by Venture Capital (VC) firms or multinational drug companies in commercial areas.

PPPs do not operate as a passive channel of funds to either their academic or industry partners, i.e. they do not provide grants in the more "hands off" way

that many public donors may be used to. This is a very important point to understand. As discussed below, in practice effective PPPs operate more like a cross between social-VC funders and multinational drug company (MNC) divisions.

Just as VC firms do when looking for optimal new products to take forward from a commercial perspective, the PPP also assesses the field to hone it down to a shortlist of the most promising R&D projects from a public health perspective. The PPP raises the funds, bears the risks, finances the chosen groups, provides support to get their products across the line, and finally reaps the (social) dividend. Likewise, the PPP plays a VC-like role in setting milestones, monitoring progress against these and making go/no-go decisions based on how well each project performs. PPPs are assisted in this task by their Scientific Advisory committees, composed of experts (often world-leaders) in industry pharmaceutical development and developing world health needs. Watching one of these committees grill R&D groups on their projects is a fascinating exercise in how public health and industry expertise can work together to ensure that the target products are not only possible from an industrial perspective, but also optimal in terms of affordability, suitability, efficacy and safety for the target developing country populations.

This VC-like role is often unacknowledged, which is a great pity since it is an area where government funders of R&D projects (for example, via grant programmes) are often most exposed to the risk of poor investments and failed decisions. Shifting these decisions to PPPs with industry and public health expertise represents a clear bonus for government funders. If allied to additional government funding of PPPs, it could also help provide the magical formula of increased public involvement and accountability, but decreased public risk. An important proviso is that the PPP must, of course, have sufficient industry and public health expertise – some groups are stronger on this than others, an issue that is addressed through proposals set out elsewhere .

PPPs also play a role that we have loosely categorized as "MNC-like". In other words, they provide smaller or less experienced drug development partners with technical and scientific skills that they may lack and, importantly, provide overall management of the lengthy and complex drug development process. MNCs often play a similar role when working with small biotech companies. For instance, PPPs can supplement their partner's skill gaps by arranging (and often funding) outsourcing to Contract Research Organisations (CROs), by finding industry partners for further development, or by putting together manufacturing deals with other firms. These activities closely mimic the modular approach that MNCs increasingly take to drug development, keeping core activities in-house but outsourcing other jobs to contracted groups who can do them more cheaply.

PPP assistance of this nature can be invaluable for academic groups, developing country firms with limited experience of registering novel drug products (as opposed to generics) or biotech firms who are strong in drug discovery but have limited, if any, experience of regulatory approval or large-scale manufacturing and distribution. In each of these instances, the PPP can contract in the necessary skills to fill the gap (e.g. a CRO skilled in toxicology or regulatory approvals; a developing country company with experience in large-scale manufacture) and provide overall management of

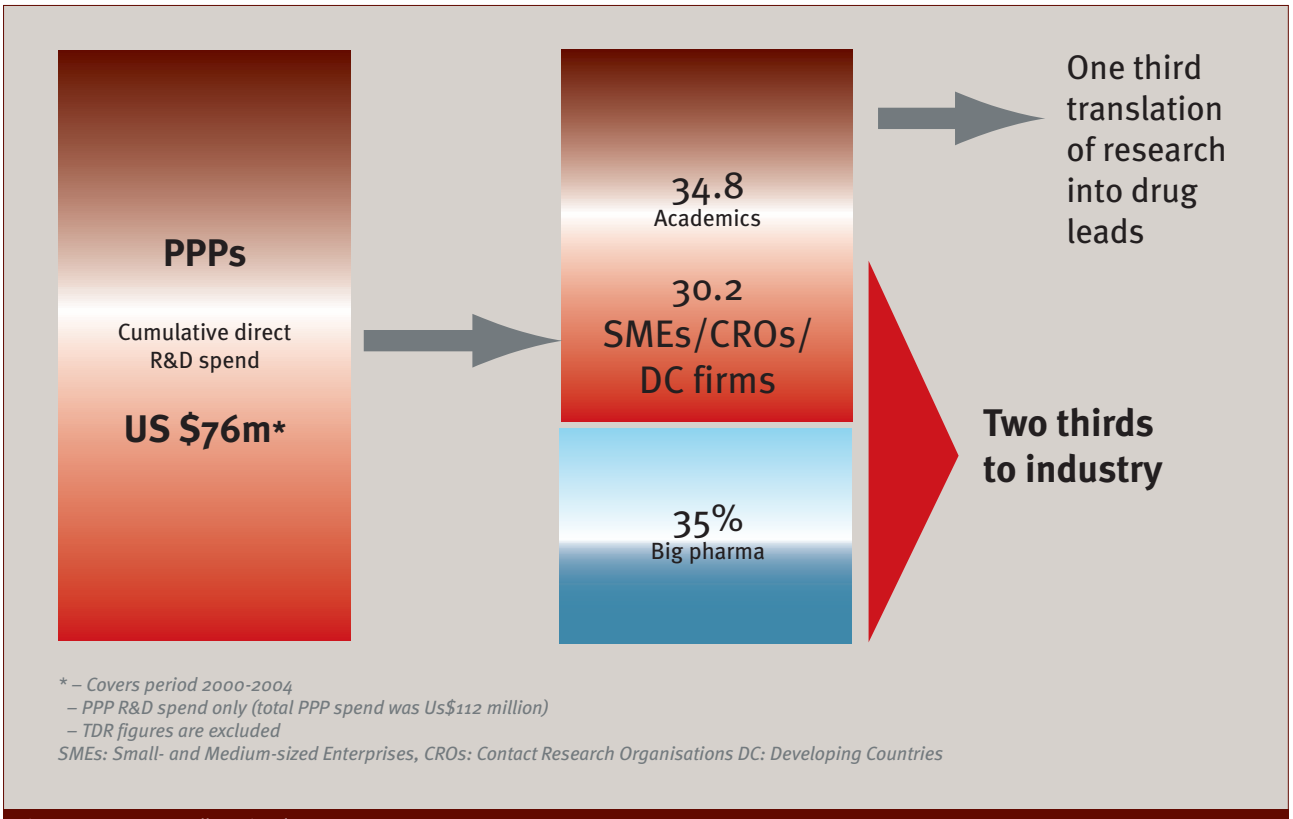

Figure 3: Resource allocation by PPPs 2000-2004

this process in a way that is usually well beyond the smaller partner's resources.

Likewise, these smaller groups – as well as many multinational companies who have limited experience in neglected disease or developing country public health markets – can benefit greatly from PPP input of neglected disease and public health knowledge, ranging from provision of partners or contractors with parasite testing facilities (unlikely to be found in most private firms), to location of suitable developing country clinical trial sites or assistance with senior contacts in developing country public health programmes.

PPP's flexible modular approach to drug development is opening up alternative R&D avenues

As noted above, under the classical model, PPPs provide funds (and sometimes skills) while the compounds being developed come from drug companies, and often large multinational companies. Under this model, PPPs (or, indeed, any public group or government) have no control over the original intellectual property (the background IP) and therefore very little control over what is or is not developed, how quickly it is developed and at what price it is made available to developing country patients. In practice, this is less a problem than perceived, since most companies agree to contractual obligations on delivery, price etc. In other words, the PPP can exercise control through contracts rather than through intellectual property (IP) ownership *per se*.

However, this model represents just under half of all PPP deals. The remaining half are more interesting, since they demonstrate quite different ways of developing drugs for public health use. In many of these cases, it is the PPP who has control over IP issues relating to the compound, for example, because the compound being developed is already in the public domain (so no one has background IP rights), because it has been licensed to the PPP by an academic or a company (so the PPP has the rights it needs for its mission), or because the PPP owns the relevant background IP (so the PPP owns all the rights). However, it is not the IP ownership itself that is central, but the fact that this ownership confers on the PPP the full responsibility for developing the product, thus giving them far greater choice in how the product is developed, by whom and how quickly, and how it will be priced, produced, registered and distributed to developing country patients.

One major outcome of this flexibility is that it allows PPPs to develop new drugs from leads that fall outside the normal commercial model i.e. the PPP does not have to rely solely on companies for access to and development of in-house compounds. For example, the PPP can develop:

- Public domain IP, i.e. drugs or compounds whose patent rights have expired. For example, paromomycin is being developed for use against Indian and African visceral leishmaniasis strains by iOWH and DNDi respectively. The interesting point is that, unlike commercial groups, PPPs do not need orphan drug monopoly provisions in Western markets (and the profits these promise) as a pre-requisite to developing these public-domain drugs since the PPP is seeking a health return, not a financial return, on their R&D investment.
- Shelved company compounds. For instance, the anti-TB drug, PA-824, was shelved by Chiron (who inherited the patent family from a smaller firm, PathoGenesis). However, Chiron were willing to license the compound to the TB Alliance for further development in return for a very modest fee and an option to buy-back the Western rights on any final product that the PPP developed. By taking the risk and cost out of developing shelved company compounds, PPPs can make it more attractive for companies to hand over unwanted compounds than to sit on them.
- Academic leads without commercial potential e.g. compounds such as synthetic peroxide for malaria, which could have a dramatic impact on malaria treatment but has limited potential for Western sales and therefore little likelihood of attracting industry development partners. PPPs offer a new route for academics to see their promising drug leads developed, i.e. PPPs offer a pathway for non-commercial leads to be developed, in addition to the traditional industry pathway for commercial leads. This option has not previously existed.

It is worth a closer examination of how PPPs are able to develop these leads from different sectors. In practice, PPPs use a variety of approaches, some of which deviate markedly from the Public-Private Partnership approach described under the classical model:

- On some projects, they choose to work with no partner, by simply subcontracting out R&D to multiple industry and academic/public groups but retaining overall control themselves. (That is, there are no "partnerships".)
- On others, they develop the compound themselves in the earlier stages using academic or industry subcontractors, but bring in an industry partner (in some cases a developing country firm) at a later stage, for example to assist with large-scale manufacture and distribution. (This is a mixed model, with industry partnering only at certain stages and if needed.)
- Others forgo industry input altogether, with R&D being conducted solely by public partners and public subcontractors. This happens particularly with early-stage projects (although industry input would be expected further down the development line), but sometimes also with late-stage registration projects, e.g. DNDi's registration of paromomycin for African leishmaniasis. (This approach has no "private" input to the R&D.)

In each of these cases, PPPs develop the product using industry's modular approach, where the relevant IP is derived from external sources, and development work is shared by the PPP on a paid or unpaid basis with a range of "partners" with different skills, some or all of whom may have no role in joint decision-making and no stake in the final product.

The modular PPP approach has two important implications. The first is that it allows PPPs to develop

compounds from many different sources even if there is no interested industry partner and no commercial potential. This runs against the oft-stated maxims that only commercial market returns can catalyse drug development; and that only pharmaceutical companies (and perhaps only large multinational companies) have the requisite experience to manage the lengthy, complex and expensive process of drug development.

Equally important is that this flexible, modular approach not only allows but stimulates different (and often far cheaper) models of drug development. For example, by actively pairing small Western companies or academics with CROs and developing country manufacturers, PPPs create a neglected disease pipeline that encourages and allows smaller-sized groups to participate, and at a substantially lower cost than the traditional commercial approach. We note that the anti-malarial synthetic peroxide has moved from laboratory into clinical at a cost of less than US$ 12 million; while the new fixed-dose antimalarial, pyronaridine-artesunate, is expected to be registered for US$ 20 million or less. The TB Alliance also estimates that its anti-TB drug, PA-824, will cost less than US$ 90 million to complete clinical development. All these projects involve academic, public domain or small company leads teamed up with contractors or a developing country manufacturing partner. PPP co-development of multinational drug company leads can also be substantially cheaper, since costs of capital (estimated to roughly double the cost of R&D) are largely avoided, and companies are able to minimize their risk and financial outlays – and therefore their final prices. Either or both of these alternative approaches may provide interesting lessons for other Western diseases where the profit motive is weak or absent: antibiotics for drug resistant bacteria and products for orphan diseases are two examples that spring to mind.

The upshot of these different approaches and choices is that, as noted above, a great deal of PPP activity deviates markedly from the standard perception of what PPPs are and how they operate. It is true that many PPP deals, and the majority of those with large multinational pharmaceutical companies, involve classical partnerships that are built on joint decision-making, majority funding from the PPP partner and in-kind donations of effort and skills from the private partner. Under these deals, the PPP can be very much the weaker party, since it relies on the charitable or strategic motivations of its private partner, which may change with the next merger or acquisition. However, an equally large number of PPP deals do NOT look like this, particularly when the PPP has control over the R&D process or the background IP. Indeed, these deals may have neither joint decision-making, in-kind donations nor private input – and may not even involve partnerships at all.

The net effect of these new models, approaches and dynamics is that the new PPP product development organisations are, in many ways, PPPs in name only. By lumping them together under a generalized "partnerships" umbrella that encompasses everything from charity to business-funded health programmes, we risk failing to understand – and therefore capitalize on – the very specific strengths and opportunities that these groups offer. In this context, we note particularly their ability to deliver high health-value new drugs to neglected disease patients, their capacity to reduce costs and risks to industry and governments, and their catalytic role in translating basic into applied research even in the absence of a commercial market.

Challenges

The first challenge is to provide policy-makers and government donors with a better differentiated understanding of PPPs generally, and a far better understanding of what product development PPPs are and how they operate – and perhaps a better name for the PDPPPs.

The second is to urgently encourage governments to translate this understanding into policies that support these product development organizations, in particular policies that specifically encourage and reward industry involvement in these groups (no such policies now exist) and new funding streams to address the noticeable, even embarrassing, lack of public funding for them, despite the fact that they are now responsible for three quarters of all neglected disease drug development. Further, industry policies need to be tailored to suit different industry groups: not only multinational drug companies, but also the smaller biotechs and CROs who are playing an increasingly active role.

PPPs also face internal challenges, the greatest – but not the only one – of which is their funding gap. Even the best-performing PPP cannot continue to contract and pursue R&D projects in the face of funding deficits of up to 50% in the near future. PPPs are also not all the same, with some performing better than others. While much of this reflects the varying difficulty of the different disease targets these groups address, all PPPs nevertheless need to seek to match industry levels of efficiency and productivity if they are to secure funds from risk-averse public donors. This is likely to require not just public health expertise, but also high in-house levels of industry expertise and understanding, including through the composition of Scientific Committees, Boards and staff; and the willingness (and funds) to contract in the necessary skills when gaps become apparent. For instance, Medicines for Malaria Venture (MMV), which already has high levels of in-house skills, has readily moved to secure CRO assistance on individual projects to maintain their performance standards.

Industry, likewise, has challenges to address, in particular multinational drug companies who have more flexibility to participate than do many smaller enterprises. Although four of the top twelve multinational companies now have active neglected disease programmes collectively employing over 200 scientists, others do little or nothing in terms of neglected disease R&D. Those companies with modest activity could review whether this could be increased – and in particular whether partnering could offer a lower-risk, more cost-effective way of pursuing greater activity. On the other hand, companies with little or no in-house expertise in infectious or veterinary diseases – who are likely to be unwilling, and perhaps unsuited, to full-blown neglected disease R&D – can also take up the challenge by contributing creatively in other

ways. For instance, by providing greater access to in-house compounds; provision of platform skills such as portfolio management or regulatory support to PPPs; or encouraging and supporting senior staff to participate in PPP Scientific Committees or Advisory Boards.

Finally, we would like to pose a challenge for our own community of experts, the international public health community. One of the concerns about PPP drug development organizations is that, since there is generally only one PPP working on each disease, patients are at the mercy of that one group and its performance, or lack thereof. (Others, in particular governments, complain that there are too many PPPs and that they should be rationalized!) In response, there have been suggestions that we need to have a more competitive market for new neglected disease drugs, with multiple products being developed by different groups, thus allowing developing country patients the kind of choice that patients in developed countries have come to expect. This may well be true, but it also raises a number of questions. How many new products can developing country health systems absorb in each disease area? How many new Artemisinin Combination Therapies do we need in the near future (we currently have five additional adult formulations in development)? What about diseases that are largely managed through national control programmes (e.g. DOTS programmes for TB, or India's planned leishmaniasis eradication programme?) Could national TB programmes cope with a new product every five years, in the happy event that this were possible? Will the previous private marketing of miltefosine, our first oral anti-leishmanial, help or hinder India's plans for a controlled roll-out of the drug as part of its leishmaniasis programme? Would it be better to hold back new anti-malarial products until resistance has appeared or to market them as they became available? Who would be responsible for a decision to hold-back or the timing of a new release, or the task of dealing with producers keen to see rapid returns on their investment? Is it better to have one PPP managing a disease portfolio (allocating R&D investments, balancing the portfolio between discovery and development projects, and controlling product registration and release) or to have several groups independently pursuing products that could each be made available to patients as soon as it was ready? Given the paucity of funds, should R&D for each disease be planned and integrated (through a PPP or otherwise) or should we rely on more traditional competitive approaches?

We stress that we do not know the answers to these complex questions. The lack of neglected disease R&D activity for many decades means we have never before had to face the question of product management for neglected diseases – for some diseases, we were lucky to have any products at all. As a result, there has been little published and little open discussion of these issues. We raise them now only because they sometimes seem to be the elephant in the room – and elephants are ultimately very hard to sweep under the carpet. ❑

Mary Moran *trained as a medical doctor, working for 13 years in Emergency Medicine in Australia. A postgraduate degree in international relations and politics at University of NSW and Monash University (1995) led her into a diplomatic career with the Australian Department of Foreign Affairs & Trade, including a posting to London where she focused on climate change negotiations and international trade. Dr Moran subsequently worked for three years with Médecins Sans Frontières, initially as Director of the Access to Essential Medicines Campaign in Australia and later as a Europe-based advocate on a range of issues relating to access to medicines for neglected patients. In 2004, she founded the Pharmaceutical R&D Policy Project (PRPP) at the London School of Economics & Political Science and subsequently moved the unit to Sydney, Australia, where it was consolidated as the Health Policy Division (HPD) of The George Institute for International Health in 2006. The HPD maintains a London office as part of the new International Development Centre in Bloomsbury and is associated with the London School of Hygiene and Tropical Medicine.*

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Anne-Laure Ropar *originally trained and worked as a mechanical engineer. After completing a master's degree in political economy and international relations at the University of Chicago, she worked for a number of years as a consultant specializing in European and developing country health systems and policies. Her clients have included the EU-based pharmaceutical industry, philanthropic organizations (Rockefeller Foundation, Bill & Melinda Gates Foundation), and government bodies (DFID, USAID). Anne-Laure Ropar's project experience spans drug procurement policy in sub-Saharan Africa, market-based mechanisms to reduce the price of essential drugs in Ghana, to drug reimbursement policies in European countries. She joined the PRPP at its creation in 2004, where she has managed research on Product Development Partnerships and the pharmaceutical industry's involvement in neglected diseases, and worked on incentive proposals for both large pharmaceutical and small biotechnology firms. Anne-Laure now heads the HPD research team in the London office of The George Institute.*

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2. Moran M et al. *The new landscape of neglected disease drug development*. London School of Economics/ Wellcome Trust, September 2005.
3. Pyronaridine-artesunate, chlorproguanil-dapsone-artesunate and dihydroartemisinin-piperaquine (Artekin) by MMV; and AS-AQ and AS-MQ by DNDi (as handovers from an earlier group). MMV are also developing the first paediatric ACT formulation (Coartem in non-tablet form, with Novartis).

Decision-making

Delivering evidence to inform health system strengthening: the role of systematic reviews

Article by Sara Bennett

Increasingly health system bottlenecks are perceived as the principle barriers to scaling up the use of critical health services and achieving public health goals[1]. While this perception perhaps started with a concern about lack of human resources, there is now broader recognition of the problems that multiple health system constraints, such as inequitable systems of health financing, poor quality services, fragmented information systems, and weak accountability structures present. At the time of writing, several new major initiatives at the global level, including the UK government International Health Access Initiative, the Norwegian government Millennium Development Goals 4 and 5 Initiative, the Canadian government African Health Systems Initiative, as well as initiatives from the GAVI Alliance and potentially the Global Fund to Fight AIDS, TB and Malaria, indicate that there will be substantially increased investments in health systems in the near future. But how best to invest these new resources in order to achieve health goals?

While there are certain similarities across low- and middle-income country contexts in terms of the nature of health system barriers, there is also wide variation in health system structures and social values that mean it is not possible to craft a "one-size-fits-all" solution. Health systems interventions will never be able to be reduced to easy to prescribe formulae such as DOTS. National-level policy-makers must craft health policies, plans and system strengthening interventions that match their country's specific needs. What role can evidence and particularly evidence drawn from systematic reviews play in ensuring that the national policies and strategies chosen are effective?

During the past ten years Evidence Based Medicine has had a major impact on how clinicians, managers and policy-makers think about clinical practices[2]. Systematic reviews have the advantage of providing findings based upon the best available evidence, and in being transparent about the source of evidence and how the evidence has been interpreted. However in the context of health policy and systems research in low- and middle-income countries, systematic reviews have only been undertaken to a very limited degree, and although there is no data on the topic, it appears that to-date they have played virtually no role in influencing policy.

This paper focuses on the potential contribution that systematic reviews could make to policy decisions regarding health systems in low- and middle-income countries, and the challenges to actually using systematic reviews for this purpose. The paper does not address the nature of demand for systematic reviews by policy-makers nor their capacity to use and apply systematic review evidence, although both of these questions raise complex issues in their own right.

Systematic reviews have the advantage of providing findings based upon the best available evidence, and in being transparent about the source of evidence and how the evidence has been interpreted

The potential for systematic reviews to contribute to policy

For many questions that health policy and decision-makers might ask (What is the best way to extend financial protection to those seeking health care? How have health workers responded to alternative incentive mechanisms? Which strategies are most effective in terms of improving quality of care?) a substantial body of evidence exists, but this evidence is often scattered and not available in a form that decision-makers find easy to appraise or use. Systematic reviews of health policy and systems research have the potential to reduce bias in the estimation of the effectiveness of a policy option by identifying all relevant studies, selecting those that meet explicit criteria, appraising their quality, and synthesizing the results using a transparent process. Systematic reviews reduce the role that chance has to play in estimating effectiveness or cost-effectiveness, and allow more precise estimation of the impact of a policy option.

Systematic reviews offer considerable advantages to the decision-maker. First, drawing on an existing systematic review constitutes a more efficient use of time for research users, enabling them to draw upon the research literature without having to comb through it themselves. Second, research users are less likely to be misled by results of a systematic review than a single investigation and therefore can be more confident about what can be expected.

Challenges in employing systematic reviews for health policy-making

While in principle systematic reviews have much to offer the policy-maker, in practice, at this point in time, there are some real challenges in terms of their use in policy development. Four main challenges are described and addressed here, namely:

- addressing non-effectiveness questions;
- making decisions when evidence is scarce;
- adapting international evidence to local contexts;
- combining systematic review evidence with other types of information.

Broadening out from effectiveness questions – over the last two decades, scientists have established a reasonable consensus regarding "best practice" for systematic reviews that inform clinical decision-making regarding effectiveness, as well as public policy-making regarding adoption, use and discontinuation of health technologies. These methods rely heavily on the use of hierarchies of levels of evidence, with randomized controlled trials given the greatest weight. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies.

However, many of the questions which policy-makers raise regarding health systems do not concern whether or not a particular strategy works, but rather, how it should best be implemented, or how it might be perceived by stakeholders. Increasingly, systematic review methodologies have been applied to questions other than those about the effectiveness of interventions, however there is less consensus about the methodologies for conducting such reviews[3]. If systematic reviews are to be used to help policy-makers address difficult decisions regarding health systems, then greater methodological consensus and clarity on addressing non-effectiveness questions is required.

Making decisions when evidence is scarce – as noted above, systematic reviews have typically focused upon synthesizing findings from studies that have used experimental designs. However in the field of health policy and systems research, relatively limited evidence is generated through randomized controlled trials. In such circumstances, systematic reviews must rely more heavily on non-experimental analyses including controlled before/after studies and interrupted time-series studies. Although methods are available for synthesizing findings from such studies, they are less well known and less well developed than those for synthesizing findings from randomized studies.

But even if this broader range of study designs are included in the review, in many instances very few studies are available. For example, Lagarde and Palmer[4] conducted a systematic review of various health financing mechanisms, focusing only on studies conducted in low- and middle-income country contexts. For many of the mechanisms which they were interested in, there were very few studies that met their inclusion criteria[5], for example no studies were found of social health insurance mechanisms, one was found for community-based health insurance, and three for contracting out of health services. When so few studies are available, the information synthesized can be frustratingly thin, and not very helpful to policy-makers. Systematic reviews may still be useful, to at least point out the flimsy nature of the evidence base supporting the policy or intervention being considered, and thus underscoring the need for the simultaneous implementation of monitoring and evaluation mechanisms to ensure that no harm is done through the policy. However this challenge also implies: (a) that much greater investment is needed in well-designed, rigorous, impact evaluations and (b) that development of methods for the synthesis of other types of study design should be accelerated, while acknowledging that, depending on the nature of the question being asked, they may provide less reliable information.

Adapting international evidence to local contexts – most systematic reviews review the international evidence base, yet, as described above, there are major differences in the health systems of different countries, and thus the effects that alternative strategies to strengthen health systems might lead to. For example, Lewin et al[6] review the evidence on lay health workers. While they found many articles[7] that met their inclusion criteria, and they concluded that there was evidence of moderate to high quality supporting the effectiveness of lay health workers in the provision of specific services such as improving immunization uptake, and reducing childhood morbidity and mortality from common illnesses, the authors noted that for some services much of the available evidence came from industrialized countries and it was not clear whether the intervention effects would be transferable to other settings. With respect to the effectiveness of lay health workers, differences in contextual factors such as the availability of routine data, the availability of resources to provide clinical and managerial support, and the availability of drugs and accessible referral services are all likely to be critical. While some systematic reviews (e.g. Lagarde and Palmer 2007) focus on low- and middle-income country contexts alone, it is not clear that focusing only on studies from countries with a particular economic status necessarily leads to more relevant conclusions. Improved approaches to ensuring and assessing the transferability of review findings are needed.

Faced with a review that synthesizes evidence from a variety of potentially very different country contexts, policy-makers need to question whether there are important relevant differences in the structure of the health system, the on-the-ground realities and constraints, the epidemiological conditions, or the perspectives of health system stakeholders, that might mean that the review findings are not transferable to the context where they are being considered. Policy-makers, or policy analysts both need sufficient skills to make this assessment and be provided with sufficient information within the review for them to be able to assess transferability.

A further factor regarding the transferability of findings regards the scale at which the intervention was implemented; often systematic reviews of effectiveness questions capture data from impact evaluations of small scale, experimental interventions. Some interventions may be effective if

Equitable access: good intentions are not enough

Article by Robert Wells (pictured) and Judith Whitworth

Most countries do not have universal health insurance and for most people living in countries without universal access, particularly the poor, illness is a substantial financial burden, and indeed often a crippling burden. Paradoxically, a far greater proportion of out-of-pocket spending occurs in those countries least able to afford it. Inevitably, health care, far from being a basic human right, is simply beyond the reach of many.

As a proportion of gross domestic product (GDP), developed countries spend around 8–9% on health (this includes both government and private spending)[1]. In contrast, in lower- and middle-income countries' proportional expenditure is usually far less, e.g. Sri Lanka spent 1.3% and India 0.9% of GDP in 2004[2]. In Ghana per capita spending on health was estimated as US$ 8 per person per year in 2004[2]. This contrasts with the United States figure of around US$ 6100 in 2004. The Macroeconomic Commission on Health considered US$ 30–40 as the minimum necessary for basic health interventions[2]. These figures reflect in part relative wealth of countries, but clearly also are dependent on spending priorities of governments. Thus in many countries basic health interventions for all are not assured.

Some countries, most particularly wealthier countries, have schemes/systems for universal health insurance e.g. Australia, UK, many European countries. Ironically the world's richest nation, the USA, stands out both as not having a system of universal health and as spending absolutely and proportionally much more on health than any other country. Developed countries with comprehensive universal health insurance tend to spend less on health than those without such systems such as the USA[1] or with more limited universal coverage (such as Canada and Australia), although health outcomes are equivalent or better, pointing out the desirability of universal access. The USA spends nearly twice as much as the UK without any comparable improvement in health outcomes, and it has been estimated that at least some premature mortality in the USA represents inadequate access[3].

Universal access is generally regarded as a highly desirable policy. Yet even in this context, there are often inequities, which may not be intended. For example, in Australia factors which inhibit access and introduce inequity include uneven geographic distribution of health services; unequal capacity to afford "out-of-pocket" expenses (such as patient co-payments, travel, or time off work); the limited range of available services e.g., shortages in some speciality areas such as geriatrics, ophthalmology; the global problem of insufficient workforce which particularly affects rural Australia; and long waiting times for high demand services, which can be bypassed by the rich (via the private sector) but not by the poor.

These problems are magnified in lower- and middle-income countries, for example, in Tanzania a 1997 scheme to implement evidence based health plans at an estimated cost of US$ 2 per capita was limited by inadequacy of infrastructure and capacity[4]. These difficulties have been widely recognized and are seen in particular where increased spending on vertical programmes in areas of limited capacity and infrastructure have led to redirection and further weakening of resources available to the system as a whole.

There are further difficult questions around our understanding of what is equitable. For example, Australia spends around 1.5 times more per head on health care for its indigenous population than for non-indigenous people. However, the health status of indigenous people is appalling; with life expectancy almost 20 years lower than for the non-indigenous population. If expenditure is considered in terms of disease burden then indigenous health is significantly under-funded. Indigenous people living in remote areas have 10–20 times higher death rates than non-indigenous Australians from diseases such as diabetes, cervical cancer, respiratory disease and infections[5]. Suggestions for the additional spending required to improve health status for indigenous people range from two to three times that for non-indigenous people but these figures seem to have no firm basis and therefore would provide no guarantee of achieving a measurable improvement. There would probably be a need also for a concomitant proportional increase on social and infrastructure support spending for indigenous people.

The research agenda

What then are the research questions around equitable access? How long is a piece of string?

For example:

1. What do we mean by equity? Which aspect has primacy – dollars spent or health status or health outcomes?
2. How do we determine what is a reasonable amount to spend (or invest)? How can this best be contextualized and

harmonized with other government priorities? This is even more problematic when we consider that other areas of government spending e.g. education, housing, transport, may all impact on health in major ways.

3. Would there be more equitable access to health services if governance and decision-making were more open to input by community stakeholders? Another aspect of this question of governance is: how can governments reasonably reorder priorities given the range of pressures on their available resources?
4. Given the resource and other infrastructure constraints, particularly in poorer countries, what are the most appropriate health care delivery models for a country to adopt?

Given this possible research agenda, are these questions capable of analysis that is likely to lead to useful outcomes? Are they universal or is the specific context of local country considerations so dominant that no general conclusions can be drawn? Is there political will to address this agenda, let alone tackle the problems on the ground?

The first question, what is equity?, seems capable of answer, albeit not in a generalizable way. What people mean and want by equity could be established in specific contexts using focus groups and standard social research methodologies, for each level of government and decision-making. If people see equity of outcome as having primacy, then simple equity around allocation will not be enough. Nevertheless, unless there is some broad agreement on the answer to this question for a given society, allocation of resources and planning of services is much more difficult.

The second question, what is a reasonable amount to invest in health? is more difficult. However data are or will be available on how much countries spend and on return on investment as determined by health metrics, status and outcomes. The new institute for global health evaluations, the Gates Foundation funded Health Metrics and Evaluation Institute at the University of Washington in Seattle should fill a critical gap by providing better information on health metrics and health system performance[6]. These will include data on mortality, cause of death, disease and disability burden, risk factors, resource flows and assessments of health systems[6]. We know that above a certain level of spending, health improvements are not evident, e.g. USA. Cuba on the other hand has excellent outcomes for modest spending. However, below a certain level of spending, health status is poor and this is reflected in poor health outcomes for the poorest countries. It may be useful to compare country performance for like countries as a guide to allocative efficiency in a particular context. Analogous with the Australian indigenous situation, some focus on health outcomes would seem desirable particularly where there are varying local ethnic, cultural, social or geographical factors.

The third set of questions address governance and how actual spending priorities are determined and set. Again, social and cultural factors have primacy here, both in the process for decision-making and in determining the particular value sets for identifying and respecting priorities. Some principles that might guide governance could include measurement of what is done and evaluation of what is achieved, along with openness and transparency of decision making, and a long-term commitment to agreed plans and their implementation.

The fourth question is very important in providing capacity to move forward within the constraints of available resources and competing priorities. For many countries a high technology health system is an unrealistic expectation even for the longer term. The priority will be in dealing with basic health needs and public health measures. Mullan and Frehywot suggest, for example, that the use of non-physician clinicians in sub-Saharan Africa might be an effective means of meeting some of the workforce demands to meet current and future demand[7].

For many countries, the governance will be a key factor in providing some stability and at least medium-term certainty to the health system. Developing and sustaining a health system is a long-term challenge. The provision of basic health infrastructure and capacity, including access to the routine services and checks that help in maintaining good health and detecting emerging health problems for the population at large, is often well beyond the political horizon. Tackling urgent problems can often be undertaken at their expense. The temptation can often be to focus on one or two high-profile health problems or diseases or skew resource allocation in these areas. A robust governance system should allow these storms to be weathered without abandoning the whole ship.

This balancing of long-term sustainability against short-term crisis can be the hardest challenge for any health system.

The experience of all countries, rich or poor, is that there is an insatiable demand for health services. Achieving equity of health status depends on a range of factors, individual, environmental and political and not simply the nature of the health system, not the quantum of available resource. There are some important questions which need to be addressed to assist countries or regions in deciding how best to determine how much they might invest in health and how this investment might be made. Most important of all is political will. Decisions about health are made, often unintentionally, in policies around finance, education, defence, agriculture, transport, housing and so on, as much as they are by decisions within the health system. Perhaps we should rephrase our debates. Just as we have moved from thinking of health research to thinking of research for health, we should think of investment for health rather than investment in health. ❑

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Using evidence for policy-making in health

Article by Tikki Pang

How is evidence used in policy-making in health? The answer to this fundamental question requires an appreciation of the different mindsets, mentalities and "world views" of researchers and public policy-makers, and how these conditions influence the way they work, or do not work, together. An insight into this key dynamic then allows consideration of various possible solutions on how to improve this critical relationship so that scientific evidence may truly drive and inform health decision- and policy-making.

Goals, priorities, attitudes towards information, time pressures, accountability mechanisms and career paths tend to be different between researchers and policy-makers. They often distrust one another's motives, lack respect for each other, have different views on the production and use of evidence, different accountabilities, and disagree on the fundamental issue of whether there should be a link between science and policy. Some possible solutions can be put forward to improve the use of evidence in policy-making: using knowledge "brokers" (translational researchers), new and better incentives to encourage researchers and policy-makers to work together, organizational capacity-building and embedding research in implementation, utilizing a broader definition of research, re-defining the starting point for knowledge transfer, and, finally, acknowledging that policy-making is a highly complex process.

In the face of continuing global health challenges, times of scarce resources and competing priorities, the use of evidence to inform policy-making becomes a moral and ethical responsibility and should be the key driver for improving health system performance.

Researchers and policy-makers are different creatures living in different worlds

Despite the intuitive, logical assumption that scientific evidence should automatically inform policy, there are problems in implementation and evidence-based policy is a goal which is not always reached[1-5]. Many researchers are sceptical about the extent to which research is used, and, in turn, many policy-makers are sceptical about the usefulness of research in general. The causes for the disconnect are complex but are probably related to some key factors including the fact that researchers and policy-makers have different goals, speak different "languages" and have different time frames for their work.

A researcher has, as his primary goal, the generation of new knowledge and the advancement of science. She/he often measures success through the publication of scientific publications in peer-reviewed academic journals, with this activity often used as the primary criteria for career advancement (the "publish or perish" syndrome). They are often less interested in broader issues, for example, the "big-picture" social or policy aspects and impact of their work. The objective in the research world is "publications, patents, and professorships"[6]. Given the unprecedented rate of increase in knowledge, researchers tend to become extremely specialized and narrow in their field of research, often resulting in others (researchers and non-researchers alike) not able to fully understand or appreciate the importance of their work. They aspire to become an "expert/professor/specialist" and work largely according to a rational, intellectual model.

In contrast to this desire for recognition by peers, the goal of policy-makers is to obtain popular support. Much of their daily work is to "put out fires" and manage political crises and they are thus more interested in broader issues, e.g. solutions that can be generally applied to a wide variety of problems and which are politically acceptable. So, in contrast to the research community, the key considerations in the policy world is "policy, practice, and people"[6]. Because of time pressures and lack of necessary skills policy-makers have very little time to read or evaluate original scientific publications of primary research. Instead, they prefer to read short summaries or even just "bullet points". They strive to become a "Mr/Ms Fix-it and Jack of all trades", and better still is if they can do this across different portfolios. They search for compromise and rapid fixes, by using an intuitive, visceral model.

Research researchers speak their own language which normally consists of at least some Greek letters and mathematical symbols. Their language often requires "translation" before it can be understood by non-researchers,

Policy-makers	Researchers
Complex policy problems	Simplification of the problem
Focused solutions	Interest in related but separated issues
Reducing uncertainties	Finding the truth
Speed	Time to think
Control and delay	Publish or peril
Manipulation	Explanation
Feasible and pragmatic solutions	Thoughtful deliberations

Source: Bensing JM. Doing the right thing and doing it right: toward a framework for assessing the policy relevance of health service research. International Journal of Technology Assessment in Health Care, *2003, 19:604-512.*

Table 1: Conflicting interests of policy-makers and researchers

or even fellow researchers in a different field. Researchers often add a standard clause at the end of their papers stating that "our research indicates that more research is needed". This is, of course, both exculpatory ("don't blame me if this isn't correct") and self-serving ("but if you give me more money I might be able to give you a better answer"). Herein lies a key point of distrust: policy-makers believe that researchers do research primarily to generate more funding for more research, and not for the potential value of the research to society.

"Policy speak" is often used to describe the language which policy-makers use and it often contains acronyms, which in turn are defined by other acronyms. Much of the communication is confidential in nature and for a closed audience, and driven by unpublicized political agendas. They often include multiple signatures or are anonymous (containing no signatures), and are often stamped as "confidential". While policy-makers do sometimes conduct research, it is rare to see their findings published in peer-reviewed scientific journals, if released at all. In general, the culture of open sharing of knowledge and information is not part of the policy-making world.

Scientific research in general is driven by fairly long time frames. Researchers want time for contemplation, thinking, formulating hypotheses, analysis, syntheses, talking to colleagues and more reflection. In general, it is believed that the longer it takes to do a research study, the better the research quality. It is also a fact that the process of science is a cumulative one and builds on the previous work of others. Many researchers spend their entire research career in one narrow subject area, in order to build up their expertise and track record, as well as national and international reputation in that area – to many, this is an end in itself.

In contrast, policy-makers work to a very different, much shorter time scale, often a matter of days or weeks. Answers are always needed instantly and the time pressures often take precedence over quality, since they must have prompt and firm opinion to look credible. This is reflected in the classic policy-makers' sentiment, "I have made up my mind, don't confuse me with the facts". Policy-makers usually have short tenure managing projects, and will move on quickly to other responsibilities, in order to build up their repertoire of expertise in a wide variety of different areas. The conflicting interests of policy-makers and researchers is given in Table 1.

Why are they different?

The incompatibilities between researchers and policy-makers lead to very real problems in terms of promoting better use of evidence for health policy development. If they are to work together, researchers and policy-makers must know each other's strengths and weaknesses, as well as likes and dislikes. There are a number of key issues that must therefore be addressed.

Researchers and policy-makers often lack trust and respect for the respective roles that they play. Researchers often have a "superiority complex" which translates into a condescending attitude and a lack of respect for those who are not researchers. They often take the view that their research is to be reviewed only by their peers and find it difficult to conduct "directed" or "applied" research, regardless of the potential benefits to society in general. They consider "academic freedom" to be sacrosanct and expect to be allowed to pursue their interests with no constraints. Therefore, they often resent the power of policy-makers to control research funding and the frequent misuse that is made of scientific data to fulfil a politically-driven policy agenda. At the same time, policy-makers resent the arrogance of researchers, the seeming self-fulfilment and self-serving nature of much of their research, and their narrow, tunnel vision approach to the world. Scientific input is often untimely, less-than-relevant, abstract and impossible to understand or contextualize. In extreme situations, they view scientific evidence as being detrimental to political and economic considerations, e.g. when evidence of an infectious disease outbreak can lead to economic loss as a result of reduced numbers of tourists.

In addition, researchers and policy-makers often have different views as to what constitutes evidence. Many scientific results are quantitative and can be assessed in rigorous, repeatable ways. Researchers obsess about research methodology and the "levels of evidence" gathered through different study designs, such as clinical trials and observational studies. Policy-makers, on the other hand, are often more informal in their assessment of information, even that of a quantitative nature. They look for important information based on quick reflections of reality for policy-making, e.g. poll results, opinion surveys, focus groups in marginal electorates, anecdotes and real-life stories. They operate on a different hierarchy of evidence – their "levels of evidence" may range from "any information that establishes a fact or gives reason for believing in something" to "available body of facts or information indicating a belief or proposition is true or valid".

Should researchers cater to the needs of policy-makers? Policy-makers are often frustrated because researchers cannot give them a quick, clear and simple answer. Researchers are frustrated because required data may not exist, or they do not know the answer or want to admit problems with their studies, or they cannot explain their complex findings in a simple language. Policy-makers believe that much of the research being conducted is pointless and lacks relevance, which is probably right as the motivation on the part of the researchers is often scientific curiosity and the

desire to publish. The core of the issue in using evidence differently lies in the differences in decision-making imperatives. Not only might scientific evidence conflict with values and beliefs of policy-makers, but the policy-maker uses evidence in the battle to control problem definition and policy solutions. Policy-makers thus look for evidence to support their claims, and thus systematic bias occurs in the way that policy-makers look for and use data. Another facet of this issue is that policy-makers are often concerned that highlighting knowledge gaps will reduce support for their programmes. They thus end up making uninformed decisions.

Further complicating the issues are the weaknesses in logic in both scientific and policy-making approaches to setting priorities and achieving outcomes. Science and policy-making are chaotic in different ways. Most scientific research is derivative, and unhelpful from a policy perspective. The 23rd paper on smoking and a certain disease may still be published, but it is not really advancing science unless the study is somehow markedly better than previous studies; too often, it is not. In other words, there is a lot of indifferent or "junk" science out there, and policy-makers are clever enough to recognize this. Policy-making is built on a history of related policies, but is also reactive to numerous and competing stakeholder demands. At the end of the day, policies are the result of compromises and are constantly framed and re-framed in response to changing contexts.

Also, researchers are always wanting to hedge their findings – they recognize the limitations of their data and are striving to provide proof "beyond reasonable doubt" – however, policy-makers need a simple one-line answer to what are often, at least to the researchers, complex issues. In presenting their results, researchers traditionally rely on so many caveats that policy-makers do not know what to believe. Policy-makers frequently have to exercise moral judgements in the face of uncertainty, so decisions are taken "on the balance of probabilities". They usually have plenty on their plates, and gravitate towards evidence that speaks to their own experiences, or that of their constituents. They seek a "one size fits all" or "cookie cutter" approach. Policy-makers want a "bottom line", but researchers are uncomfortable giving one.

Facilitators	Number of studies
Personal contact between researchers and policy-makers	13
Timeliness and relevance of the research	13
Research that includes a summary with clear recommendations	11
Research that confirms current policy or endorses self-interest	6
Good quality research	6
Community pressure or client demand for research	4
Inclusion of effectiveness data	3
TOTAL studies	24
Barriers	**Number of studies**
Absence of personal contact between researchers and policy-makers	11
Lack of timeliness and relevance of research	9
Mutual mistrust between researchers and policy-makers	8
Power and budget struggles	7
Poor quality of research	6
Political instability or high turnover of policy-making staff	5
TOTAL studies	24

Table 2: Facilitators and barriers to use of research by policy-makers, identified in a systematic review of 24 interview studies (tabulation of data provided by Innvaer et al., 2002[7])

Researchers and policy-makers also tend to have different accountability mechanisms. Researchers are essentially accountable to editors of peer-reviewed journals, fellow researchers and those who fund their research. They may be interested in policy but, at the end of the day, are not required to focus on issues that have policy relevance or application. On the other hand, policy-makers are usually accountable to political parties, government and taxpayers, if not the voters, and must focus on things that are consistent with political agendas. Complicating this however is the increasing pressure on researchers to comply with views of governments that are increasingly responsible for setting priorities in the way research funds are allocated. So smart researchers will have their research proposals reviewed by policy-makers before submitting their grant proposals.

There is unfortunately no correlation between the quality of science and the policy derived from it. Good science does not always guarantee good policy; bad or even no science does not necessarily lead to bad policy. It is true that good policy does not always depend on waiting for good evidence. For example, condom promotion makes good common sense when setting policies to tackle sexually transmitted diseases. On the other hand, having a policy, no matter how carefully thought out, is no guarantee that it works. Having a policy for clean water, for example, does not necessarily make the water clean. It must be realized that science is needed both to help develop the policy and to evaluate the policy.

Another issue is related to the public image. Researchers are often respected as "wise and objective people", free from political and economic interests and pressures. Policy-makers are often regarded as "powerful people", but are not necessarily respected. It is not that either researchers or policy-makers are "wrong" or "bad". One responds to scientific rationality, while the other responds to political pressures. Furthermore, the societies within which they work also have norms and expectations, which might be considered "cultural rationality". The coming together of these competing rationalities is necessary to resolve the seeming incompatibilities and ultimately ending up with the adoption of evidence-based health policies.

Some suggestions on bridging the gap

How can we bridge this chasm and gap between researchers and policy-makers? Arguably, a key first step might be an attempt to understand what may be the predictors of success (and failure) in the way researchers and policy-makers communicate and value each others' efforts. Innvaer et al. reviewed 24 interview studies with health policy-makers (a total of 2041 interviews) concerning their perceptions of the use of research evidence in health policy decisions[7]. The most commonly reported facilitators were personal contact (13/24

interview studies), timely relevance (13/24), and the inclusion of summaries with policy recommendations (11/24) (Table 2). The most commonly reported barriers were absence of personal contact (11/24), lack of timely relevance of research (9/24), and mutual mistrust (8/24). The question then is how to fully recognize the incompatibility problems and to promote successful experiences in the collaboration between researchers and policy-makers, i.e. promote facilitators and suppress barriers. Also, the solutions to the questions run deeper than simply putting the researchers and policy-makers in personal contact, or just asking researchers to provide timely and relevant findings. Some specific suggestions can be proposed.

Knowledge brokers

Given the differing values, perspectives and language described above, a suggestion has been made that one possible mechanism to consider is the development of a cadre of knowledge "brokers" or "facilitators"[2,4,8]. Such knowledge brokers may serve as a catalyst to look for, and nurture if possible, the relationship between the two groups. In other words, they can ensure that policy-makers are employing "the right science", and that researchers are doing "the science right"[3]. For example, by integrating and synthesizing scientific information into more accessible formats, good knowledge brokers may be able to say to the policy-makers who are swamped with information, "Here is the list of the top 10 major issues in this country according to current knowledge". The knowledge broker may then turn to the researchers, "Give me the science on what works to tackle these issues" and then produce an inventory of evidence-based best practices. The demand for evidence and information should, ideally, come from the policy-makers themselves but this often does not happen. A critical role of the knowledge broker is to "translate" this demand and "re-translate" information which comes from the research community – in a way which is understandable and transparent, including evidence which is "in conflict" with what policy-makers have already decided. Knowledge brokerage can also be seen as initiatives to simplify and present the information in a way that is more attractive to policy makers – a good example is the Health Evidence Network set up recently by the World Health Organization (WHO), which goes a step beyond Cochrane style systematic reviews and tries to come up with one-page policy briefs in response to questions posed by policy-makers[9]. Another variation on this theme is the idea of "trading places", a temporary "job exchange" programme where policy-makers and researchers take each others' places for a period of time to enable them to obtain insights into the other's point of view. This practice has been tried, for example, between chief executives and lobbyists in Canada.

Better incentives

Research funding does not usually provide for information dissemination to policy- and decision-makers. Engagement with the public and with policy-makers, is not rewarded. Incentives are also needed to encourage policy-makers to acquire a higher level of scientific training than is the present norm. Scientific thinking and results can be dumbed down only so much before becoming meaningless. On the other hand, at least some researchers need to develop a sense of the "big picture" and work on ways to make scientific work understandable and usable by intelligent lay people. Unfortunately, none of these will happen unless there are incentives for them. The current reward mechanisms simply do not work optimally to encourage policy-makers and researchers to work together. However, what incentives are there for this partnership? New incentives may have to be created in order for changes to take place. An obvious starting point would be to include links to policy as another criteria in academic promotion, instead of solely relying on the number of papers published.

Building organizational capacity and embedding research into implementation

Attempts should also be made to include mechanisms, processes and structures within organizations to ensure there is input from researchers and policy-makers. For example, the American Association for the Advancement of Science (AAAS) has a programme where researchers are actively encouraged to enter the policy-making arena[10] by putting them into staff roles at the federal and local levels thus creating a cohort of politically informed citizens-researchers. A range of possible workforce development approaches and appointment strategies could be considered, e.g. requiring diverse skills, secondments, job rotations, dual appointments, liaison units, etc. Skills required of policy-makers in the future will likely be different because the world of public administration is changing. The idea of a "chief knowledge officer"[11,12] has been put forward and there are suggestions that this individual should actually be the chief medical officer of a country. In an attempt to "do the science within government", the World Health Organization has launched an initiative called EVIPNet (Evidence-informed Policy Networks)[13] which aims to establish national mechanisms and structures to facilitate better linkages and dialogue between researchers and policy-makers. WHO followed a model recently established in East Africa where Tanzania, Kenya and Uganda have jointly established the REACH-Policy (Regional East African Community Health-Policy) initiative, which has as its goal the more effective use and application of knowledge to strengthen health policy and practice.

A broader definition of research

If research is defined more broadly, it may be easier to argue that research is an investment, not a cost; that all countries should have a health-research system that drives health-sector reform; that research should be applied to improve health equity; that research must be conducted according to universal ethical standards; and that the results of research should be accessible to all. A key challenge in public health is the use of knowledge in strengthening health systems[4]. To strengthen health systems, there is a need for human resource development through, among other things, strengthening capacity for operational research in health

systems development. Partnerships are urgently needed between government policy bodies and academic/research organizations experienced in this area.

Re-defining the starting point

It is time perhaps to change the starting point, i.e. public policy-makers must be placed at centre stage and researchers should aim to serve their needs. In addition, citizens and civil society have a vital – and so far neglected – role to play in setting research priorities[14] and having an influence on policy formulation. There is an important role of the citizen or community in evidence-based policy, for example, in the increasing community engagement and citizen participation in health systems and the increasing trend towards including patient and public input into research. Research-funders and policy-makers have to become a lot more skilled at ensuring that researchers spend a lot of their time researching the questions that have the greatest potential to improve society. They should be encouraged to fund synthesis research and impact assessments in support of policy decisions. The trick here is to connect science with policy, and policy with science. It is desirable to have both "evidence-based policy" and "policy-based evidence"[15]. In other words, policies should be based on evidence, and once policies have been formulated, there should be evidence on how to achieve the set goals, and to develop, implement and evaluate needed strategies. There is no better way than to have policy-makers intimately engaged in the science. However, one must be careful to make sure that "evidence-based policy-making" does not become "policy-based evidence-making", i.e. creating and selecting evidence that suits and justifies certain formulated policies. Sometimes policy-makers want to stretch the interpretation of research findings to reinforce the "validity" of the policies they are already decided upon. There are potential problems when researchers get too close to policy, e.g. concerns about loss of objectivity and freedom to criticize government policy, and how to guard against this.

Policy-making is complex

It should be acknowledged that it is too simplistic to think that policy-making could ever be based solely on scientific evidence. In addition to scientific evidence, policies are also based on values, emotions, "know-how", intuition, "gut feeling" and the wishes of interest groups, for example. The reality of how decisions are made dictates that scientific evidence is only one consideration among several. Such evidence can even in its best form be only background. In some cases, it is perfectly possible for wise policy-makers to develop good policies without research. In other cases, policy-makers listen more to the voters than to the researchers. We should perhaps admit this and not set unrealistic expectations for the role of scientific evidence, and acknowledge that, on the other hand, failing to grab accessible evidence may delay intervention opportunities. For example, it took 263 years after the discovery of the preventive value of citrus juice against scurvy before sailors' shipboard diets were routinely supplemented with it at the end of the 19th century. The link of smoking to lung cancer was found in 1950 but it was not until 1957 that any legislative action was initiated. How long will it take to tackle the current epidemic of obesity if our will to intervene awaits the delivery of perfect evidence that proposed solutions will work? Thus, the balance between action and further research is an interesting and important one. When do we need policy decisions and when do we need more research? ❑

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Towards evidence-informed policy-making in human resources for health: the state of research

Article by Manuel M Dayrit (pictured), Mario Roberto Dal Poz, Hugo Mercer and Carmen Dolea

Health systems in many countries are failing to respond to the health needs of their population. Part of the reason for this is the current crisis in the health workforce, which is expressed in severe shortages, imbalances and a poor knowledge base on effectiveness of interventions. In order to make health systems more responsive to current and emerging health needs, countries must strengthen their health workforce. Research can help policy-makers pose and find answers to the critical questions regarding the status of their workforce, its level of performance and the problems health workers face.

Need for more evaluation studies to know what works and what does not

Research is required – not only to give policy-makers a better understanding of the present situation of their country's health workforce, but also to discover which policy interventions work or do not work. What can we say about the status of research in human resources for health?

First, the knowledge base in human resources for health development is weak and uneven overall, compared to other domains of health systems research, such as health financing or health sector reform, even though efforts to identify priorities in the health workforce research agenda have already started[1,3]. Given that close to half of health expenditure is spent on the health workforce, it seems incredible that there is so little research investment or solid evidence in this area. Moreover, the existing knowledge base is largely skewed towards high-income countries, medical doctors and descriptive reports, as opposed to intervention studies or best practice assessments[1,2].

An examination of the Cochrane Collaboration systematic reviews identified only 12 reviews on topics related to human resources for health, most of them in the domain of health workforce management[4]. A more detailed analysis points out that not only is there a very limited number of systematic

Title of Cochrane systematic review	Research question	Number of studies (initial/final)	Total number of subjects	Results
Substitution of doctors by nurses in primary care	To investigate the impact of nurses working as substitutes for primary care doctors on: ✣ health outcomes ✣ process of care ✣ resource use ✣ costs	4253 articles initially 25 articles, relating to 16 studies, met inclusion criteria	n/a	✣ No difference in quality of care and health outcomes between appropriately trained nurses and doctors. ✣ Nurses tend to provide more health advice and achieve higher levels of patient satisfaction, compared with doctors. ✣ Even though using nurses may save salary costs, nurses may order more tests and use other services, which may decrease the cost savings of using nurses instead of doctors.
Lay health workers (LHW) in primary and community health care	To assess the effects of LHW interventions in primary and community health care on health care behaviours, patients' health and well-being, and patients' satisfaction with care	8637 abstracts initially 400 potentially eligible 43 eventually included	210 110 consumers	✣ LHWs show promising benefits in promoting immunization uptake and improving outcomes for acute respiratory infections and malaria, when compared to usual care. ✣ For other health issues, evidence is insufficient to justify recommendations for policy and practice. ✣ There is also insufficient evidence to assess which LHW training or intervention strategies are likely to be most effective.
Audit and feedback: effects on professional practice and health care outcomes	Are audit and feedback effective in improving professional practice and health care outcomes?	85 RCTs Only 10 of the 85 included studies to be of high methodological quality	>3500 health professionals	✣ Audit and feedback can improve professional practice, but the effects are variable. ✣ When it is effective, the effects are generally small to moderate. ✣ The results of this review do not provide support for mandatory or unevaluated use of audit and feedback.

Table 1: Short description of results of three Cochrane systematic reviews on human resources for health

reviews in this field, but the final number of studies that met the selection criteria is very limited, too, compared to the initial pool of abstracts. This may mean that either the selection criteria for systematic reviews were too rigid, or the actual number of good quality evaluative studies in the field of human resources for health has been limited (see Table 1 for a detailed analysis of three of the systematic reviews). Also, most of the studies come from developed countries.

Second, much of the research is descriptive. For example, available studies have pointed to global shortages, regional imbalances and increasing migration of health workers, as well as dissatisfaction of health workers with their working conditions[5-9]. On the other hand, many country-based situation analyses have pointed towards geographical imbalances and significant understaffing in rural areas. There are paradoxical in-country shortages of nurses even where many nurses remain unemployed. And there are situations where doctors engage in dual employment[10, 11].

Third, the knowledge about effective solutions to address challenges described is far less developed[5, 12, 13]. And herein lies a major gap. From a country perspective, policy-makers need to know what solutions are available to them. They would also like to know how much an intervention will cost, how difficult it is to implement and its likely impact in the short run. Knowing what sort of interventions have worked in other settings would give them an idea of what they can try in their own context.

Currently, there are very few evaluation studies of effective interventions or impact assessment studies on human resources for health. Also, there are very few sources of best practice collections in health workforce development. Efforts have started to systematize the knowledge about effective interventions, but only a very small number of promising policy levers were identified through an extensive search of recent systematic reviews[14].

Need for more operations and context-specific research

What is really needed is more operational research and context-specific research. Policy-makers in countries may not have the means to support sophisticated research such as systematic reviews, but they should certainly have the capacity to use it. Hence there is a need to develop the critical mass of researchers in countries, with the appropriate skills to do research, use it and make its relevance evident to policy-makers. Also, country-based studies should be encouraged by policy-makers, within the umbrella of a national strategy of health research that should accommodate the priorities of Human Resources for Health (HRH) research within the priorities of overall health system research.

In general, preference should be given to research that:

- develops and evolves from purely descriptive studies to conceptual research, policy analysis and operations research;
- promotes international and comparative research by considering multi-site, multi-level and multi-country research projects to improve comparability and transferability of findings, such as the African migration study or the European nursing exit study;
- integrates research into ongoing or planned interventions and processes such as health sector reforms so that lessons can be drawn, compared and shared from the experiences of different countries[1].

Bringing the answers into the policy-making process

Once research has provided us with the answers we need, we should move to the next stage: using that knowledge.

In the field of human resources for health, effective action must cut across many sectors. These include, among others: health, education, labour, civil service, the private sector – which operates many educational institutions – and the regulatory system. Gathering all the various actors, researchers and policy-makers from the different sectors around the same table will take some doing. A recent example from Canada may provide inspiration for similar processes to be developed in other settings.

In the year 2000, the Canadian government established a new national programme of Research Chairs to attract and retain some of the best researchers. One of the specific aims of the Chairs is to promote the best possible use of research resources through strategic institutional planning and through collaboration among institutions and between sectors. For example, in the domain of health workforce research at the University of Toronto, research topics are both agreed upon and discussed with local and national policy-makers. The process of engaging policy-makers in the development of research topics, keeping them informed of the results of research and cultivating champions among policy-makers has helped to address some crucial policy issues in nursing workforce development in Canada (L O'Brien-Pallas, oral presentation at World Health Organization (WHO), Geneva, January 2006).

Regional and national observatories are other potential mechanisms for harvesting and disseminating new knowledge, provided they effectively engage the full range of stakeholders and their institutions. The experience of the Observatory on Human Resources for Health in the region of the Americas demonstrates that the observatory can be an effective mechanism to improve information and evidence and to advance the advocacy for human resources issues. The recently launched Africa HRH Observatory is hoped to provide a new impetus for research and evidence for that region[15].

The way forward: encourage local production and reach out to external research

In conclusion, without good research to answer the policy questions in health workforce development, we will fail to find innovative solutions to long-festering problems. Policy-makers must reach out to researchers in their own countries and facilitate the development of national research within the framework of a national strategy of health systems research.

Therefore, this policy brief recommends that both policy-makers and researchers at country level:

- develop a critical mass of researchers in the field of health workforce research;
- build health workforce research into national health systems research agendas;
- strengthen the link between policy-makers and researchers at country level;
- promote innovative approaches to bridge the gap between producers and users of research – for example, by organizing workshops that bring together policy-makers and researchers;
- harness the production of and increase the access to locally developed research, including operational research;
- promote access to external research by creating networks of researchers and building libraries of best practices. ❑

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Inequities in health status: findings from the 2001 Global Burden of Disease study

Article by Alan Lopez (pictured) and Colin Mathers

The 1990 Global Burden of Disease (GBD) study developed a comprehensive framework for integrating, validating, analyzing, and disseminating fragmented information on the health of populations so that it is truly useful for health policy and planning[7]. Features of this framework included the incorporation of data on nonfatal health outcomes into summary measures of population health (described in the next subsection), the development of methods and approaches to estimate missing data and to assess the reliability of data, and the use of a common metric to summarize the disease burden both from diagnostic categories of the international classification of diseases (ICD) and the major risk factors that cause those health outcomes.

The basic philosophy guiding the burden of disease approach is that almost all sources of health data are likely to have information content provided that they are carefully screened for plausibility and completeness and that internally consistent estimates of the global descriptive epidemiology of major conditions are possible with appropriate tools, investigator commitment, and expert opinion. This philosophy remains central to the GBD 2001 study, which has expanded the framework of the original GBD study to:

- quantify the burden of premature mortality and disability by age, sex, and region for 135 major causes or groups of causes;
- develop internally consistent estimates of incidence, prevalence, duration, and case fatality rates for more than 500 *sequelae* resulting from the foregoing causes;
- analyze the contribution to this burden of major physiological, behavioural, and social risk factors by age, sex, and region.

Estimating mortality: methods and data

Complete death registration data cover only one third of the world's population. Some information on another third is available through the national sample registration systems and urban death registration systems of India and China. For the remaining one third of the world's population, including most countries in sub-Saharan Africa, only partial information is available from epidemiological studies, disease registers, and surveillance systems.

To estimate the number of deaths by cause we drew on the following four broad sources of data:

- **Death registration systems.** Complete or incomplete death registration systems provide information about causes of death for almost all high-income countries and for many countries in Europe (Eastern) and Central Asia and in Latin America and the Caribbean. Some vital registration information is also available in all other regions.
- **Sample death registration systems.** In China and India, sample registration systems for rural areas supplement urban death registration systems. Information systems now provide information on causes of death for several other large countries for which information was not available at the time of the original GBD study.
- **Epidemiological assessments.** Epidemiologists have estimated deaths for specific causes, such as HIV/AIDS, malaria, and tuberculosis (TB), for most countries in the regions most affected. These estimates usually combine information from surveys on the incidence or prevalence of the disease with data on case fatality rates.
- **Cause of death models.** The cause of death models used in the original GBD study[7] were substantially revised and enhanced for estimating deaths by broad cause group in regions with limited information on mortality. The CodMod software developed for this study and described later drew on a data set of 1613 country-years of observation of cause of death distributions from 58 countries between 1950 and 2001.

For the GBD 2001 study, age- and sex-specific death rates were calculated from the death and population data provided by countries, with adjustments made for completeness of the registration data where needed, and then total deaths by age and sex were calculated for each country by applying these rates to the United Nations Population Division estimates of de facto populations for 2001.

Four methods were used to construct life tables for each country depending on the type of data available[2]:

- **Countries with death registration data for 2001.** Such data were used directly to construct life tables for 56 countries after adjusting for incomplete registration if necessary.
- **Countries with a time series of death registration data.** Where the latest year of death registration data available

was prior to 2001, a time series of annual life tables (adjusted if the registration level was incomplete) between 1985 and the latest available year was used to project levels of child and adult mortality for 2001. For small countries with populations of less than 500 000, moving averages were used to smooth the time series. Projected values of child and adult mortality were then applied to a modified logit life table model[6], using the most recent national data as the standard, to predict the full life table for 2001, and HIV/AIDS and war deaths were added to total mortality rates for 2001 where necessary. This method was applied for 40 countries using a total of 711 country-years of death registration data.

- **Countries with other information on levels of child and adult mortality.** For 37 countries, estimated levels of child and adult mortality were applied to a modified logit life table model[6], using a global standard, to estimate the full life table for 2001, and HIV/AIDS deaths and war deaths were added to total mortality rates as necessary. For most of these countries, data on levels of adult mortality were obtained from death registration data, official life tables, or mortality information derived from other sources such as censuses and surveys. The all-cause mortality envelope for China was derived from a time series analysis of deaths for every household in China reported in the 1982, 1990, and 2000 censuses. The extent of underreporting of deaths in the 2000 census was estimated at about 11.3% for males and 18.1% for females[1]. The all-cause mortality envelope for India was derived from a time series analysis of age-specific death rates from the sample registration system after correction for underregistration (88% completeness)[8].
- **Countries with information on levels of child mortality only.** For 55 countries, 42 of them in sub-Saharan Africa, no information was available on levels of adult mortality. Based on the predicted level of child mortality in 2001, the most likely corresponding level of adult mortality (excluding HIV/AIDS deaths where necessary) was selected, along with uncertainty ranges, based on regression models of child versus adult mortality as observed in a set of almost 2000 life tables judged to be of good quality[2,6]. These estimated levels of child and adult mortality were then applied to a modified logit life table model, using a global standard, to estimate the full life table in 2001, and HIV/AIDS deaths and war deaths were added to total mortality rates as necessary. Evidence on adult mortality in sub-Saharan African countries remains limited, even in areas with successful child and maternal mortality surveys.

Classification of causes of disease and injury

Disease and injury causes of death and of burden of disease were classified using the same tree structure as in the original GBD study[7]. The first level of disaggregation comprises the following three broad cause groups:

- Group I: communicable, maternal, perinatal, and nutritional conditions;
- Group II: noncommunicable diseases;
- Group III: injuries.

Each group was then divided into major cause subcategories, for example, cardiovascular disease (CVD) and malignant neoplasms (cancers) are two major cause subcategories of Group II. Beyond this level, two further disaggregation levels were used, resulting in a complete cause list of 135 categories of specific diseases and injuries.

Group I causes of death consist of the cluster of conditions that typically decline at a faster pace than all-cause mortality during the epidemiological transition. In high-mortality populations, Group I dominates the cause of death pattern, whereas in low-mortality populations, Group I accounts for only a small proportion of deaths. The major cause subcategories are closely based on the ICD chapters with a few significant differences. Whereas the ICD classifies chronic respiratory diseases and acute respiratory infections into the same chapter, the GBD cause classification includes acute respiratory infections in Group I and chronic respiratory diseases in Group II. Note also that the Group I subcategory of "causes arising in the perinatal period" relates to the causes included in the corresponding ICD chapter, principally low birth weight, prematurity, birth asphyxia, and birth trauma, but does not include all causes of deaths occurring during the perinatal period, such as infections, congenital malformations, and injuries. In addition, the GBD includes only deaths among children born alive and does not estimate stillbirths.

The GBD classification system does not include the ICD category "Symptoms, signs, and ill-defined conditions" as one of the major causes of deaths. The GBD classification scheme has reassigned deaths assigned to this ICD category, as well as some other codes used for ill-defined conditions, to specific causes of death. This is important from the perspective of generating useful information to compare cause of death patterns or to inform health policy-making, because it allows unbiased comparisons of cause of death patterns across countries or regions.

Deaths are categorically attributed to one underlying cause using ICD rules and conventions. In some cases where the ICD rules are ambiguous, the GBD 2001 follows the conventions used by the GBD 1990 study[7]. It should also be noted that a number of causes of death act as risk factors for other diseases. Total mortality attributable to such causes may be substantially larger than the mortality estimates for the cause in terms of ICD rules for underlying causes. For example, the GBD 2001 estimates that 960 000 deaths were due to diabetes mellitus as an underlying cause, but when deaths from CVD and renal failure attributable to diabetes are included, the global total of attributable deaths rises to almost 3 million[9]. Other causes for which important components of attributable mortality are included elsewhere in the GBD cause list include hepatitis B or C (attributable liver cancer and renal failure), unipolar or bipolar depressive disorders and schizophrenia (attributable suicide), and blindness (mortality attributable to blindness whether from infectious or non-infectious causes).

		Deaths (millions)	Crude death rate per 1000	% of deaths under 5	% of deaths over 60	Probability of dying per 1000 5q0	Probability of dying per 1000 45q15	Probability of dying per 1000 60q0	Probability of dying per 1000 20q60	Expectation of life at birth (years)
Low- and middle-income	1990	22.5	10.1	27.9	39.5	98	269	351	712	59.9
	2001	22.5	9.7	21.2	42.2	86	269	341	667	61.2
East Asia and Pacific	1990	6.6	8.0	16.3	50.6	54	215	265	699	64.9
	2001	6.9	7.4	10.2	56.2	41	189	228	623	67.8
Europe and Central Asia	1990	2.5	11.1	7.9	55.9	45	286	323	696	63.6
	2001	3.0	13.0	3.2	59.6	32	328	353	711	63.0
Latin America and the Caribbean	1990	1.7	7.8	19.5	44.7	56	245	294	640	64.5
	2001	1.8	7.0	12.4	49.1	38	218	252	572	67.6
Middle East and North Africa	1990	1.0	8.2	34.9	34.2	83	247	318	688	62.0
	2001	1.1	6.8	21.6	45.2	56	216	267	674	65.2
South Asia	1990	6.8	11.7	32.4	35.0	122	310	407	754	56.4
	2001	7.1	9.9	25.1	39.2	94	285	362	710	59.9
Sub-Saharan Africa	1990	3.9	15.6	54.1	17.0	191	386	517	758	49.6
	2001	5.6	16.9	42.2	16.9	178	518	616	760	46.0
High-income	1990	3.9	9.1	1.7	76.2	12	148	160	542	72.9
	2001	4.0	8.8	1.0	78.7	7	124	132	469	75.5
World	1990	26.4	10.0	24.0	44.8	91	245	323	667	61.7
	2001	29.5	9.6	18.5	47.2	80	243	312	618	63.1

Note: a) Estimates for 1990 based on country-level life tables from vital registration data or Modmatch (see methods section)
b) Estimates for 2001 derived from Lopez et al. 2002 c) Estimates for child mortality to nearest whole number. Source: Lopez et al. 2006

Table 1a: Selected mortality characteristics in males by World Bank region, 1990 and 2001

		Deaths (millions)	Crude death rate per 1000	% of deaths under 5	% of deaths over 60	Probability of dying per 1000 5q0	Probability of dying per 1000 45q15	Probability of dying per 1000 60q0	Probability of dying per 1000 20q60	Expectation of life at birth (years)
Low and middle-income	1990	19.4	8.9	29.7	44.6	95	182	270	585	64.2
	2001	22.8	8.8	22.5	48.3	86	191	271	554	64.9
East Asia and Pacific	1990	5.5	7.0	17.8	56.2	53	152	204	577	68.8
	2001	6.1	6.8	11.4	64.6	44	127	171	519	71.3
Europe and Central Asia	1990	2.4	9.9	6.4	77.5	37	125	162	503	72.3
	2001	2.7	10.8	2.9	81.5	26	133	159	511	72.8
Latin America the Caribbean	1990	1.3	5.7	20.1	53.9	45	138	182	493	71.3
	2001	1.4	5.4	12.5	61.3	32	124	155	434	73.9
Middle East and North Africa	1990	0.8	6.9	37.7	36.1	76	174	245	593	66.1
	2001	0.8	5.5	23.5	49.7	51	144	193	562	69.5
South Asia	1990	6.1	11.2	37.0	33.7	131	243	357	680	57.9
	2001	6.5	9.6	28.3	40.2	101	226	317	645	61.5
Sub-Saharan Africa	1990	3.3	12.9	54.8	19.6	168	265	403	664	55.1
	2001	5.2	15.5	40.9	18.3	166	437	545	680	48.9
High-income	1990	3.6	8.2	1.3	87.3	9	74	83	346	79.7
	2001	3.9	8.2	0.8	88.3	6	65	73	297	81.6
World	1990	23.0	8.8	25.2	51.3	88	161	244	516	66.6
	2001	26.7	8.7	19.3	54.1	80	168	244	487	67.3

Note: a) Estimates for 1990 based on country-level life tables from vital registration data or Modmatch (see methods section)
b) Estimates for 2001 derived from Lopez et al. 2002 c) Estimates for child mortality to nearest whole number. Source: Lopez et al. 2006

Table 1b: Selected mortality characteristics in females by World Bank region, 1990 and 2001

Global and regional mortality in 2001

Slightly more than 56 million people died in 2001, 10.5 million, or nearly 20%, of whom were children younger than five. Of these child deaths, 99% occurred in low- and middle-income countries. Those age 70 and over accounted for 70% of deaths in high-income countries, compared with 30% in other countries. Thus a key point is the comparatively large number of deaths among the young and the middle-aged in low- and middle-income countries. In these countries, 30% of all deaths occur at ages 15 to 59, compared with 15% in high-income countries. The causes of death at these ages, as well as in childhood, are thus important in assessing public health priorities.

Trends in mortality levels

The 1990s were characterized by significant economic gains in most regions, with growth in gross national product per capita ranging from 18% in South Asia and sub-Saharan Africa to more than 100% in East Asia and the Pacific and the Middle East and North Africa. Overall, gross national product per capita grew by about 33% in low- and middle-income countries during the decade. One would expect this to have led to a significant improvement in life expectancy, and this indeed occurred in most regions with the notable exception of Europe and Central Asia and, in particular, sub-Saharan Africa (Table 1a and 1b). In the former region, life expectancy was largely unchanged at around 72.5 years over the decade, primarily because of the massive rise in adult mortality in countries such as Russia and its neighbours during the first part of the decade, which negated the declines in child mortality. Much of this extraordinary increase in adult mortality, which rose by about 50% between 1987 and 1994, has been attributed to alcohol abuse, particularly among men (Leon et al. 1997).

Economic development and better coverage of the population with essential child health services have ensured continued declines in levels of child mortality, as measured by the risk of death from birth to age five, in all regions. The notable exception is sub-Saharan Africa, where child mortality among girls remained unchanged at around 165 per 1000, with only a modest decline (5%) in the risk of death for boys. The absence of significant declines in child mortality in the 1990s in sub-Saharan Africa is most likely largely due to the impact of HIV/AIDS. Overall, the risk of child death declined from 90 per 1000 in 1990 to 80 per 1000 in 2001, with the risk being remarkably similar for males and females (Table 1a and 1b); however, the differential in child mortality between the world's richest and poorest populations is stark, with a newborn in sub-Saharan Africa facing 25 times the risk of death before the age of five than a newborn in a high-income country.

Despite the much greater uncertainty in relation to levels of adult mortality compared with those for children, the estimates shown in Table 1a and 1b nonetheless indicate substantially different trends in adult mortality across different regions between 1990 and 2001. For most regions, the risk of death between ages 15 and 60 fell by about 10 to 17% over the decade. This was not the case in Europe and Central Asia, where policy shifts, particularly in relation to alcohol, together with broader social change, have largely been responsible for the 15% rise in adult male mortality and the 6% increase in the risk of death for women. Note that these estimates mask the large cyclical fluctuations in adult mortality in Russia, in particular, that characterized the region's mortality trends in the 1990s.

Table 1 also reveals the large increase in adult mortality in sub-Saharan Africa, which was due primarily to the unfolding of the HIV/AIDS epidemic in southern Africa. Notwithstanding the substantial uncertainty surrounding these estimates, the epidemic appears to have been of proportionately greater consequence for women, with the rise in their risk of death (67%) being twice that of males, among whom other causes of death such as violence were more common. If these estimates are correct, then 52% of African males reaching age 15 and 44% of females will die before their 60th birthdays, compared with, for instance, 6.5% of women in high-income countries, who despite their already low risk enjoyed a further 11% decline in mortality during the 1990s. These reversals in mortality decline have effectively negated gains elsewhere, with the results that the global risk of adult death has remained essentially unchanged for males, and may even have risen slightly for females.

Taken together, the probability of death up to the age of five and between the ages of 15 and 60 are a better reflection of the risk of premature death than either alone, although both have particular public health implications. Some argue that health policy should be equally concerned with keeping adults alive into old age as it is with keeping children alive into adulthood. A convenient metric to measure this is the risk of death between birth and age 60 (Table 1a and 1b). In high-income countries, given 2001 mortality rates, only about 7% of females and 13% of males would be dead by age 60, compared with 55 to 62% in sub-Saharan Africa. Significant improvements in this summary measure of premature death can be observed in all regions except Europe and Central Asia and sub-Saharan Africa. Worldwide, the index appears to have changed slightly for males and not at all for females.

Other features of global mortality summarized in Table 1a and 1b are worth highlighting. First is the impressive evidence of a continued decline in mortality among older age groups in high-income countries that began in the early 1970s. The risk of a 60-year-old dying before age 80 declined by about 15% for both men and women in high-income countries so that at 2001 rates, fewer than 33% of women who reach age 60 will be dead by age 80, as will less than 50% of men. Second, crude death rates in East Asia and the Pacific, Latin America and the Caribbean, and the Middle East and North African region are lower than in high-income countries, reflecting the impact of the older age structure of rich countries, and are particularly low in Latin America and the Caribbean. Third, the proportion of deaths that occur below age five, while declining in all regions, varies enormously across them, from just over 1% in high-income countries to 44% in sub-Saharan Africa. In some low- and middle-income regions, particularly East Asia and the Pacific,

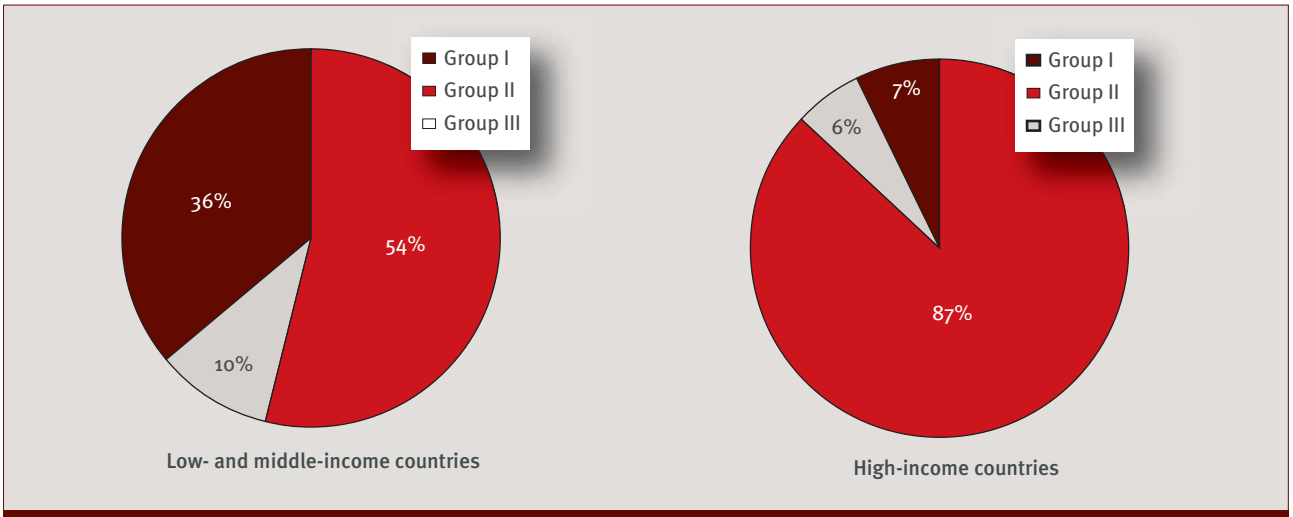


Figure 1: Deaths by broad cause group, 2001 *Source: Mathers et al. 2006*

Europe and Central Asia, and Latin America and the Caribbean, the proportion is well below 20%. The net effect of these changes in age-specific mortality since 1990 has been to increase global life expectancy at birth by 0.7 years for females and by about twice this for males: a modest scorecard.

Distribution of deaths by major cause group

Worldwide, one death in every three is from a Group I cause. This proportion remains almost unchanged from 1990 with one big difference: whereas HIV/AIDS accounted for only 2% of Group I deaths in 1990, it accounted for 14% of Group I deaths in 2001. Excluding HIV/AIDS, Group I deaths fell from 33% of total deaths in 1990 to less than 20% in 2001. Virtually all of the Group I deaths are in low- and middle-income countries. Just under 10% are from Group III causes (injuries) and almost 60% of deaths are from Group II causes (noncommunicable diseases). Figure 1 shows the proportional distribution of these major cause groups for low- and middle-income countries and high-income countries.

Group I causes remain the leading cause of child deaths in all regions, although they are now responsible for fewer child deaths than Group II and Group III combined in high-income countries (Figure 2). In contrast, Group II causes are now responsible for more than 50% of deaths in adults age 15 to 59 in all regions except South Asia and sub-Saharan Africa, where Group I causes, including HIV/AIDS, remain responsible for 33 and 67% of deaths, respectively. For adults age 15 to 59, death rates from Group II causes are higher for all low- and middle-income regions than for high-income countries, and in Europe and Central Asia are almost double the rate for the high-income countries. These results show that premature mortality from noncommunicable diseases is higher in populations with high mortality and low incomes than in the high-income countries.

Leading causes of death

Table 2 shows the top 10 disease and injury causes of death in 2001 for low- and middle-income countries and for high-income countries. Ischaemic Heart Disease (IHD) and cerebrovascular disease (stroke) were the leading causes of death in both groups of countries in 2001, responsible for 12 million deaths globally, or almost one quarter of the global total. Only 1.4 million of the 7.1 million who died of IHD were in the high-income countries. Stroke killed 5.4 million, of whom less than 1.0 million were in high-income countries.

Whereas lung cancer, predominantly due to tobacco smoking, remains the third leading cause of death in high-income countries reflecting high levels of smoking in previous years, the increasing prevalence of smoking in low- and middle-income countries has not yet driven lung cancer into the top 10 causes of death for these countries. HIV/AIDS is the fourth leading cause of death in low- and middle-income countries, and HIV/AIDS death rates are projected to continue to rise, albeit at a slower pace, despite recent increased efforts to improve access to antiretroviral drugs.

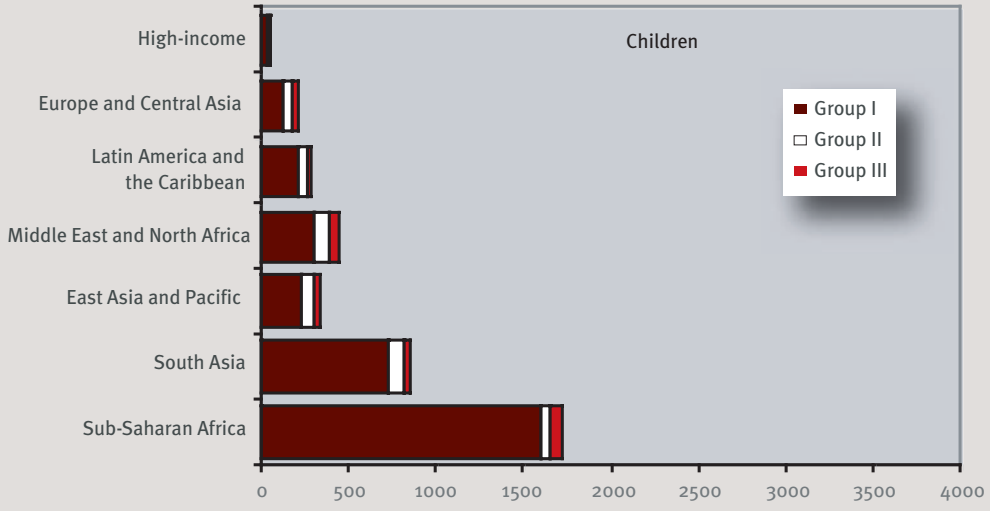
Lower respiratory infections, conditions arising during the perinatal period, and diarrhoeal diseases remain among the top 10 causes of death in low- and middle-income countries. In 2001, these three causes of death together accounted for nearly 60% of child deaths globally.

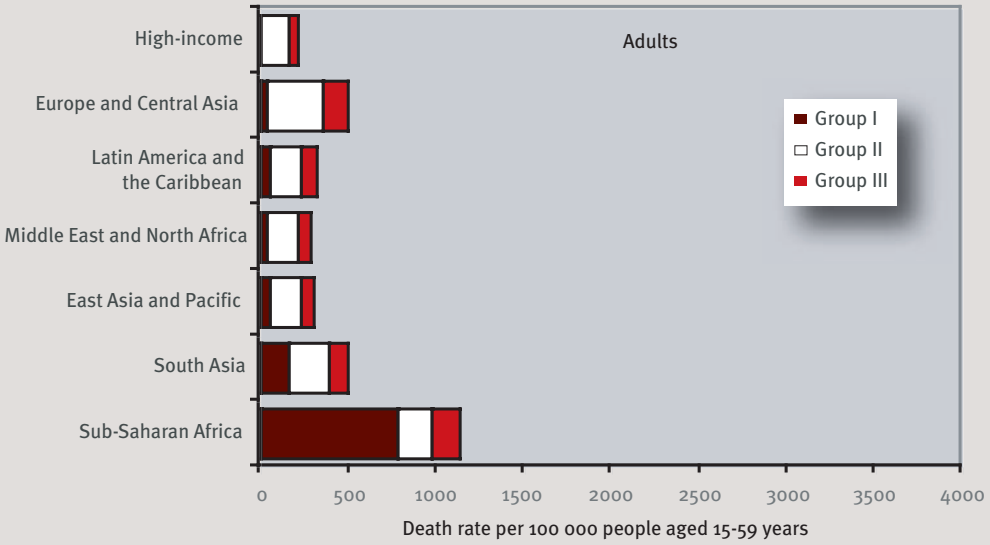
Table 3 shows the 10 leading causes of death in low- and middle-income countries by sex in 2001. Leading causes of death are generally similar for males and females, although road traffic accidents appear in the top 10 only for males and diabetes appears only for females.

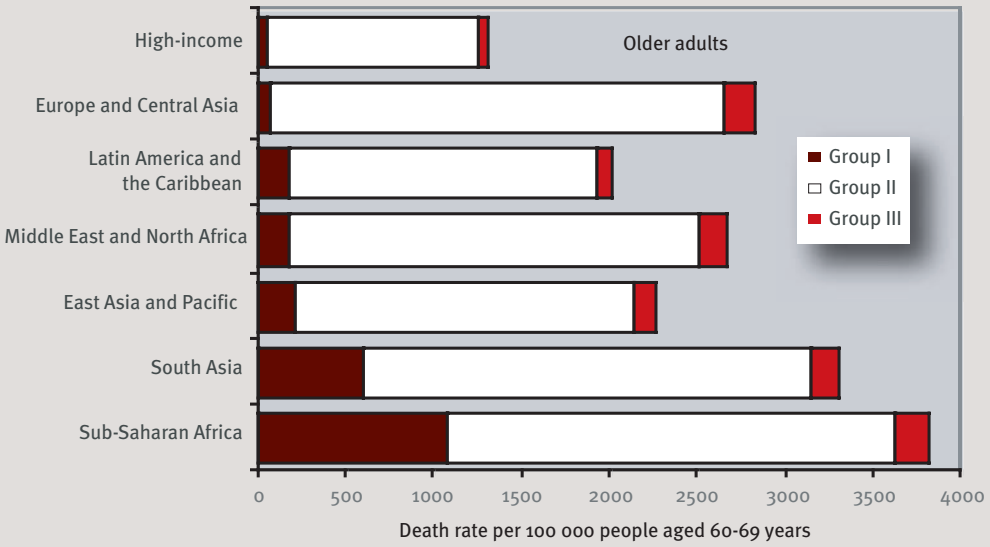
Leading causes of death in children

Infectious and parasitic diseases remain the major killers of children in the developing world. Although notable success has been achieved in certain areas, for example, polio, communicable diseases still account for 7 out of the top 10 causes and are responsible for about 60% of all child deaths. Overall, the 10 leading causes in low- and middle-income countries represent 80% of all child deaths in those countries, and also worldwide (Table 4).

Many Latin American and some Asian and Middle Eastern countries have shifted somewhat towards the cause of death pattern observed in developed countries. In these countries, conditions arising during the perinatal period, including birth asphyxia, birth trauma, and low birth weight, have replaced infectious diseases as the leading cause of death and are now







Source: Mathers et al. 2006

Figure 2: Death rates from each broad cause group, by region, children aged 0–14, adults aged 15–59, and older adults aged 60–69, 2001

	Low- and middle-income countries				High-income countries			
	Cause	Deaths (millions)			Cause	Deaths (millions)		
1	Ischaemic heart disease	5.70	11.8%	1	Ischaemic heart disease	1.36	17.3%	
2	Cerebrovascular disease	4.61	9.5%	2	Cerebrovascular disease	0.78	9.9%	
3	Lower respiratory infections	3.41	7.0%	3	Trachea, bronchus, lung cancers	0.46	5.8%	
4	HIV/AIDS	2.55	5.3%	4	Lower respiratory infections	0.34	4.4%	
5	Perinatal conditions	2.49	5.1%	5	Chronic obstructive pulmonary disease	0.30	3.8%	
6	Chronic obstructive pulmonary disease	2.38	4.9%	6	Colon and rectum cancers	0.26	3.3%	
7	Diarrhoeal diseases	1.78	3.7%	7	Alzheimer and other dementias	0.21	2.6%	
8	Tuberculosis	1.59	3.3%	8	Diabetes mellitus	0.20	2.6%	
9	Malaria	1.21	2.5%	9	Breast cancer	0.16	2.0%	
10	Road traffic accidents	1.07	2.2%	10	Stomach cancer	0.15	1.9%	

Table 2: The ten leading causes of death, by broad income group, 2001

responsible for 21 to 36% of deaths. Such a shift in the cause of death pattern has not occurred in sub-Saharan Africa, where perinatal conditions rank in fourth place and malaria, lower respiratory infections, and diarrhoeal diseases continue to be the leading causes of death in children, accounting for 53% of all deaths.

About 90% of all HIV/AIDS and malaria deaths in children in developing countries occur in sub-Saharan Africa, which accounts for 23% of the world's births and 42% of the world's child deaths. The immense surge of HIV/AIDS mortality in children in recent years means that HIV/AIDS is now responsible for 332 000 child deaths annually in sub-Saharan Africa and nearly 8% of all child deaths in the region.

Some progress has been made against diarrhoeal diseases and measles. While the incidence of diarrhoeal diseases is thought to have remained stable, mortality from diarrhoeal diseases has fallen from 2.5 million deaths in 1990 to about 1.6 million deaths in 2001, and now accounts for 13% of all deaths of children under age 15. Deaths from measles have declined modestly, although more than 0.5 million children under five still died from this disease in 2001. Malaria causes more than a million child deaths per year or nearly 11% of all deaths of children under five.

Leading causes of death in adults

Table 5 shows the leading causes of deaths among adults age 15 to 59 worldwide in 2001. Despite a global trend of declining communicable disease burden in adults, HIV/AIDS has become the leading cause of mortality and the single most important contributor to the burden of disease among adults in this age group.

Nearly 80% of the 2.1 million adult deaths from HIV/AIDS in 2001 occurred in sub-Saharan Africa. In this region, HIV/AIDS is the leading cause of death, resulting in more than 6000 deaths every day and accounting for almost 1 in 5 deaths for all ages and 1 in 2 deaths of adults age 15 to 59. HIV/AIDS has reversed mortality trends among adults in the region, and in many countries, life expectancies have declined since 1990.

The 4.5 million adult injury deaths in 2001 were heavily concentrated among young adults, particularly men. In the 15 to 59 age group, road traffic accidents and suicide were among the 10 leading causes of death in high-income and low- and middle-income countries, and violence (homicide) was also among the 10 leading causes in low- and middle-income countries. Among adults age 15 to 44 worldwide, road traffic accidents were the leading cause of death for men after HIV/AIDS, followed by TB and violence. Suicide was the third leading cause of death for women in this age group, after HIV/AIDS and TB, with road traffic accidents in fifth place.

The risk of death rises rapidly with age among adults aged

	Males				Females			
	Cause	Deaths (millions)			Cause	Deaths (millions)		
1	Ischaemic heart disease	3.01	11.8%	1	Ischaemic heart disease	2.69	11.8%	
2	Cerebrovascular disease	2.17	8.5%	2	Cerebrovascular disease	2.44	10.7%	
3	Lower respiratory infections	1.72	6.7%	3	Lower respiratory infections	1.68	7.4%	
4	Perinatal conditions	1.38	5.4%	4	HIV/AIDS	1.18	5.2%	
5	HIV/AIDS	1.38	5.4%	5	Chronic obstructive pulmonary disease	1.17	5.1%	
6	Chronic obstructive pulmonary disease	1.21	4.7%	6	Perinatal conditions	1.11	4.9%	
7	Tuberculosis	1.04	4.1%	7	Diarrhoeal diseases	0.85	3.7%	
8	Diarrhoeal diseases	0.93	3.6%	8	Malaria	0.63	2.8%	
9	Road traffic accidents	0.78	3.1%	9	Tuberculosis	0.55	2.4%	
10	Malaria	0.58	2.3%	10	Diabetes mellitus	0.42	1.8%	

Table 3: The 10 leading causes of death, by sex, low- and middle-income countries, 2001

	Low- and middle-income countries				High-income countries			
	Cause	Deaths (millions)			Cause	Deaths (millions)		
1	Perinatal conditions	2.49	20.7%	1	Perinatal conditions	0.03	33.9%	
2	Lower respiratory infections	2.04	17.0%	2	Congenital anomalies	0.02	20.0%	
3	Diarrhoeal diseases	1.61	13.4%	3	Road traffic accidents	0.01	5.9%	
4	Malaria	1.10	9.2%	4	Lower respiratory infections	0.00	2.5%	
5	Measles	0.74	6.2%	5	Endocrine disorders	0.00	2.4%	
6	HIV/AIDS	0.44	3.7%	6	Drownings	0.00	2.4%	
7	Congenital anomalies	0.44	3.7%	7	Leukemia	0.00	1.9%	
8	Whooping cough	0.30	2.5%	8	Violence	0.00	1.8%	
9	Tetanus	0.22	1.9%	9	Fires	0.00	1.2%	
10	Road traffic accidents	0.18	1.5%	10	Meningitis*	0.00	1.2%	

Table 4: The 10 leading causes of death in children aged 0–14, by broad income group, 2001

60 and over in all regions. Globally, 60-year-olds have a 55% chance of dying before their 70th birthday. Regional variations in the risk of death are smaller at older ages than at younger ages, ranging from around 40% in the developed countries of Western Europe to 60% in most developing regions and 70% in sub-Saharan Africa. Historical data from countries such as Australia and Sweden show that life expectancy at age 60 changed slowly during the first six to seven decades of the 20th century, but started to increase substantially since around 1970. Life expectancy at age 60 has now reached 25 years in Japan. In Eastern Europe from 1990 onwards, Hungary, and Poland started to experience similar improvements in mortality for older people, but Russia has not, and is actually experiencing a worsening trend.

Regional variations in causes of death

The 10 leading causes of mortality differ greatly between regions (Table 6). IHD and cerebrovascular disease are among the top four causes of death in all low- and middle-income regions except sub-Saharan Africa, where they are 8th and 7th, respectively. Cerebrovascular disease is the leading cause of death in East Asia and the Pacific, unlike in most other regions, where IHD causes more deaths than cerebrovascular disease. In sub-Saharan Africa, 6 of the top 10 causes are communicable diseases, with HIV/AIDS being the leading cause of death, followed by malaria and lower respiratory infections.

South Asia (mainly India) and Latin America and the Caribbean are the only two other low- and middle-income regions where HIV/AIDS is one of the top 10 causes of death. Lower respiratory infections, primarily pneumonia, are the third leading cause of death, especially among children under five, who account for 60% of these deaths. Chronic obstructive pulmonary disease kills more people (1.4 million) in the East Asia and Pacific region, primarily China, than anywhere else in the world, with 50% of global mortality from the disease occurring there.

Europe and Central Asia differs from all other low- and middle-income regions in the size of the CVD epidemic (with almost 60% of deaths due to CVD), followed by trachea, bronchus, and lung cancers in third place. Self-inflicted injuries (suicide) are the fifth leading cause of death in this region. South Asia is the only other region where suicide is in the top 10 causes of death. Latin America and the Caribbean is distinguished as the only region where violence falls in the top 10 causes of death, responsible for 1 in 25 deaths. In all low- and middle-income regions apart from Europe and Central Asia, road traffic accidents are included among the top 10 causes of death, reaching fifth position in the Middle East and North Africa, where they are responsible for 1 in 20 deaths.

Global burden of disease in 2001

The 20 leading causes of burden of disease for both sexes together are shown in Table 7. While the two leading causes

	Low- and middle-income countries				High-income countries			
	Cause	Deaths (millions)			Cause	Deaths (millions)		
1	HIV/AIDS	2.05	14.1%	1	Ischaemic heart disease	0.13	10.8%	
2	Ischaemic heart disease	1.18	8.1%	2	Self-inflicted injuries	0.09	7.2%	
3	Tuberculosis	1.03	7.1%	3	Road traffic accidents	0.08	6.9%	
4	Road traffic accidents	0.73	5.0%	4	Trachea, bronchus, lung cancers	0.08	6.8%	
5	Cerebrovascular disease	0.71	4.9%	5	Cerebrovascular disease	0.05	4.4%	
6	Self-inflicted injuries	0.58	4.0%	6	Cirrhosis of the liver	0.05	4.4%	
7	Violence	0.45	3.1%	7	Breast cancer	0.05	4.0%	
8	Lower respiratory infections	0.33	2.3%	8	Colon and rectum cancers	0.04	3.1%	
9	Cirrhosis of the liver	0.32	2.2%	9	Diabetes mellitus	0.03	2.1%	
10	Chronic obstructive pulmonary disease	0.32	2.2%	10	Stomach cancer	0.02	2.0%	

Table 5: The 10 leading causes of death in adults aged 15–59, by broad income group, 2001

	Europe and Central Asia			Latin America and Caribbean	
1	Ischaemic heart disease	29.7%	1	Ischaemic heart disease	10.9%
2	Cerebrovascular disease	18.2%	2	Cerebrovascular disease	8.2%
3	Trachea, bronchus, lung cancers	2.9%	3	Perinatal conditions	5.0%
4	Chronic obstructive pulmonary disease	2.3%	4	Diabetes mellitus	5.0%
5	Self-inflicted injuries	2.1%	5	Lower respiratory infections	4.8%
6	Hypertensive heart disease	1.9%	6	Violence	4.0%
7	Poisonings	1.9%	7	Chronic obstructive pulmonary disease	3.0%
8	Lower respiratory infections	1.8%	8	Road traffic accidents	2.7%
9	Cirrhosis of the liver	1.8%	9	Hypertensive heart disease	2.7%
10	Stomach cancer	1.8%	10	HIV/AIDS	2.5%
	Sub-Saharan Africa			**Middle East and North Africa**	
1	HIV/AIDS	19.0%	1	Ischaemic heart disease	16.9%
2	Malaria	10.1%	2	Cerebrovascular disease	6.8%
3	Lower respiratory infections	10.0%	3	Lower respiratory infections	5.6%
4	Diarrhoeal diseases	6.6%	4	Perinatal conditions	5.5%
5	Perinatal conditions	5.3%	5	Road traffic accidents	5.1%
6	Measles	4.1%	6	Hypertensive heart disease	3.9%
7	Cerebrovascular disease	3.3%	7	Diarrhoeal diseases	3.9%
8	Ischaemic heart disease	3.2%	8	Congenital anomalies	2.4%
9	Tuberculosis	2.9%	9	Nephritis and nephrosis	2.2%
10	Road traffic accidents	1.8%	10	Chronic obstructive pulmonary disease	2.1%
	South Asia			**East Asia and Pacific**	
1	Ischaemic heart disease	13.6%	1	Cerebrovascular disease	14.6%
2	Lower respiratory infections	10.4%	2	Chronic obstructive pulmonary disease	10.8%
3	Perinatal conditions	8.0%	3	Ischaemic heart disease	8.8%
4	Cerebrovascular disease	6.8%	4	Lower respiratory infections	4.2%
5	Diarrhoeal diseases	5.1%	5	Tuberculosis	4.1%
6	Tuberculosis	4.5%	6	Perinatal conditions	3.8%
7	Chronic obstructive pulmonary disease	4.3%	7	Stomach cancer	3.4%
8	HIV/AIDS	2.0%	8	Trachea, bronchus, lung cancers	3.0%
9	Road traffic accidents	1.8%	9	Liver cancer	2.9%
10	Self-inflicted injuries	1.7%	10	Road traffic accidents	2.8%

Table 6: Leading causes of death in low- and middle-income countries, by region, 2001

of death, IHD and cerebrovascular disease, remain among the top four causes of the burden of disease, four nonfatal conditions are also among the top 20 causes of burden: unipolar depressive disorders, adult-onset hearing loss, cataracts, and osteoarthritis. This once again illustrates the importance of taking nonfatal conditions into account, as well as deaths, when assessing the causes of loss of health in populations.

In 2001, the leading causes of the burden of disease in low- and middle-income countries were broadly similar to those for the world as a whole (Table 8), and included six Group I causes among the top 10, but the leading causes in high-income countries consisted entirely of Group II conditions, including three (unipolar depressive disorders, adult-onset hearing loss, and alcohol use disorders) for which direct mortality is low.

Age and sex differences in the burden of disease

Children younger than 15 accounted for 36% of the world's total burden of disease and injury in 2001 and adults age 15 to 59 accounted for almost 50%. Low- and middle-income countries accounted for the vast majority of the disease burden for children (Figure 3). While the proportion of the

	Low- and middle-income countries			High-income countries			
	Cause	DALYs (millions) of years		Cause		DALYs (millions) of years	
1	Perinatal conditions	90.48	5.9%	11	Road traffic accidents	35.06	2.3%
2	Lower respiratory infections	85.92	5.6%	12	Hearing loss, adult onset	29.99	2.0%
3	Ischaemic heart disease	84.27	5.5%	13	Cataracts	28.64	1.9%
4	Cerebrovascular disease	72.02	4.7%	14	Congenital anomalies	24.95	1.6%
5	HIV/AIDS	71.46	4.7%	15	Measles	23.11	1.5%
6	Diarrhoeal diseases	59.14	3.9%	16	Self-inflicted injuries	20.26	1.3%
7	Unipolar depressive disorders	51.84	3.4%	17	Diabetes mellitus	20.00	1.3%
8	Malaria	39.97	2.6%	18	Violence	18.90	1.2%
9	Chronic obstructive pulmonary disease	38.74	2.5%	19	Osteoarthritis	17.45	1.1%
10	Tuberculosis	36.09	2.3%	20	Alzheimer and other dementias	17.11	1.1%

Table 7: The 20 leading causes of burden of disease, DALYs, world, 2001

	Low- and middle-income countries				High-income countries			
	Cause	DALYs (millions) of years			Cause	DALYs (millions) of years	
1	Perinatal conditions	89.07	6.4%	1	Ischaemic heart disease	12.39	8.3%
2	Lower respiratory infections	83.61	6.0%	2	Cerebrovascular disease	9.35	6.3%
3	Ischaemic heart disease	71.88	5.2%	3	Unipolar depressive disorders	8.41	5.6%
4	HIV/AIDS	70.80	5.1%	4	Alzheimer and other dementias*	7.47	5.0%
5	Cerebrovascular disease	62.67	4.5%	5	Trachea, bronchus, lung cancers	5.40	3.6%
6	Diarrhoeal diseases	58.70	4.2%	6	Hearing loss, adult onset	5.39	3.6%
7	Unipolar depressive disorders	43.43	3.1%	7	Chronic obstructive pulmonary disease	5.28	3.5%
8	Malaria	39.96	2.9%	8	Diabetes mellitus	4.19	2.8%
9	Tuberculosis	35.87	2.6%	9	Alcohol use disorders	4.17	2.8%
10	Chronic obstructive pulmonary disease	33.45	2.4%	10	Osteoarthritis	3.79	2.5%

Table 8: The 10 leading causes of burden of disease, DALYs, by broad income group, 2001

total burden of disease borne by adults age 15 to 59 was the same in both groups of countries, adults older than 60 accounted for a significantly larger share of the disease burden in high-income countries.

Although injuries become more important for boys beyond infancy, the causes of the burden of disease are broadly similar for boys and girls. However, striking gender differences emerge in adulthood. In low- and middle-income countries, 5 of the 10 leading causes of DALYs for men age 15 to 44 are injuries. Indeed, after HIV/AIDS, road traffic accidents were the second leading cause of the burden of disease for men in this age group. Other unintentional injuries and violence were the third and fourth leading causes, with self-inflicted injuries and war also appearing in the top 10 causes. Injuries were also important for women age 15 to 44, although road traffic accidents were the tenth leading cause, preceded by other unintentional injuries in fourth place and self-inflicted injuries in sixth place. Unipolar depressive disorders were the second leading cause of the burden for women in this age group, after HIV/AIDS.

The growing burden of noncommunicable diseases

The burden of noncommunicable diseases is increasing, accounting for nearly half the global burden of disease for all ages, a 10% increase from estimated levels in 1990. While the proportion of the burden from noncommunicable disease in high-income countries has remained stable at around 85% in adults age 15 and older, the proportion in middle-income countries has already exceeded 70%. Surprisingly, almost 50% of the adult disease burden in low- and middle-income countries is now attributable to noncommunicable disease. Population ageing and changes in the distribution of risk factors have accelerated the epidemic of noncommunicable disease in many developing countries.

CVD accounted for 13% of the disease burden among adults age 15 and older in 2001. IHD and cerebrovascular disease (stroke) were the two leading causes of mortality and disease burden among adults age 60 and older and were also among the top 10 causes of disease burden in adults age 15 to 59. In low- and middle-income countries, IHD and cerebrovascular disease (stroke) were together responsible for 15% of disease burden in those aged 15 and older, and DALYs rates were higher for men than for women.

The proportion of the burden among adults age 15 and older attributable to cancer was 6% in low- and middle-income countries and 14% in high-income countries in 2001. Of the 7.1 million cancer deaths estimated to have occurred in that year, 17%, or 1.2 million, were attributable to lung cancer alone, and of these, three quarters occurred

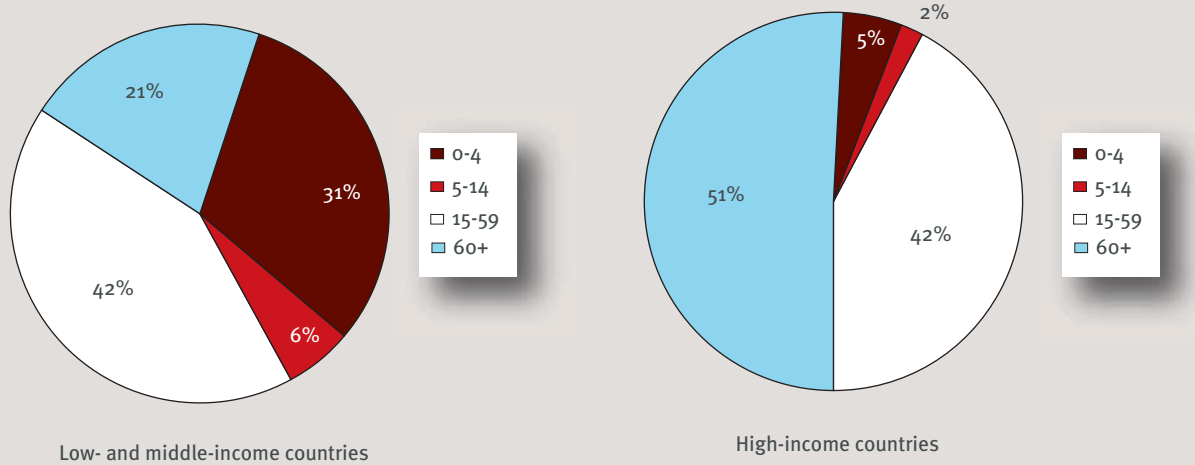


Figure 3: Age distribution of disease burden (DALYs), by income group, 2001 *Source: Mathers et al. 2006*

	Europe and Central Asia			Latin America and Caribbean	
1	Ischaemic heart disease	15.9%	1	Perinatal conditions	6.0%
2	Cerebrovascular disease	10.8%	2	Unipolar depressive disorders	5.0%
3	Unipolar depressive disorders	3.7%	3	Violence	4.9%
4	Self-inflicted injuries	2.3%	4	Ischaemic heart disease	4.2%
5	Hearing loss, adult onset	2.2%	5	Cerebrovascular disease	3.8%
6	Chronic obstructive pulmonary disease	2.0%	6	Endocrine disorders	3.0%
7	Trachea, bronchus, lung cancers	2.0%	7	Lower respiratory infections	2.9%
8	Osteoarthritis	2.0%	8	Alcohol use disorders	2.8%
9	Road traffic accidents	1.9%	9	Diabetes mellitus	2.7%
10	Poisonings	1.9%	10	Road traffic accidents	2.6%

	Sub-Saharan Africa			Middle East and North Africa	
1	HIV/AIDS	16.5%	1	Ischaemic heart disease	6.6%
2	Malaria	10.3%	2	Perinatal conditions	6.3%
3	Lower respiratory infections	8.8%	3	Road traffic accidents	4.6%
4	Diarrhoeal diseases	6.4%	4	Lower respiratory infections	4.5%
5	Perinatal conditions	5.8%	5	Diarrhoeal diseases	3.9%
6	Measles	3.9%	6	Unipolar depressive disorders	3.1%
7	Tuberculosis	2.3%	7	Congenital anomalies	3.1%
8	Road traffic accidents	1.8%	8	Cerebrovascular disease	3.0%
9	Whooping cough	1.8%	9	Vision disorders, age-related	2.7%
10	Protein-energy malnutrition	1.5%	10	Cataracts	2.3%

	South Asia			East Asia and Pacific	
1	Perinatal conditions	9.2%	1	Cerebrovascular disease	7.5%
2	Lower respiratory infections	8.4%	2	Perinatal conditions	5.4%
3	Ischaemic heart disease	6.3%	3	Chronic obstructive pulmonary disease	5.0%
4	Diarrhoeal diseases	5.4%	4	Ischaemic heart disease	4.1%
5	Unipolar depressive disorders	3.6%	5	Unipolar depressive disorders	4.1%
6	Tuberculosis	3.4%	6	Tuberculosis	3.1%
7	Cerebrovascular disease	3.2%	7	Lower respiratory infections	3.1%
8	Cataracts	2.3%	8	Road traffic accidents	3.0%
9	Chronic obstructive pulmonary disease	2.3%	9	Cataracts	2.8%
10	Hearing loss, adult onset	2.0%	10	Diarrhoeal diseases	2.5%

Table 9: Leading causes of burden of disease in low- and middle-income countries, by region, 2001

among men. The number of cases of lung cancer increased nearly 30% since 1990, largely reflecting the emergence of the tobacco epidemic in low- and middle-income countries.

Stomach cancer, which until recently was the leading site of cancer mortality worldwide, has been declining in all parts of the world where trends can be reliably assessed, and in 2001 caused 842 000 deaths, or about two thirds as many as lung cancer. Liver cancer was the third leading site, with 607 000 deaths in 2001, more than 60% of them in the East Asia and Pacific region. Among women, the leading cause of cancer deaths was breast cancer. Breast cancer survival rates have been improving during the past decade, but the chance of survival varies according to the coverage of and access to secondary prevention. Globally, neuropsychiatric conditions accounted for 19% of the disease burden among adults, primarily from nonfatal health outcomes.

Injuries: the hidden epidemic

Injuries, both unintentional and intentional, primarily affect young adults, and often result in severe, disabling *sequelae*. In 2001, injuries accounted for 16% of the adult burden of ill-health and premature death worldwide. In parts of Latin America and the Caribbean, Europe and Central Asia, and the Middle East and North Africa more than 30% of the entire disease and injury burden among male adults age 15 to 44 was attributable to injuries, and road traffic accidents, violence, and self-inflicted injuries were all among the top 10 leading causes of the burden of disease. Globally, road traffic accidents were the third leading cause of burden in the same age and sex group, preceded only by HIV/AIDS and unipolar depression. The burden of road traffic accidents has been increasing, especially in the developing countries of sub-Saharan Africa and South and Southeast Asia, and particularly affects males.

Intentional injuries, which include self-inflicted injuries and suicide, violence, and war, accounted for an increasing share of the burden, especially among economically productive young adults. In developed countries, suicides accounted for the largest share of the intentional injury burden, whereas in developing regions, violence and war were the major sources. The former Soviet Union and other high-mortality countries of Eastern Europe have rates of death and disability resulting from injury among males that are similar to those in sub-Saharan Africa.

Regional variations in the burden of disease

Table 9 summarizes the 10 leading causes of burden for each of the low- and middle-income regions.

In 2001, IHD and stroke dominated the burden of disease in Europe and Central Asia, and together accounted for more

than a quarter of the total disease burden. In contrast, in Latin America and the Caribbean, these diseases accounted for 8% of disease burden. However, this region also had high levels of diabetes and endocrine disorders compared with other regions. Violence was the third leading cause of burden in Latin America and Caribbean countries, but did not reach the top 10 in any other region.

HIV/AIDS was the leading cause of burden of disease in sub-Saharan Africa, followed by malaria. Seven other Group I causes also appear in the top 10 causes for this region, with road traffic accidents being the only non-Group I cause.

Group I, II, and III causes all appear among the top 10 causes of the disease burden for the Middle East and North Africa. Of particular note, road traffic accidents were the third leading cause and congenital anomalies were the seventh leading cause.

Group I causes of disease burden remained dominant in South Asia, and this burden fell particularly on children, but noncommunicable diseases such as IHD, stroke, and chronic obstructive pulmonary disease also featured in the list of top 10 causes.

In East Asia and the Pacific, stroke was the leading cause of disease burden in 2001, with IHD in fourth place, although Group I causes such as conditions arising during the perinatal period, TB, lower respiratory infections, and diarrhoeal diseases remained important.

Conclusions

The analysis presented has confirmed some of the conclusions of the original GBD study about the importance of including nonfatal outcomes in a comprehensive assessment of global population health, and has also confirmed the growing importance of noncommunicable diseases in low- and middle-income countries. However, it has also documented some dramatic changes in population health in some regions since 1990. The key findings include the following:

- HIV/AIDS is now the fourth leading cause of the burden of disease globally and the leading cause in sub-Saharan Africa.
- In low- and middle-income countries, the epidemiological transition has resulted in a 20% reduction in the per capita disease burden due to Group I causes since 1990. Without the HIV/AIDS epidemic, this reduction would have been closer to 30%. Several of the "traditional" infectious diseases, such as TB and malaria, have not declined, in part because of weak public health services and the increased numbers of people with immune systems weakened by HIV/AIDS.
- The per capita disease burden in Europe and Central Asia increased by nearly 40% during 1990–2001, meaning that this region now has worse health than all other regions except South Asia and sub-Saharan Africa. The unexpected increase in the disease burden, and the concomitant reduction in life expectancy, in countries of this region appear to be related to such factors as alcohol abuse, suicide, and violence, which seem to be associated with societies facing social and economic disintegration. The rapidity of these declines has dramatically changed our perceptions of the time frames within which substantial changes in the burden of chronic disease can occur and of the potential for such adverse health trends to occur elsewhere.
- Adults under the age of 70 in low- and middle-income countries face a substantially greater risk of death from noncommunicable diseases than adults of the same age in high-income countries.
- In Europe and Central Asia, Latin America and the Caribbean, and the Middle East and North Africa, more than 30% of the entire disease burden among male adults age 15 to 44 is attributable to injuries, including road traffic accidents, violence, and self-inflicted injuries. In addition, injury deaths are noticeably higher for women in some parts of Asia and the Middle East and North Africa than in other regions, partly because of high levels of suicide and violence. Combined with higher rates of infant and child mortality for girls, this results in a narrower differential between male and female healthy life expectancy than in any other region. ❑

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The potentials of involving communities in health research

Article by Selemani S Mbuyita

"…We live, after all, in a world of increasing polarization of power and wealth into North and South, into overclasses and underclasses. Materially, those in the overclasses have more and more, and are increasingly linked by instant communications. At the same time, the numbers in the underclasses of absolute poverty continue to rise. Among them, many millions have less and less, and remain isolated both from the overclasses and from each other. Almost by definition, the poor and powerless have no voice. It may be politically correct to say that they should be empowered and their voices heard. But cynical realists will point to inexorable trends, vested interests and pervasive self-interest among the powerful, and argue that little can be changed" (Robert Chambers, Whose Voice*?).*

For anyone who has been in research and applied any of the many b ranches of participatory research methods, turning back to the conventional empiricist survey approaches or any other "quick and dirty" data collection techniques would be difficult. The facts revealed, the knowledge acquired and the skills unveiled from the people in communities where the research process is implemented, differentiate distinctly participatory research (that involves communities) from other research methodologies.

Literally, participation can be defined in different ways. However, in general terms the concept of participation reflects the action of taking part in an activity. People "participate" in local development every day through their family life, livelihood activities and community responsibilities. The degree of control that men and women have over these activities varies. The same holds true for initiatives that are initiated or involve "outsiders" such as *research projects*, development programmes or advocacy campaigns[2].

The potential of participatory research comes from the researched people as active analysts of the researched subjects. With participatory research, solutions to research questions *come from the people supported with data, and not from data supported by trained data analysts*. Interventions and/or programmes developed using data from the first scenario are more reliable, feasible and sustainable in their implementation than the latter. Historically, health policies that have been designed without a community participatory approach, some of which have acquired a global attention, often have failed to solve people's health problems. The trend will be the same and the vicious cycle maintained unless the participatory research community can succeed to show, demonstrate, convince and prove to local and global health policy-makers that participatory research has the potential to solve many of our health problems.

Literally, participation can be defined in different ways. However, in general terms the concept of participation reflects the action of taking part in an activity. People "participate" in local development every day through their family life, livelihood activities and community responsibilities

To address these concerns, special attention has been paid for the past few decades to the development and analysis of participatory research methods. One stream of participatory research, with new inventions, evolved as a family of approaches and methods known as Participatory Rural Appraisal (PRA). As PRA evolved, it soon became evident that it had applications for policy. Thematic and sectoral studies were carried out and resent as reports to decision-makers, sometimes within only days or weeks of the field work. The World Bank, through trust funds from bilateral donors, initiated Participatory Poverty Assessments (PPAs). Some of these used PRA methods to enable poor people to express their realities themselves. The insight from these thematic studies was striking, convincing and unexpected. However, it was (*and still is*) too scattered and/or fragmented for full mutual learning or for its significance to be fully seen[3].

Health programmes that were later proposed and implemented worldwide, with elements of involving communities in their implementation had their roots in evidence revealed by participatory research. Today, we identify programmes and interventions such as School Health Programmes, Community Based Health Initiatives etc. that were designed to respond to unveiled potentials of beneficiaries' involvement in such programmes. For example, the concepts of the *Health-Promoting School* and of *Comprehensive School Health Education and Promotion*, as discussed and defined by WHO, have highly considered participation concepts[1]. Partly, this programme aims to counter the views adults and teachers commonly hold of children and young people as ignorant-to be taught;

irresponsible-to be disciplined; immature-to be brought up; incapable-to be protected; a nuisance-to be seen and not heard; or a resource-to be made use of[7]. Participatory research, resulting in participatory data to generate participatory solutions through participatory interventions and/or programmes, were demonstrated to be successful in averting and/or changing such views.

Community involvement in health research and in other domains of development is a strong tool towards such change. It helps to teach those who hold such views and perceptions that they can learn a lot from children, poor people, and unschooled and illiterate men and women – that there is much to appreciate, so many skills to acquire and adopt. Learning such lessons is important if our research is to bring positive effects and make a difference. These realities are easily seen once one gets involved in the process of participatory research.

The following sets of questions and case studies will help to demonstrate the potential of applying community participation in health research, and will help bring everybody aboard – including those with practical experiences of participatory research in health and those without. Indeed, they might assist in changing even those *cynical realists who usually point to inexorable trends, vested interests and pervasive self-interest among the powerful, and who argue that little can be changed*.

What does participatory health research look like?

Most of us have some understanding of what it *means* to use participatory approaches in health but *how* to make it happen may be less clear. There are some basic principles to using participatory methods:

1. Local people are creative and capable of undertaking their own investigations, analyses and planning.
2. Outsiders (*field workers, facilitators, researchers etc.*) have a role as facilitators of this process.
3. Local people can and should be empowered to solve their own problems themselves[4].

This means that, when conducting health research using a participatory approach the method:

1. should not only extract information from people, but should also recognize local knowledge and make use of it;
2. should not end at collecting data but, should stimulate a process that would discuss issues identified from the data;
3. should not try to create solutions to the identified issues, but rather involve the people themselves to formulate ideas and initiatives to solve their own problems.

Due to its nature of involving people, methods applying community participation are usually intertwined; issues raised are of time taken, expectations aroused and whose realities are expressed.

As a result, participatory research is time-consuming. The methods used, especially the visual ones like mapping, diagramming and matrices, tend to be fun and engage people's full attention.

Expectations are liable to be raised. After being helped to analyze their conditions, problems and opportunities, people often expect action[3]. Unfortunately, many research activities end at this point, instead of proceeding two steps further where planning for action and follow-up would actually be instituted.

Throughout the process of community participation in health research, transparency must be maintained. Outside researchers should make clear from the start who they are, what they are doing, and why, and what can and cannot be expected.

Can every health research question be answered using participatory research?

The classical classification of research is usually very wide. Some research questions traditionally have been associated only with specific research design and methods. For example, a malaria vaccine trial typically would be seen to appropriately require a clinical trial design. However, it is possible to argue that, participatory methods are also important to answer questions in clinical trials. For example, in preparing for a malaria vaccine trial in Bagamoyo, Tanzania, a component applying participatory research methods was included for introducing the study objectives and creating awareness within the community in the study area. It also helped to extract information about people's expectations, worries and fears and increase the readiness of the research project to address individual and community concerns before the vaccine was introduced. The participatory research component also helped to solicit people's views (from the people who would later be the active participants of the process) on how best to make the project, and ultimately the vaccine intervention, a success.

The experience of this participatory approach to the malaria trials was that some of the issues raised by involving the community at that early stage of the project had not been well thought out nor understood in advance

The experience of this participatory approach to the malaria trials was that some of the issues raised by involving the community at that early stage of the project had not been well thought out nor understood in advance – *and actually could not have been known by "professionals"*. Had the trials proceeded without this process, the existing "knowledge" would definitely have misled the trial.

This example, and others that can be sited, support the argument that participatory research in health can be applied to a wide range of research questions, including those that usually seem to be too scientific to involve local people. However, the nature of the participation of various partners in the research process (local people, key community persons, community leaders, political leaders etc.) varies with the nature of the study, research design and scope of work involved in the research process.

Generally, any research question can apply and employ participatory approaches. In the Tanzania Essential Health Interventions Project (TEHIP), the Community Voice Component employed Participatory Action Research (PAR) in trying to answer the question, "How can communities be effectively involved in district health planning processes?". The initial objective was to develop a procedural framework for incorporating Community's Voice into District Health Plans[5]. Traditionally, stern professionals with a sound background in participatory methods and community involvement would have been contracted to develop such a framework. However, by using a participatory action research approach, communities in selected study districts significantly contributed to the design of such a framework (planning tool). The result was the availability of a practical tool that took into account the views of both professionals and the community.

What can participatory health research achieve?

Like in any other type of research model, the key product of community participation and involvement is data. Data generated through a participatory process normally produces richer information than that from a classical data set. The form in which the data is normally made available is clearer and easier to be understood by all those involved in the research process – as well as by those who were not – than are classical data sets from surveys.

Apart from the data, an additional value of a participatory health research process is the interaction that happens between the *outsiders* and the communities. This interaction is very important for understanding social factors, such as how people understand disease, that may influence people's health-seeking behaviours and patterns of health care use[4]. In a later stage, this understanding is important in designing health services that reflect people's culture and use local knowledge, which in turn has been shown to increase acceptability of the services, compared to services that do not take these into account. Even where health infrastructures are available, providing information in one's own language, ensuring culturally appropriate care or supporting community networks for prevention and follow-up of illness, are all important factors in improving access to care. Research processes that have involved people as active participants have brought about these effects and impacts.

There are three main levels of impacts on the community, from which we can deduce what community involvement in health research can achieve. Each level has a different scope, but each is equally important:

1. The immediate impacts and direct benefits for individuals and families.
2. The broader impact on "social capital" or local organizations, namely the empowerment and representation of communities and their members.
3. The overall impact on local society.

At each level, the forms of expected impacts may also vary. Impacts may have material, human and spiritual attributes. These are seen across a continuum of tangible and intangible impacts, including environmental, productive, and physical changes, as well as overall transformations at the individual and community level. Tangible impacts are changes that can be observed directly, and measured and documented quickly. Intangible impacts are more subtle, internal or attitudinal changes that can also be documented but often in a more "qualitative" manner[6].

Can participatory health research approaches achieve everything?

Participatory approaches that involve communities are basically reflective and are primarily qualitative in nature. People who are used to drawing conclusions using numbers and figures might be a bit disappointed, although even quantitative information can be gathered through participatory methods. Tools used in participatory research are designed to gather people's knowledge generated from their own opinions and experiences. By definition, much of this knowledge is not measurable in the scientific sense of the word but, nevertheless, vital if communities and outsiders are to work successfully together in improving the health and well-being of individuals, communities and the nation.

At the same time, this does not mean participatory research and action ignores quantitative data i.e. data that is counted or measured. There are examples of participatory methods for research in health that provide evidence that is quantitative. We can use participatory methods in health research to produce averages and other quantitative information[4].

Who should be involved when community participation in health research is applied?

Beyond the immediate networks of households and families, there are *social groupings* within "communities". These social groups share a common experience or situation. For example they share the same social class, income level, gender, geographical area, age, ethnic or religious group, political status or other social and economic factors or experiences. These factors and experiences can influence how healthy they are, how they are able to create and sustain their own health, how they are exposed to disease, and how much they are affected by ill health. It can also influence how well they are served by health or other community services that affect their health, or how they access those services. For example, disabled people as a social group face particular difficulties in achieving the conditions needed to create and sustain their health. They are often subject to stigma, discrimination, and social marginalization and exclusion that prevent them from participation in the lives of their families and communities, schools, workplaces and income-generating activities and from benefiting from the results of that participation. Often, their health needs are not recognized and they may experience exclusionary criteria from medical and other community services necessary to their health. In addition, access to health services is often made difficult or impossible because of architectural barriers, lack of accessible transport and inappropriately planned and designed health services.

Several strategies are needed for each of the identified social groups we have identified to build interest and become actively involved in health activities. One of the first of these is for people to be aware. **Information is power**. The community that is well informed about the existing health activities stands a better chance to raise their voice, debate and demand inclusion, participation and social justice. We thus need to include in the design of any programme, components that provide for awareness creation, for listening to inputs from communities and feeding information back to communities.

It is practically impossible to involve everybody throughout all stages of implementation of a health research, programme or activity. Different stages of the programme will involve different people in the community. For example, during the introduction, awareness creation and sensitization of the health activity, all community members would preferably be involved. However, at a stage such as planning, representation is important as it is not possible to have all the community members in a planning meeting. Representation is more easily achieved if we know the different groups that need to be represented and ensure that their interests are all addressed.

It is important when we talk of participatory research in health to look beyond community involvement. If for example our research is to influence the policy-making process, it is very essential to identify other partners of the process and involve them in earlier stages of the research process rather than waiting to involve them at results dissemination and programme design. This would include policy-makers, the media and other key stakeholders.

Policy development is complicated and involves a number of players with diverse interests. Policy interests at local level may differ from those at global level. Take for example medicines. At the community level, the interest is to make sure that when people fall ill, that they have medicines at the nearest health facility. At the district level, decision-makers may balance the priorities for drugs for treatment against spending on prevention, water supplies, improving antenatal services and so on. At national level there may be issues about how much foreign currency is spent on drugs versus fuel and other essential goods. At the global level, there may be trade rules to do with protecting patents for large companies that may limit the options of what countries can do[4].

Therefore, for communities to effectively work with, engage or influence institutions at different levels it is necessary to understand how these institutions are organized, their roles, how information flows between them, and who their authorities are. If possible, a research process that intends to engage communities, should also consider other partners from the public departmental sectors, NGOs and Civil Societies with shared values and interests in the area being researched.

In summary

Community involvement in health research is about facilitating change. If it is used as it should be used, it can lead to major shifts in the way people and organizations think and act. When using participatory approaches, practitioners are encouraged to move away from the concept of "them" and "us" to recognizing that health "belongs to us all". The attitude and behaviours of the practitioner is central – listen to people's own knowledge, create dialogue, involve people and institutions at all levels in decisions and activities.

Everybody can learn and acquire "knowledge of" participatory methods but not everybody has the skills to implement them. Participatory skills are not "acquired by learning" but rather "by doing after having learned". This makes community participation an area where skills grow through practice and through getting feedback from colleagues and communities.

Health research applying a community participation approach uses a diversity of methods that is limited only by our own imaginations, which are limitless. The methods are flexible and can be adapted to different circumstances. Participatory methods are very strong tools for generating qualitative data; however, some methods can also generate quantitative data. Participants with guidance from facilitators can do their analysis in the field, producing results quickly and discussing and moving ahead with actions. This is cost effective and results/reports are produced and shared in a timely fashion.

Involving communities in health research can be time consuming, but can often be done with local resources and may not be costly. They are not like "quick and dirty surveys". They need significant listening skills. Some issues may call for several rounds of reflection, action and then analysis and reflection leading to further action.

Approaches that empower people and lead to change may be threatening to some groups or interests in communities, and change may be resisted. There may be opposition and resistance to participatory research for these reasons. Like any other method, participatory methods are also open to abuse, and can be used in the wrong way for the wrong reasons. Not every method can work everywhere[4]. ❑

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To achieve better health, particularly among the poor and marginalized in low- and high-income countries alike, there is a need to improve health systems and services, to ensure equitable and affordable access to these and to good quality medicines, and to address social inequities that produce and exacerbate poor health. Beyond the treatment of ill-health, much more attention is needed to create the conditions that enable individuals, communities and countries to promote better health.

The fourth Volume of the *Global Forum Update on Research for Health* reflects the current state of health research in ensuring equitable access. The topics covered range from access to health, innovation and research resources to decision-making and governance.

This Volume is produced to coincide with the Global Forum for Health Research's annual meeting, Forum 11, and contains articles from some of the leading institutions and public health professionals from across the world.

Front cover image: Over one third of the population in developing countries lack access to essential medicines. The provision of safe and effective traditional medicine could become a critical tool to increase access to health care.

Traditional medicine is the sum total of the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, whether explicable or not, used to treat, diagnose and prevent illnesses or maintain well-being.

The cover image represents "acupressure", a traditional Chinese medicine technique whereby an appropriate pressure and manipulation is applied to prescribed acupuncture points using the fingers instead of needles. This technique is widely used as a safer alternative to needling for a broad range of conditions. The Publishers would like to thank Dr Xiaorui Zhang from the World Health Organization for providing this explanation.

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