Chapter 4

Priority setting in health research

Section 1

About priority setting

1. Priority setting is a long-term process

Priority setting is as critical as conducting the research itself. Since the funding available for health research is low in comparison to its very high potential benefits, it is essential that it be based on a rational priority-setting process. The use of a sound methodology and a scientific process are critical to ensure the identification of the research priorities which will make the greatest contribution to people's health.

Priority setting is a long term, iterative process. Priorities are not static and need to be regularly reviewed. Priority setting must be based on evidence of potential impact and use of comparative advantages of the various actors, rather than on short-term political considerations. However, this long-term perspective often hinders political approval for research, as the benefits are not always immediately available, causing research to be misunderstood as a 'luxury' item.

2. Deficiencies in priority setting and consequences

The failure in practically all countries to establish a process for priority setting based on the burden of diseases and their causes has led to a situation in which only about 10% of health research funds from public and private sources are devoted to 90% of the world's health problems (measured in Disability-Adjusted Life Years or DALYs).[1,2,3] This extreme imbalance in research funding has a very high economic and social cost for individuals, countries and the world as a whole. To make matters worse, even the 10% of funds allocated to the 90% of the world's health problems are not used as effectively as they should be.

Reasons for this imbalance in health research funding include the following:

(a) In the public sector

- Over 90% of research funds are in the hands of a small number of countries (see chapter 5) which, understandably, have given priority to their own immediate national health research needs, even though this may be a short-sighted position.
- Decision-makers are often unaware of the magnitude of the problems outside their own national borders. In particular, they are unaware of the impact on their own country of the health situation in the rest of the world both directly (e.g. rapid growth in travel, re-emerging diseases, development of antimicrobial resistance) and indirectly (e.g. lower economic growth, migration).
- The decision-making process is influenced by a range of factors including the personal preferences of influential scientists or decision-makers, competition between institutions, donor preferences, career ambitions and tradition.

[1] Global Forum for Health Research. *The 10/90 Report on Health Research 2000.*
[2] Global Forum for Health Research. *The 10/90 Report on Health Research 2001-2002.*
[3] Ad Hoc Committee on Health Research Relating to Future Intervention Options. *Investing in Health Research and Development,* WHO, September 1996.

- There is insufficient understanding of the role the public sector could play in supporting the private sector in the discovery and development of drugs for 'orphan' diseases.

(b) In the private sector

- Decision-makers in the private sector are responsible for the survival and success of their enterprise and for the satisfaction of their shareholders. Their decisions are based largely on profit perspectives which inevitably limit investment in diseases prevalent in low- and middle-income countries, as market potential is often underestimated.
- In low- and middle-income countries, pharmaceutical companies have the potential to develop and produce products for diseases prevalent in those countries. However, their funding capacity is comparatively small in global terms and therefore this potential remains largely untapped.

3. Priority setting in health research: tools versus process

In everyday life, setting priorities is a difficult process. This is much more so in the field of health research, where a larger number of factors and actors enter into the equation.

It is important to differentiate between the *process* of priority selection and the *tools* used for that purpose.[4] The process is the mechanism by which constituencies and stakeholders are involved and decide upon research priorities. It is evident that ensuring the participation of communities and users is a necessary part of the process.

The tools are the instruments which facilitate (i) the organization of the huge mass of information (regarding burden of disease, available resources, determinants, present knowledge) which is necessary to establish priorities on a scientific basis and (ii) its presentation in a way which permits analysis and comparison of the various possible fields of research, eventually permitting the identification of the areas with the most promising impact on people's health.

4. From local research priorities to national and global priorities

The exercise of priority setting should take place at the local, national and global levels, as resources are invested in health research, in one form or another, at all three levels. The challenge is to relate, in an efficient and effective way, the results of exercises undertaken at the local and country levels with those at the regional and global levels for specific diseases and conditions, based on the respective comparative advantages. A practical way to relate the three levels is presented in section 4 below, "Application of the Combined Approach Matrix".

5. Whose priorities?

Lists of priorities are only as good as their inputs and the process leading to the identification of these priorities. As far as the process is concerned, the dominating constituency will invariably tend to impose its own view of the problem. The Commission on Health Research for Development[5] drew attention to the fact that the "perception of health problems may differ according to the people consulted." It made its point by reporting on a study in which the priority ranking of health problems by citizens in Bangkok contrasted markedly with that analysed by health professionals. In that study, citizens' views only vaguely matched the views expressed by epidemiologists.

[4] De Francisco A. Paper presented in Forum 7, Geneva, December 2003.

[5] Commission on Health Research for Development. *Health Research, Essential Link to Equity in Development,* 1990.

Lomas[6] defines 'technical' and 'interpretative' models of priority setting, the former being based on available data and the latter on more subjective judgements made by participants taking part in the exercise. The objective of the priority-setting process is to ensure that the views of a range of health professionals, citizens and other stakeholders are well represented and balanced, if not entirely reconciled.

In summary, the priority-setting process is a *subjective* process, i.e. the priorities identified at the end of the process are those of the actors having participated in the process. In order to make the results as *objective* as possible, i.e. as representative as possible of the priorities of the *whole* local community, the *whole* nation, or the world as a *whole*, it is essential (i) to adopt a priority-setting *process* which is as transparent and as participatory as possible, and (ii) to apply a methodology which is as scientific as possible, even though both are costly in terms of the financial and human resources needed.

6. From research to action

A fundamental requirement for research to be effective is to ensure that the results of research are transformed into actual and measurable improvements in people's health. Unfortunately, too many priority-setting exercises end when the priorities are identified. The link between research and people's health is largely embedded in the health and health research systems in all their dimensions and complexities. An important contribution of research is to throw light on the reasons why, in particular instances, the findings of health research do not result in improvements in people's health.

The preliminary results of a three-year study on health research systems in a number of countries were presented in Forum 7,[7] underlining the difficulties of translating research results into policies. In his analysis, Hanney[8] indicated that priority should be given to the following themes: (i) priority setting; (ii) the interface between the health system, the health research system and policy-making; and (iii) the role of the beneficiaries of health research. In this context, it is not only important to know whether research was used in policy formulation, but also to know how it was used.[9]

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[6] Lomas J et al. "On being a good listener: setting priorities for applied health services research" in *The Milbank Quarterly*. Volume 81, Number 3, 2003.

[7] Sadana R. Towards analyses of national health research systems - update on a pilot study involving some 20 countries. Paper presented in Forum 7, Geneva, December 2003.

[8] Hanney SR et al. "The utilisation of health research in policy-making: concepts, examples and methods of assessment" in *Health Research Policy and Systems* 2003, 1:2

[9] Lavis J et al. "Measuring the impact of health research" in *Journal of Health Services Research and Policy*, Vol 8 No 3, July 2003.

Section 2

Comparison of experiences in priority setting: processes and methods

Since the Commission on Health Research for Development in 1990,[10] priority-setting exercises have used various methods and processes. The objective of this section is to compare these various efforts on prioritization in health research in order to highlight their similarities and complementarity. An overview of this analysis is presented in Insert 4.1 which summarizes and compares the characteristics of the major priority-setting approaches for health research which have emerged since the Commission's Report. Recent developments in each of the approaches are briefly summarized below.

1. Priority setting using the Essential National Health Research strategy (1991)[11]

Based on the Commission's recommendation to "encourage all countries to undertake Essential National Health Research (ENHR)," the Council on Health Research for Development (COHRED) was established in 1993 to assist developing countries with the implementation of this strategy to organize and manage research (See chapter 9, section 15 below).

COHRED has worked in about 65 countries (see Insert 9.15.2) and has made a significant contribution to health research in low- and middle-income countries by advocating for the ENHR strategy and by supporting countries to prioritize and manage health research resources more efficiently.[12,13] In its promotion of the ENHR concept, COHRED emphasized the following principles: countries as the key actors in health research for development;[14,15] the need for solid evidence to underpin an inclusive health research agenda; the need to involve all stakeholders in the prioritization process; and the need to link research results to policy and to action.

(a) Process

The three essential stages to increase the potential success of the priority-setting process are the following:

Planning the priority-setting process

- Identifying leadership for the process, namely the central government or a body officially assigned by the government to coordinate health research in the country.
- Identifying and involving stakeholders, i.e. decision-makers (at various levels), researchers, health service providers and communities.
- Gathering and analysing information for setting priorities (situation analysis) in three broad categories:
  – health status (main health problems,

[10] Commission on Health Research for Development. op. cit.
[11] Paper contributed by Sylvia de Haan, Carel Ijsselmuiden and Lisa Myers, COHRED, January 2004.
[12] See COHRED website for information on specific countries (http://www.cohred.ch).
[13] COHRED (2002). *Health Research Priority Setting: Lessons Learned*. Learning Brief 2002.6
[14] Neufeld V and Johnson N (eds). *Forging Links for Health Research. Perspectives from the Council on Health Research for Development*, IDRC, 2001.
[15] COHRED. *Health Research. Powerful Advocate for Health and Development, based on Equity*. Document 2000.2

common diseases, determinants or risk factors)
  - health care system (current status, deficiencies and problems)
  - health research system (availability of human, fiscal and institutional resources for research).

Setting the priorities

- Preparation of the information into a manageable list of priority health problems and related research areas/issues.
- Step-by-step process of stakeholders who determine the criteria for selecting priorities and a method for weighting the priorities.
- Determination of the scope of the expected outcome (from broad lists of priority health problems to a detailed list of priority research questions).

Implementing the priorities

- From research priority areas to research portfolio: transformation of the broad list of research priority areas into a research portfolio.
- From meeting report to policy decision: integration of priorities into an appropriate governmental plan, agenda or policy to ensure political backing.
- Research priorities and a changing environment: periodic review, update of priorities.
- Investing in research priorities.

Insert 4.1

Comparison of various priority-setting approaches[16]

Characteristics	Essential National Health Research Approach	Ad Hoc Committee on Health Research Approach	Advisory Committee on Health Research Approach	Global Forum Combined Approach Matrix
1. Objective of priority setting	Promote health and development on the basis of equity. Help decision-makers make rational choices in investment decisions.	Help decision-makers make rational choices in investment decisions so as to have the greatest reduction in the burden of disease for a given investment (as measured by number of DALYs averted).	Address problems of critical significance for global health: population dynamics, urbanization, environment, shortages of food and water, new and re-emerging infectious diseases.	Help decision-makers make rational choices in investment decisions so as to have the greatest reduction in the burden of disease for a given investment (as measured by number of DALYs averted), on the basis of the practical framework for priority setting in health research (matrix presented in Insert 4.2).
2. Focus at the global or national level?	Focus on situation analysis at country level; residual problems to be studied at global level.	Focus on situation analysis at the global level; method also applicable at the country level.	Priority to "significant" and "global" problems, requiring "imperative" attention.	Method applicable at both global and national level.
3. Strategies/ principles	Priorities set by all stakeholders. Process for priority setting should be iterative and transparent. Approach should be multidisciplinary.	Five- step process. Process should be transparent.	Priorities should be set by all stakeholders. Process should be transparent and comparative. Multidisciplinary approach.	Priorities should be set by all stakeholders. Transparent and iterative process. Approach should be multidisciplinary (biomedical sciences, public health, economics, environmental sciences, education sciences, social and behavioural sciences).
4. Criteria for priority setting				
Burden of disease	Based on an estimate of severity and prevalence of disease.	Measured by DALYs (number of years of healthy life lost to each disease).	Allocate resources to the problems deemed of "greatest global burden".	Measured by DALYs (number of years of healthy life lost to each disease) or other appropriate indicators.
Analysis of determinants of disease burden	Analysis of multidisciplinary determinants (biomedical, economic, social, behavioural, etc.).	Analysis of mostly biomedical determinants. Other determinants implicit.	Analysis of multidisciplinary determinants (biomedical, economic, social, behavioural, etc.).	Analysis of determinants at following intervention levels: – individual/family/ community – health ministry and research institutions – sectors other than health – government macro-economic policies.
Cost-effectiveness of interventions (resulting from planned research)	Some attempts at measurement in terms of impact on severity and/or prevalence.	Cost-effectiveness measured in terms of DALYs saved for a given cost.	Implicit reference to cost-effectiveness analysis.	Cost-effectiveness measured in terms of DALYs saved for a given cost.

Source: Global Forum for Health Research

[16] Global Forum for Health Research: *The 10/90 Report on Health Research 2001-2002* (Insert 4.1, pages 50-51).

Insert 4.1 (continued)

Comparison of various priority-setting approaches

Characteristics	Essential National Health Research Approach	Ad Hoc Committee on Health Research Approach	Advisory Committee on Health Research Approach	Global Forum Combined Approach Matrix
4. Criteria for priority setting (continued)				
Effect on equity and social justice	Central criterion in ENHR approach (not directly measured).	Inbuilt equity orientation, based on same weights given to year of healthy life saved for poor and rich population (effect on equity not directly measured as yet).	A number of indicators in the VHIP draw attention to the situation of the poorer segments of the population.	Inbuilt equity orientation, based on same weights given to year of healthy life saved for poor and rich population (effect on equity not directly measured as yet).
Ethical, political, social, cultural acceptability	This criterion is present, although in varying degrees, in various approaches, either explicitly (particularly in the ENHR approach) or implicitly.			
Probability of finding a solution	Specifically mentioned in the ENHR approach.	Part of the cost-effectiveness analysis (step 4).	Implicit.	Part of the cost-effectiveness analysis.
Scientific quality of research proposed	Pre-condition in all approaches.			
Feasibility (availability of human resources, funding, facilities)	Specifically mentioned in the ENHR approach.	Implicit.	Implicit.	Feasibility is part of the list of criteria.
Contribution to capacity strengthening	Explicitly mentioned in the ENHR approach.	Not mentioned. Could be integrated in the cost-effectiveness analysis.	Not mentioned. Could be integrated.	Can be integrated in the cost-effectiveness analysis.
5. Critical problems and priority research areas	Will depend on each country's situation.	Infectious diseases, malnutrition and poor maternal/child health. New and re-emerging infectious diseases due to antimicrobial resistance (TB, STD, HIV/AIDS, malaria). Increase in NCD and injuries. Inequities and inefficiencies in delivery of health services.	Infectious diseases: TB, vaccine-preventable childhood diseases, STD, HIV/AIDS, tropical diseases, maternal and child health. Noncommunicable diseases: cardiovascular diseases, diabetes, cancer, injuries, mental disorders, substance abuse. Health policies and health systems. Environment, nutrition, behaviour.	Health system research (efficiency and equity of health systems). Child health and nutrition (diarrhoea, pneumonia, HIV, malaria, vaccine-preventable diseases, nutritional deficiencies, TB). Maternal and reproductive health (mortality, STDs and HIV, nutrition, family planning). Noncommunicable diseases (cardiovascular, mental and neurological conditions). Injuries.
6. Implementation tools	Essential national health research plans.	Forum for investors in international health research. National agendas. Public/private collaboration.	Under preparation.	Analytical work for priority setting. Research networks (initiatives) for priority diseases. Annual meeting of partners to help correct the 10/90 gap.

(b) Tools

Over the past decade, there has been significant progress in health research priority setting, both in the process and the development of methodologies, tools and approaches.[17,18] The outstanding challenges and opportunities are discussed in chapter 9 (see section 15 on COHRED).

2. Ad Hoc Committee on Health Research (1996)

The characteristics of the priority-setting approach proposed by the Ad Hoc Committee are presented in Insert 4.1. It involves a so-called "five-step process" that focuses on the "economic dimensions" of priority setting.

3. Advisory Committee on Health Research (1997)

In its 1997 publication,[19] the Advisory Committee on Health Research set out the Visual Health Information Profile, a computer-based visual display showing the "totality of the health status of a country" in a way that enables comparisons of health status (i) for a given country over time and (ii) between countries at a given point in time. It draws attention to the large diversity of actors and factors affecting the health status of a population and defines indicators of a country's health status permitting these comparisons over time and across countries.

4. National Institutes of Health (NIH), USA

A paper presented in Forum 5[20] explored the process of setting priorities at the National Institutes of Health (NIH) in the United States. The aim of the paper was to identify the extent to which disease burden was a criterion in the allocation of research funds. The NIH is one of the 12 operative agencies of the US Department of Health and Human Services (DHHS). It is the only agency within DHHS with a singular mission of biomedical research and training to improve the health of the American population and people worldwide. In addition to the Office of the Director, it is composed of 27 centres, independently funded from yearly Congressional appropriations. Even though the centres focus mainly on the domestic health research priorities of the United States, the majority of them also have a substantial international programme. The Fogarty International Center is specifically charged with the promotion and support of international research and research training.

NIH funding increased over the past decade from approximately US$ 10 billion in 1992 to approximately US$ 23 billion in 2002. This has further increased to US$ 27 billion in 2004. Over recent years, funding for collaborative research between US and foreign investigators, direct funding of foreign researchers, and training of non-US scientists increased at a faster rate than the rest of the NIH programme. About US$ 300 million dollars were provided in 2002 for international research collaboration or direct funding (including about one third for training).

(a) Selection of research projects

Each year NIH receives a large number of research grant proposals for peer review. The number has risen from about 22 000 in 1992

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[17] *A Manual for Research Priority Setting using the ENHR Strategy*. Prepared by David Okello, Pisonthi Chongtrakul and the COHRED Working Group on Priority Setting, COHRED, Document 2000.3. Also available in French and Spanish.

[18] *Health Research for Policy, Action and Practice, Training Modules. Module I: Priority Setting*. Collaborative Training Programme, 2002. The Collaborative Training Programme is supported and coordinated by the Alliance for Health Policy and Systems Research, COHRED, the Global Forum for Health Research and the INCLEN Trust.

[19] Advisory Committee on Health Research. *A Research Policy Agenda for Science and Technology to Support Global Health Development, A Synopsis*, WHO, December 1997.

[20] Paper presented by Gerald T Keusch (then Director, Fogarty International Center, USA) in Forum 5.

to almost 35 000 in 2003. Approximately 70% are investigator-initiated, on any topic of interest to the investigator, and address research questions developed by the investigator. The remaining 30% are submitted in response to programme areas defined by the NIH itself.

(b) Method used to identify priorities

NIH uses the following five major criteria in setting its research priorities:

- *Public health needs*, based on the prevalence and severity of the problem, as reflected in national and international data.
- *Scientific quality of the proposed research*, based on a stringent two-stage peer review mechanism. This factor, essential to the NIH mission, is designed to separate politics and science and is firmly embedded in the culture of the NIH. Strict procedures are also in place to help eliminate conflict of interest in the decision-making process itself.
- *Potential for scientific progress*, based not only on the soundness of the research design, but also on the potential for scientific advances that open new lines of inquiry or the development of new instruments or methods that make it feasible to explore long-standing questions with greater sophistication or open up new questions to investigation.
- *Portfolio diversification*, to ensure that a broad base of science is being explored. This includes multiple studies on similar topics but using a multiplicity of approaches, as well as a large number of different topics being supported. The research portfolio ranges from basic, through clinical and translational research to applied research, including studies of rare or orphan diseases as well as those common in the population. Portfolio diversification also means that funding encompasses both national and international health research priorities.
- *Human resources and infrastructure support*. The support for human capital is of paramount importance to NIH and includes considerable attention to gender and minority issues.

5. WHO's Department of Reproductive Health and Research (RHR)[21]

(a) Process of priority setting

In 2002, a process was carried out by RHR to define priorities for work in 2004-2009 in research, normative work and technical support to countries. It involved the following steps:

Step 1: Surveying current issues and needs in sexual and reproductive health. A document prepared in-house, together with other WHO departments, reviewed the current issues in the field of reproductive health, to elicit feedback from advisory bodies. Criteria used to select priorities included the following: public health significance, utility and sustainability of products, impact on reproductive rights and gender issues, feasibility, and time and cost implications. These priorities were not for WHO but for the field at large.

Step 2: Seeking feedback from expert resource. A questionnaire was used to take the 'pulse' of the international community. In all, experts were asked to score 25 issues in sexual and reproductive health on the basis of their assessment of the needs at national and global level, practical guidelines at national and global level, and country support at national level, for each issue. This served to consolidate the review prepared under step 1.

Step 3: Selecting potential operating areas for WHO. This was implemented using the logical

[21] Catherine d'Arcangues, RHR/WHO. Presentation in WHO, 2003.

framework approach and taking into consideration the WHO/RHR comparative advantages. The selection among the priorities defined under step 1 was based on the following factors: credibility as a technical organization of high scientific standards, neutrality, objectivity and independence, convening power, wide resource base, position as an inter-governmental agency focusing on the needs of developing countries, capacity building, leadership role, avoiding duplication with other WHO departments and other agencies/institutions.

Step 4: Redefining priority setting. A ranking exercise was undertaken on the basis of the outputs of step 3 above. The ranking was undertaken in a workshop in which experts used a combination of 'scoring' and 'ranking' of identified priorities. Consideration was given to the feasibility and likely impact of projects and to the ability of the programme to deliver.

Step 5: Presentation to governing bodies of RHR. The Strategic and Technical Advisory Group discussed the process and results in February 2003. They commended the methods and outcomes, and advised on further prioritization of the selected themes based on the strengths of the programme and on financial resource allocation.

(b) Methods used to identify priorities

As a result, priority areas were identified in each of the eight areas of sexual and reproductive health listed below, thus operating a shift in focus for RHR:

- technical cooperation with countries
- family planning, including infertility
- maternal and neonatal health
- sexually-transmitted infections (STIs) and reproductive tract infections (RTI) including HIV/AIDS and cervical cancer
- prevention of unsafe abortion
- sexual health, including female genital mutilation
- gender issues and reproductive rights
- adolescent sexual and reproductive health .

6. The Combined Approach Matrix

Based on previous methodologies for priority setting, in particular those proposed by the ENHR, the Ad Hoc Committee on Health Research and the Advisory Committee on Health Research, the Global Forum for Health Research proposed the Combined Approach Matrix (CAM) in 2000.[22] The developments in the method over the past three years are presented in Section 3 below, while Section 4 deals with the concrete application of the matrix for identifying priorities. Section 5 discusses the technical issues surrounding the economic dimensions of priority setting.

[22] Global Forum for Health Research. *The 10/90 Report on Health Research 2000*, Geneva, May 2000 (pages 37-41).

Section 3

The Combined Approach Matrix

1. Principles

The CAM is a tool (i) to help classify, organize and present the large body of information which enters into the priority-setting process; (ii) to identify gaps in health research; and, on this basis, (iii) to identify health research priorities, based on a process which should include the main stakeholders in health and health research.

Priority setting in health research must take into account an "economic dimension" as underlined in the Five-Step Process of the 1996 Ad Hoc Committee as well as an "institutional dimension", which is emphasized by the 1991 ENHR approach and the 1997 Visual Health Information Profile proposed by the Advisory Committee on Health Research. The institutional approach argues that the health status of a population depends on actors and factors outside the health sector just as much as on the national health system itself.

The objective of the CAM is to incorporate both the economic and institutional dimensions into a single tool for priority setting. The resulting matrix for priority setting is presented in Insert 4.2.

For practical purposes, information on disease burden and resource flows will only be considered at the global level and not disaggregated by broad category of actors and factors. The advantage of the proposed matrix is that it will help organize, summarize and present all available information on one disease and facilitate comparisons between the likely cost-effectiveness of different types of interventions at different levels. The information will inevitably be partial, and probably even sketchy in some cases, but it will progressively improve and even limited information is sometimes sufficient to indicate promising avenues for research.

Insert 4.2

The Global Forum Combined Approach Matrix for priority setting

	Global level	A. Individual family and community	B. Ministries of health, research institutions, health systems	C. Sectors other than health.	D. Central government and macro-economic policies
1. Disease burden					
2. Determinants for persistence					
3. Present level of knowledge					
4. Cost and effectiveness					
5. Resource flows					

Source: Global Forum for Health Research

2. The main elements of the CAM

(a) The economic dimensions of priority setting

The components of the Five-Step Process identified in the 1996 Report of the Ad Hoc Committee are the following:

Step 1: Magnitude of the disease burden

Measure the disease burden as years of healthy life lost due to premature mortality, morbidity or disability. Summary measures, such as the DALY, can be used to measure the magnitude. Other methods serving the same purpose can also be used.

Step 2: Determinants (risk factors)

Analyse the factors responsible for the persistence of the burden, such as lack of knowledge about the condition, lack of tools, failure to make use of existing tools, limitations of existing tools or factors outside the health domain.

Step 3: Current level of knowledge

Assess the current knowledge base available to help solve the health problem and evaluate the applicability of solutions, including the cost and the effectiveness of existing interventions.

Step 4: Cost-effectiveness

Assess, against other potential interventions, the promise of the R&D effort and examine if future research developments would reduce costs, thus allowing interventions to be compared and applied to wider population segments.

Step 5: Resources

Calculate the present level of investment in research on the specific disease and/or determinant.

(b) The institutional dimensions of priority setting

The institutional dimensions include the following groups of actors and factors:

- Individual, family, community: in the CAM, this column will review elements which are relevant to the reduction of disease burden and can be modified at the individual, family or community level. This includes relevant interventions on, primary care, prevention and education. In the case of malaria, for example, prevention using barrier methods such as insecticide-impregnated bednets is a key intervention at the individual level.
- Health ministry, health systems and services, health research community: this column in the matrix will review the contribution of the ministry of health and health research systems to the control of the specific disease or condition being explored. The column focuses on (i) biomedical interventions and their application throughout the health system as a whole; (ii) policies and structures which can help the health system reduce the burden of a specific condition; and (iii) the potential for the health research community to provide tools, processes and methods for the same purpose.
- Sectors other than health with a major impact on people's health: examples include the role of the transport sector in the prevention of road traffic injuries, or the role of the education system (both formal and informal) in changing people's health behaviour (washing hands, smoking, substance abuse, avoiding risky behaviour in general).
- Central government and macroeconomic policies: this column in the matrix focuses on elements at the central government level or those outside the country which can have a role in the control of diseases or conditions. An example of this is the impact of World Trade Organization agreements concerning intellectual property rights on the provision of antiretrovirals for the treatment of people living with HIV/AIDS.

3. Functions of the CAM

The CAM combines the respective advantages of the methods developed in the 1990s (ENHR, the Five-Step Process of the Ad Hoc Committee on Health Research and the Visual Health Information Profile of the Advisory Committee on Health Research), while remaining relatively simple.

Thus information gathered in past priority-setting exercises conducted at country, regional and global levels can be introduced into the CAM as a common framework to organize and present the collected information (as a basis to identify gaps in health research and health research priorities).

In summary, the CAM:

1. Brings together in a systematic framework all information (current knowledge) related to a particular disease or risk factor.
2. Identifies gaps in knowledge and future challenges.
3. Relates the Five-Step Process in priority setting (economic axis) with actors and factors (institutional axis) determining the health status of a population.
4. Permits the identification of "common factors" by looking across the diseases or risk factors.
5. Is applicable to priority setting in the field of:
   - national, regional or global problems
   - diseases as well as risk factors.
6. Permits the linkage of priorities in the field of health and health research.
7. Enables the rapid identification of the effect of a change in one of the 'boxes' of the matrix on the other 'boxes'.
8. Permits taking into account the large number of factors outside the health sector which have an important impact on people's health.

Section 4

Application of the Combined Approach Matrix

1. How to use the CAM at the national level

The first step is to estimate the burden for each of the main diseases and risk factors in the country and to engage with all institutions and stakeholders in the country with particular knowledge of that disease. Each institution will feed into the matrix the information at its disposal. As a result, the matrix will gradually incorporate the best available information regarding a specific disease or risk factor. In many cases, instead of solid information, the matrix will reveal how little information is available to make rational, cost-efficient and effective decisions in the fight against specific diseases. These gaps in the information matrix are all candidates for research.

The second step is to identify which information would have the largest impact on the disease. This will be a time-consuming process as it is likely that various stakeholders will have different opinions as to the most important factor(s) to be studied to reduce the burden of that particular disease. It should be an iterative process in which each institution presents its point of view and listens to the point of view of other institutions, until gradually a consensus and a list of research priorities for each disease emerges from the discussion and the comparison of the arguments.

The next step is to compare the research priorities across diseases and come up with a final list of top priorities in the various research fields, comprising those research topics likely to have the greatest impact in reducing the burden of disease for the country (i.e. those research topics likely to lead to the largest number of 'healthy life years' for a given research budget).

This overall list of research priorities for the country is then divided up among the various research institutions in the country based on their respective comparative advantages.

Similar types of processes can be followed at the local and global levels to determine the health research priorities at these levels. Such processes can be applied by individual institutions as well as by local and national governments and development agencies, to identify their priority areas for engagement in, or support to, health research.

This is a long-term effort. The information will inevitably be partial in the first exercises, probably even sketchy in some cases, but the tool should demonstrate its usefulness at an early stage by highlighting the most important gaps in the information needed to make evidence-based decisions and by enabling some decisions to be made despite the limited information available.

Insert 4.3

Generic steps to use the CAM to identify key research projects at national level

1. Estimate the burden for each of the main diseases and risk factors.
2. For each disease and risk factor, bring together all institutions and stakeholders in the country with particular knowledge of that disease or risk factor.
3. For each of the selected diseases and risk factors, feed into the matrix the information at the disposal of each institution, thus gradually incorporating into the table the best available information regarding that disease or risk factor.
4. Complete the matrix with information from other sources which may be relevant for your country.
5. Identify which missing information would, if made available, be likely to contribute the most to decreasing the burden of that disease or risk factor.
6. Identify research projects which can fill these gaps in information. This would be the list of research priorities for that disease or risk factor.
7. Compare research priorities thus identified across diseases and risk factors and come up with a final list of top priorities in the various research fields, which will be composed of those research topics likely to save the largest number of 'healthy life years' for a given budget.
8. Allocate the priority research projects among the research institutions in the country based on their comparative advantages.

Source: Global Forum for Health Research

2. Linking research priorities at the local, national and global levels

Theoretically, health research priorities should be established by local communities, based on the local burden of disease and determined through a participatory process involving the use of scientific tools. A comparison of the priorities identified at community level will enable the identification of those priorities which are common to several or possibly all communities, thus indicating that these may become national priorities.

National authorities should then identify the national health research priorities, based on information about the national burden of disease and the results of the priority-setting exercises of the local communities, again through a participatory process and the use of scientific tools. The definition of the national and local priorities and actual research activities should be the result of an iterative process between the two levels, the ultimate result being based on comparative advantages.

International organizations and institutions with a global remit should then identify global health research priorities, based on the global burden of disease and the national priorities defined by as many countries as possible, using a participatory process and scientific tools. Here also, the definition of the global and national health research priorities should be the result of an *iterative process* between the two levels, the ultimate result being based on comparative advantages.

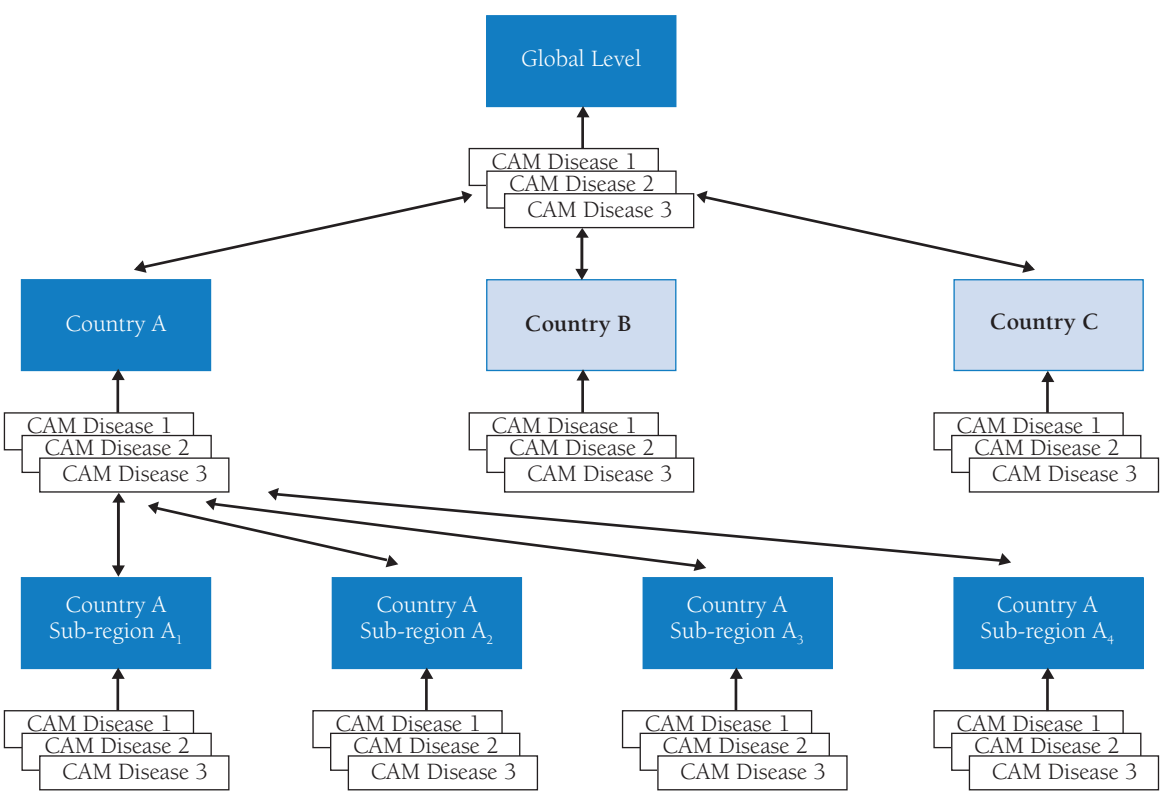
In practice, the process can start anywhere in the chain of responsibilities between the local community level, the national level and the global level, the important points being the following:

- since few if any countries and institutions have instituted a scientific process for identifying health research priorities, it is important that the process should now get under way and that the 'mosaic' should be gradually filled; an attempt is made in Insert 4.4 to represent the system and the linkages between the various levels;

- for a given disease or risk factor, priorities are unlikely to be determined once and for all, but rather to evolve over time, based on new discoveries and the evolution of the disease burden anywhere in the system; thus, it is important that the process of defining research priorities be continuous and iterative between the local, national and global levels;
- it is also unlikely that a priority problem will be researched at only one of the three levels; in reality, a research programme is more likely to have local, national and global components, with the solution depending on the optimum combination of the solutions found at each of the three levels.

Insert 4.4

Iterative process for the definition of disease research priorities at the local, national and global levels



Source: Global Forum for Health Research

3. Experiences using the CAM at the global level

(a) Early experiences

A first application of the CAM at the global level focused on epilepsy and was presented in a table entitled "Epilepsy: risks, obstacles and opportunities for interventions" in *The 10/90 Report on Health Research 2000* (Insert 5.2, pages 90-91).

Further applications in 2000 and 2001 focused on malaria, onchocerciasis and indoor air pollution and were presented in *The 10/90 Report on Health Research 2001-2002* (Inserts 4.11, 4.12 and 4.15 respectively).

(b) The example of TDR

Based on these first experiences, a priority-setting exercise was undertaken in 2002-2003 to re-align TDR's strategic focus in research to address the disease control priorities of the next five years. A summary of this exercise is presented below:[23]

The first step in the prioritization process of TDR was to bring together the TDR Disease Research Coordinators, TDR staff, disease control experts from within WHO, country programme managers and disease experts (Disease Reference Group and Scientific Working Groups) to analyse rationally and transparently the current situation of each disease. This included taking into account the current status of research and the comparative advantages of TDR. The result was the definition of a set of "strategic TDR emphases" (or priorities) in the scientific and technical areas of work for the following five years.

The exercise was based on the following documents:

- the analyses carried out by TDR, WHO and the World Bank between 1993 and 1996 which culminated in the 1996 Ad Hoc Committee Report;[24]
- the Global Forum's proposed CAM for setting priorities in health research.[25]

A modification of the Combined Approach Matrix led to the definition of the following seven steps used in the TDR prioritization process:

(i) What is the size and nature of the disease burden and epidemiological trends?
(ii) What is the current disease control strategy?
(iii) What are the major problems/challenges for disease control?
(iv) What research is needed to address these problems/challenges?
(v) What is currently being done in R&D, and what research opportunities exist?
(vi) What are TDR's comparative advantages?
(vii) Strategic emphases for R&D.

A comparison of the CAM of the Global Forum for Health Research and the TDR seven-step approach (Insert 4.5) shows the close parallels between the two methods.

[23] Lazdins J, TDR. Presentation in Forum 7, Geneva, December 2003.
[24] Report of the Ad Hoc Committee. op. cit.
[25] See Insert 4.2.

Insert 4.5

Comparison of the CAM[26] and the 2003 TDR 'Seven-Step Process' [27]

Combined Approach Matrix	TDR Seven-Step Process
1. Disease burden: measure the disease burden as years of healthy life lost due to premature mortality, morbidity or disability.	(i) What is the size and nature of the disease burden and epidemiological trends?
2. Determinants for persistence: assess factors responsible for the persistence of the burden (lack of knowledge, lack of tools, failure to make use of existing tools, limitations of existing tools or factors outside the health domain).	(ii) What is the current disease control strategy?
3. Present level of knowledge: assess the current knowledge base to solve the health problem and evaluate the applicability of solutions, including the cost and the effectiveness of existing interventions.	(iii) What are the major problems/challenges for disease control?
4. Cost and effectiveness: assess, against other potential interventions, the promise of the R&D effort and examine if future research developments would reduce costs, thus allowing interventions to be compared and applied to wider population segments.	(iv) What research is needed to address these problems/challenges?
5. Resource flows: calculate the present level of investment on research for specific diseases and/or determinants.	(v) What is currently being done in R&D and what research opportunities exist?
Other: specific to TDR only	(vi) What are TDR's comparative advantages?
	(vii) Strategic emphases for R&D.

Source: Global Forum for Health Research

The TDR prioritization strategy led to the following results: a transparent and objective prioritization process, the active participation of partners from both health research and disease control, a direct link between strategic emphases and the research needs of disease control, an efficient mechanism to communicate its strategic choices to its partners, and a continuous monitoring system for incorporating new priority needs.

Diseases in which TDR is working were categorized into the following three groups:

Group 1: Emerging and uncontrolled diseases. Diseases in this group include African trypanosomiasis, dengue and leishmaniasis. The epidemiological pattern of these diseases indicates that these are increasing in prevalence and the tools are not well developed or applicable to large segments of

[26] Ibid.

[27] Full results of the TDR priority-setting exercise are presented in "Strategic emphases for tropical diseases research: a TDR perspective" in *Trends in Parasitology*, December 2002.

the population. Research is required to improve the tools and the strategies to implement mass programmes.

Group 2: Control strategy available but disease burden persists. Diseases in this group include malaria, schistosomiasis and TB. Effective interventions are available which can be applied on a wide scale with the potential to reduce the disease burden but this has not yet taken place.

Group 3: Control strategy effective and elimination is planned. Diseases in this group include Chagas disease, leprosy, lymphatic filariasis and onchocerciasis. There are tools and strategies available to control these diseases and probably to eliminate them in the medium-term. Operations research to achieve these objectives is required as the prevalence is declining and elimination targets are evident.

(c) Ongoing experiences

Priority-setting exercises using the CAM are under way focusing on various diseases and risk factors. Work on TB and schizophrenia is presented in Insert 4.6 and Insert 4.7 respectively.

Insert 4.6

Tuberculosis: application of the CAM

Levels of potential intervention →	A. Level of the individual, family & community	B. Level of the health ministry, health research institutions, and health systems & services	C. Level of sectors other than health	D. Level of central government and macroeconomic policies
1. Disease burden				
2. Why does the burden still persist? What are the determinants?	• Exposure to infections (by sputum smear-positive PTB) • Poverty – poor housing – overcrowded conditions – undernourishment • HIV impact (relative risk for TB is 30 times higher for people infected by both HIV and Mycobacterium tuberculosis) • Inadequate care seeking • Non-compliance with treatment regime • Inadequate access to health services	• Neglect of the problem – inadequate case detection, diagnosis and cure – inadequate organization of services – unavailability of TB drugs – lack of quality control – inaccessibility of services for many patients • Inadequate case management – failure to cure cases that were diagnosed • Inadequate treatment regimes – failure to ensure directly observed treatment – lack of an information management system for rigorous evaluation of treatment outcomes • Over-reliance on BCG (i. e. vaccination for children) • Spread of multidrug-resistant (MDR) strains of M. tuberculosis • Inappropriate research agenda • Changed role of the MoH under "health sector reform", away from service provider to regulator/purchaser	• Poor infrastructure due to poverty – communication – transportation • Poor drug distribution • The HIV pandemic (high risk of TB in HIV patients) • Stigma against patients suffering from TB, e.g. at workplace • Insufficient diagnosis & treatment of TB in prison populations	• Poverty • Weak governance – inadequate political commitment – no transparent resource allocation – inadequate drug supply – poor control of private & public sectors • Inadequate financing within and between countries • Lack of knowledge of economic burden caused by TB and cost-effectiveness of control • Changing role of State away from service provision

3. What is the present level of knowledge?	a. Interventions currently available	• WHO´s DOTS strategy • Preventive therapy • BCG vaccination	• WHO´s DOTS strategy • Preventive therapy • BCG vaccination • Environmental controls	• Programmes to raise awareness of politicians, health professionals and the general public about the efficacy of existing interventions programmes against TB • Education programmes about the nature and treatment of TB, particularly in schools, the workplace, related to prison populations • Programmes against poverty – poor housing – overcrowded conditions – undernourishment • Support to DOTS strategy by some parts of civil society, e.g. faith-based organizations	
	b. How cost-effective are current interventions?	• DOTS highly cost-effective in most settings. Exceptions are: – isolated areas – when stigma is attached to TB (particularly in HIV areas) – in very poor areas when indirect costs cannot be met • Preventive therapy is cost-effective in some high HIV settings only (and even this is disputed) • BCG suffers random variations in effectiveness; it is, however, affordable and acceptable	• DOTS highly cost-effective in most settings. Exceptions are: – Dense urban & remote rural areas – In some countries where it is considered too labour intensive & expensive • Preventive therapy unfeasible due to low capacity in health sector • BCG feasible and cost-effective and widely applied • Environmental controls generally ineffective and costly	• Awareness and education programmes: not very feasible in many settings, due to poverty & lack of political will • DOTS in private sector cost-effective • Involvement of civic society cost-effective	

Insert 4.6 (continued)

Tuberculosis: application of the CAM

Levels of potential intervention →		A. Level of the individual, family & community	B. Level of the health ministry, health research institutions, and health systems & services	C. Level of sectors other than health	D. Level of central government and macroeconomic policies
4. What is to be expected in the future?	a. Interventions	• Social mobilization • Health education (regarding TB) • Improving health seeking behaviour of patients	• Strategies to extend coverage DOTS and increasing its applicability and acceptability • Improved treatment (better drugs & drug supply) • Improved diagnostics and clinical algorithms for the detection of smear-negative patients • New prophylactic interventions – a new vaccine (broader application than BCG for children) – mass chemoprophylaxis • MDRTB case management	• Involvement of civil society in TB control • Involvement of industry in TB control • Involvement of prisons in TB control	• Involvement of civil society in TB control • Involvement of industry in TB control • Involvement of prisons in TB control
	b. Cost-effectiveness	• Unknown	• Operational interventions: some evidence of cost-effectiveness • New tools: unknown cost-effectiveness	• Unknown	• Unknown
5. Resource flows					

Source: Global Forum for Health Research

Insert 4.7

Schizophrenia: application of the CAM

Levels of potential intervention →	A. Level of the individual, family & community	B. Level of the health ministry, health research institutions, and health systems & services	C. Level of sectors other than health	D. Level of central government and macroeconomic policies
1. Disease burden				
2. Why does the burden still persist? What are the determinants?	• There is no proven method of primary prevention of schizophrenia • Biological risk factors include – Genetic vulnerability (polygenic); heritability 69% - 80% – Early developmental insults (low birth weight; perinatal brain damage; early neuroinfection) • Environmental/psychosocial risks – Urban birth – Stigma – Social isolation • High co-morbidity (e.g. substance misuse)	• There is no cure for schizophrenia • Insufficient recognition in treatment programmes that level of burden is shaped by interaction between intrinsic vulnerabilities caused by the disease and the psychosocial environment • Hospitalization with the aim of removing people with schizophrenia from public places or facilities, or otherwise restricting their freedom • Severe adverse effects of antipsychotic drugs (neurological extrapyramidal effects), interfering with psychosocial and vocational adjustment, lead to non-compliance with medication, and contribute to stigma. • Treatment gap in developing countries: 67% or 17 million patients are not receiving treatment • Lack of specialists and general health workers with the knowledge and skills to manage schizophrenia across all levels of care • Lack of resources	• Stigmatizing environment (including workplace) • Mental health legislation inadequate or absent • Neglect of the large number of patients who have lost their supportive network and are homeless, vagrant or in prison • Poor coordination between services including non-health sector	• Insufficient awareness of the size of the problem and the existence of cost-effective interventions capable of reducing the burden of the disease • Lack of a coherent mental health policy

Insert 4.7 (continued)

Schizophrenia: application of the CAM

<table>
<tr><th>Levels of potential intervention →</th><th>A. Level of the individual, family & community</th><th>B. Level of the health ministry, health research institutions, and health systems & services</th><th>C. Level of sectors other than health</th><th>D. Level of central government and macroeconomic policies</th></tr>
<tr><td rowspan="3">a. Interventions currently available</td><td colspan="3">• In contrast to prevention, there is sufficient knowledge of interventions that can substantially ameliorate the course of schizophrenia and reduce the resulting impairments and disabilities:</td><td rowspan="2">• Formulation of mental health policy (e.g. as part of health sector reforms)
• Mental health awareness programmes (e.g. declaration of a mental health day)</td></tr>
<tr><td>• Reduction of stigma
• Protection of patient's human rights
• Prevention of premature mortality (e.g. suicide)
• Prevention of criminal and offending behaviour
• Skills training and illness self-management</td><td>• Antipsychotic medication (conventional antipsychotics, (e.g. phenothiazines) and atypical antipsychotics (e.g. clozapine)
• Cognitive-behavioural therapy for psychotic symptoms
• The Primary Health Care model
• Family interventions
• Group interventions focused on the patient
• Therapeutic communities
• Short-term hospitalization for acute care in accordance with ethical guidelines by international bodies, such as WHO</td><td>• Supported employment approach to vocational rehabilitation
• Nonstigmatization programmes
• Mental health legislation
• Consumer empowerment</td></tr>
<tr><td colspan="3">• Community-based management programmes involving at least three operational components:
– Pharmacological treatment aimed at symptom control in acute episodes, maintenance of stabilization and prevention of relapse, and means of ensuring adherence to treatment protocol
– Mobilization of family and community support, including provision of education about the nature of schizophrenia and its treatment, involving the family in simple problem-solving skills training, and involving the local community in providing a supportive and nonstigmatizing environment
– Local rehabilitation, such as maintaining the patient in appropriate work and social roles within the community, and creating opportunities for occupational and social skills training</td><td></td></tr>
<tr><td>b. How cost-effective are current intervention?</td><td></td><td>• Antipsychotic medication: conventional drugs are effective and inexpensive (chlorpromazine) but cause severe adverse effects. Atypical drugs cause fewer</td><td></td><td></td></tr>
</table>

3. What is the present level of knowledge?			adverse effects, but are more expensive. Cost-effectiveness studies of conventional vs. atypical antipsychotics originate in developed world. To achieve universal availability at low cost conventional antipsychotics are clearly to be preferred (pending that current atypicals come off-patent).		
		• Many of the psychological approaches have not been evaluated by economists, nor have the newest atypical antipsychotics. • There are few if any evaluations of specific combinations of pharmacological and psychological therapies. • There is little evidence of the economic consequences of side effects or non-compliance, yet one would suspect these to be important drivers of long-term costs. • Research findings point to areas where cost savings may be achieved in principle, but they may not lead to cost savings in practice: with the growth of community-based care involving multiple agencies with their own budgets and their own ways of working, there is little evidence about the incentives and constraints that might help or hinder integrated responses to schizophrenia			
4. What is to be expected in the future?	a. Interventions	• Research into the aetiology of schizophrenia, particularly genetic epidemiology, neurobiology • Research into prognosis and outcome of schizophrenia in developing countries	• Research into interactive interventions involving the patient, the family, and the community, cognizant of the fact that biological vulnerability and environmental influences interact and potentiate each other at every stage of schizophrenia (treatment, stabilization, and residual) • Research into preventive intervention, e.g. through early detection and avoidance of treatment delay		
		• Research capacity building through on-site education, exchange programmes and distance learning • Development of local networks that link centres with the requisite expertise to their surrounding community, and creation of regional networks linking such centres through joint training programmes, staff exchanges and collaborative research • Partnerships between lead institutions in high-income countries and such collaborative networks in low-income countries			
	b. Cost-effectiveness				
5. Resource flows					

Source: Global Forum for Health Research

4. Experiences using the CAM at the country level

The CAM is currently being used as a tool to help identify research priorities in the following exercises:

(a) Perinatal and neonatal health in Pakistan
In Pakistan, the CAM was used to assess potential research priorities in perinatal and neonatal care, widely acknowledged to be a greatly under-researched and under-resourced area.[28] The following main areas were highlighted for targeted research in future programmes:

- better regional and national estimates of perinatal and neonatal mortality/morbidity;
- evaluation of the socio-behavioural determinants of perinatal and neonatal mortality/morbidity in diverse but representative settings;
- evaluation of the current barriers for care-seeking and potential acceptability of future intervention strategies.

It was highlighted that there were several large and community-based data sets on reproductive health and related behaviour already available from several government agencies and autonomous bodies.

As a specific proposal, it was suggested that these disparate data sets and additional information could be pooled under a collaborative research exercise to yield composite national estimates of disease burden. This composite analysis would give a comprehensive picture of existing reproductive health behaviour and practices that impact on perinatal and neonatal care in Pakistan. Any gaps remaining could be the subject of further research.

Recommendations were made for studies to be conducted on cost-effective interventions in perinatal and neonatal care, especially those that combine elements of maternal and postnatal care. A specific attempt was made to address one such area, low birth-weight, using the CAM. Further assessment of other priority areas in perinatal and neonatal care – for example, birth asphyxia, infections and prematurity – is under way.

(b) The Indian Council of Medical Research
A paper presented in Forum 7[29] described the priority-setting exercise undertaken in 2003 by the Indian Council of Medical Research (ICMR) using the Combined Approach Matrix, which included the following steps:

(i) The concept of priority setting was first discussed with the ICMR staff.
(ii) A workshop was carried out amongst workers in ICMR and other agencies in India (including civil society) on health research and health research priorities.
(iii) Directors of all ICMR Institutes met to discuss priorities in their area of work.
(iv) An expert group of scientists from various disciplines in each Institute summarized the current knowledge in their respective fields and fed this information into the CAM.
(v) A Strengths, Weaknesses, Opportunities and Threats (SWOT) analysis was undertaken using the completed CAM tables. Major achievements and contributions in the field were listed.
(vi) Consultations with government officials,

[28] Ali N. Deputy Director, Save the Children, USA. A preliminary assessment of priorities in perinatal and neonatal care in Pakistan using the combined approach matrix. Paper presented in Forum 7, Geneva, December 2003.
[29] Kant L. Application of CAM to Identify Research Priorities of Indian Council of Medical Research. Paper presented in Forum 7, Geneva. December 2003.

NGOs and the community were undertaken on the basis of the results of the exercise. This helped to compare lists of priorities and gaps identified with those already set out by other groups in India, and by bilateral and international agencies.

(vii) Gaps in health research relevant to India were then identified, among which ICMR selected malaria and visceral leishmaniasis for a more detailed analysis and identification of priority health research projects. The tables on malaria will be compared with those prepared by TDR. The two exercises will highlight the respective advantages and complementarity of the two institutions in malaria research (TDR at the global level and ICMR at the national level in India).

(viii) The next step is for ICMR and its partner institutions to determine which institution in the Indian context will take responsibility for which priority research project in the fields of malaria and visceral leishmaniasis (in which ICMR has a comparative advantage). Other research institutions will take responsibility for the other priority research projects, based on their own comparative advantages.

In summary:

- The priority-setting exercise compels institutions to think rationally and focus institutionally.
- The exercise requires training and practice to fill in the CAM.
- In the first phase, the exercise often identifies more gaps than priorities as a large amount of information essential for rational decisions on research priorities is unavailable, particularly in the fields of cost-effectiveness data, factors affecting health behaviour and the impact on people's health of sectors other than health and of macroeconomic policies.

Section 5

Technical issues concerning the economic dimensions of priority setting

1. Comparison of mortality with DALYs

In the past, mortality figures were the leading concern of policy-makers. Deaths attributable to specific diseases had the power to advocate for specific interventions focusing on the causes of mortality. However, this mortality-focused approach has gradually shifted following the development in the early 1990s of the summary measures integrating mortality, morbidity and disability in a single burden of disease index.

As shown in Insert 4.8, mortality measures and summary measures (such as DALYs) lead to a very different ranking of diseases by burden.

Insert 4.8

Comparison of mortality measures and DALY measures for all countries

Mortality measure	% of total	Ranking	DALY measure	% of total	Ranking
Ischaemic heart disease	12.6	1	Ischaemic heart disease	3.9	6
Cerebrovascular disease (stroke)	9.6	2	Cerebrovascular disease (stroke)	3.3	7
Lower respiratory infections	6.6	3	Lower respiratory infections	5.8	2
HIV/AIDS	4.9	4	HIV/AIDS	5.8	3
Chronic obstructive pulmonary disease	4.8	5	Chronic obstructive pulmonary disease	1.9	>10
Perinatal conditions	4.3	6	Perinatal conditions	6.5	1
Diarrhoeal diseases	3.1	7	Diarrhoeal diseases	4.1	5
Tuberculosis	2.8	8	Tuberculosis	2.4	10
Trachea, bronchus, lung cancers	2.2	9	Trachea, bronchus, lung cancers	0.8	>10
Malaria	2.1	10	Malaria	3.0	8
			Unipolar depressive disorders	4.5	4
			Road traffic accidents	2.6	9

Source: Global Forum for Health Research

Note: Ischaemic heart disease and cerebrovascular disease (stroke) are the two leading causes of death globally, followed by lower respiratory infections and HIV/AIDS. However, among the diseases accounting for the highest disease burden (i.e. including mortality, morbidity and disability) perinatal conditions, lower respiratory infections, HIV/AIDS and unipolar depressive disorders are ranked highest. In terms of age-related DALYs, 36% of the world's burden of disease and injury, in 2002, was accounted for by children aged less than 15 years, and almost 50% by adults aged 15–59 years.

2. Developments regarding DALYs

The measure of DALYs has been used in the Global Burden of Disease Study (GBD)[30] and in a number of National Burden of Disease Studies. One DALY can be thought of as one year of 'healthy' life lost and the burden of disease as a measurement of the gap between current health status and an ideal situation where everyone lives into old age free from disease and disability.

WHO is currently undertaking version 3 of the GBD Project for the year 2000,[31] using DALYs as a summary measure. The primary objective of the GBD study is the development of comparable, valid and reliable epidemiological information on a wide range of diseases, injuries and risk factors. In summary, the objectives of the GBD 2000 study are the following:

- develop internally consistent estimates of mortality from 135 major causes of death, disaggregated by age and sex, for the world and major geographic regions;
- develop internally consistent estimates of the incidence, prevalence, duration and case-fatality for over 500 sequelae resulting from the above causes;

[30] Murray CJ and Lopez A. *Global Burden of Diseases and Injuries*. Volume 1, WHO, 1996.

[31] Global Programme on Evidence for Health Policy, Discussion Paper No. 54, WHO, 2003.

- quantify the burden of premature mortality and disability by age, sex and region for 135 major causes or groups of causes;
- analyse the contribution to this burden of major physiological, behavioural and social risk factors by age, sex and region.

The *World Health Report 2003* presents burden of disease estimates for 2002 based on Version 3 of the GBD study. The data sources and methods used for Version 3, together with methods used to prepare country-specific estimates of burden of disease and healthy life expectancy, are also documented.

3. Further research on disease burden measurement

(a) Deficiencies in contextual measurement

Current assessments of population health that attempt to account for the burden of morbidity tend to ignore the contexts in which the health conditions occur, i.e. the social, cultural or environmental context. This failure to take account of contextual considerations has important implications, as a study funded by the Global Forum has highlighted.[32] The authors argue that the disability weights associated with each condition are currently fixed across all social, cultural and environmental contexts. Thus, blindness in the UK is given the same disability weight as blindness in Niger in spite of structural interventions in the UK that make the disability less severe than in Niger. The authors conclude that the lack of consideration of contexts results in a measure that will underestimate the burden associated with morbidity in disadvantaged populations and overestimate the burden in advantaged populations.

Using qualitative and quantitative techniques, the study examined the impact of two health conditions (epilepsy and paraplegia) on people living in different contexts. The contexts were varied by country (Australia and Cameroon) and by environment (urban and rural); the effects of gender and socioeconomic status were also examined.[33] In each context, the participants completed a variety of tests and interviews.

Not surprisingly, both qualitative and quantitative tools revealed that people with paraplegia in Australia were substantially better off than those in Cameroon. The lack of infrastructure in Cameroon in general and in the rural areas in particular made coping with paraplegia extremely difficult. Indeed, in Cameroon paraplegia is generally regarded as a terminal condition, while facilities available in Australia make it possible to cope with this condition. In addition, it was evident that participants who were financially better off could buy the equipment and services they required to improve their quality of life.

The study underlined the importance of distinguishing summary measurement of health (using measures such as DALYs which attempt to quantify average levels of health in the population) from measurement of broader quality of life or well-being. Ignoring the context in which health conditions occur may reinforce existing inequalities in health. In the past two years, WHO has embarked on large-scale efforts to improve the methodological and empirical basis for the valuation of health states.

(b) Co-morbidity

It is also important to quantify the effect of co-morbidity (i.e. more than one disease or condition affecting the same individual). The GBD 1990 study used an additive model in

[32] Reidpath D et al. " Measuring health in a vacuum: examining the disability weight of the DALY" *Health Policy and Planning* 18(4):351-356.

[33] Ibid.

which, for the same individual, the average time spent in two different health states were combined. The GBD 2000 work being undertaken at WHO is examining co-morbidity in more detail, particularly for mental disorders.

(c) Measuring the impact of a health problem on third parties

A condition affecting one individual can also have a major impact on others (e.g. a relative of an alcoholic or drug addict). While the measurement of disease burden would estimate the impact of alcohol or drugs on morbidity, disability and mortality, it would not estimate the time invested by third parties in caring for these patients.

Taking these effects on third parties into account could substantially increase the assessment of burden of certain diseases and change the ultimate ranking of diseases, in a way that would reflect the different context in each country or community. This has important implications for health research policies.

(d) Future steps

Over the past decade, information on the global burden of disease has had a powerful influence on policy-makers and led to a radical shift in policy. The challenge now is to continue promoting and refining these methods as a quantitative tool, and to use the information to guide research priorities and the allocation of funding. Continued work is needed to improve the usefulness of these summary measures, in particular with respect to contextual measurement, co-morbidity, and measuring the impact of ill health on third parties. Ignoring these factors may reinforce already existing inequalities in health.

4. Challenges in research into risk factors

The expansion of focus from disease burden to risk factors is an important step for future improvements in policies. Modification of risk factors, such as reducing malnutrition in a given population, is likely to have a large impact on a variety of diseases. In some cases, determinants may not only be relevant in efforts to prevent disease but also in treatment, as in the case of reducing salt intake for high blood pressure, for example.

Version 2 estimates of the GBD 2000 study measured the prevalence of selected major causes of disease burden by sub-region.[34] It formed the basis for the comparative risk assessments for 20 major risk factors and the analyses of the cost-effectiveness of interventions for these risks which were the main topic of the *World Health Report 2002*.

Over 30 countries are at various stages in undertaking these assessments and WHO support to these efforts through the provision of best "prior" estimates of national burden of disease not only ensures better data for planning but also enables further development and testing of tools to facilitate burden of disease assessments. This iterative process contributes towards the ongoing updating of the global and regional burden of disease estimates.

Work is under way to develop national 'comparative risk assessment' software tools for the assessment of the attributable burden of 20 major risk factors.

Insert 4.9 details the selected risk factors to be studied in the GBD 2000 study.

[34] World Health Organization, *World Health Report 2002*.

Insert 4.9

Risk factors included in the CRA component of the Global Disease Burden 2000 Study

1. Alcohol	11. Selected occupational risks
2. Blood pressure	12. Ambient air pollution
3. Cholesterol	13. Physical inactivity
4. Climate change	14. Tobacco
5. Illicit drugs	15. Unsafe injection practices in medical settings
6. Indoor smoke from biofuels	16. Unsafe sex and unplanned pregnancies
7. Lead	17. Unsafe water, sanitation and hygiene
8. Childhood and maternal under-nutrition	18. Non-breastfeeding
9. Obesity and overweight	19. Childhood sexual abuse
10. Lack of fruit and vegetable intake	20. Distribution of risk factors by poverty

Source: GBD 2000

The GBD 2000 study selected risk factors on the basis of the following criteria:
(i) leading causes of disease burden
(ii) neither too specific nor too broad
(iii) high likelihood of causality
(iv) reasonably complete data
(v) potentially modifiable.

These characteristics are more likely to fit proximal determinants in the causal web rather than distal determinants. Poverty is an example of a distal determinant (see chapter 1, section 1 on the vicious circle between poverty and ill health). The distribution of risk factors by level of poverty has been attempted and may lead to new approaches to tackle these problems. The challenge now is to expand this analysis and to obtain better estimates of the contribution of risk exposure to disease.

5. Challenges in the cost-effectiveness analysis of health interventions

Cost-effectiveness analysis requires the following information: (i) the extent to which current and potential interventions improve population health (i.e. effectiveness); and (ii) the resources required to implement the interventions (i.e. costs).

Cost-effectiveness analysis is a useful tool to help policy-makers and programme managers decide between different ways of spending scarce resources in efforts to improve population health. It provides information on which interventions are likely to provide the greatest improvements in health for the available resources, a key input for decision-makers. Cost-effectiveness analysis can identify whether a new tool or product is likely to lead to larger number of healthy life years gained for a given cost.

Some of the main difficulties encountered in cost-effectiveness analysis are summarized below:

(a) Little information available from low- and middle-income countries

There is a dearth of information on the cost-effectiveness of interventions in low- and middle-income countries. Transfer of findings

from high-income to low- and middle-income countries is not reliable given the extensive differences in causal relationships, infrastructure, costs and capacity.

Economic evaluation has acquired significant prominence among decision-makers, and many ministries of health in low- and middle-income countries have expressed an interest in designing a national package of essential health services using this method. Given the high cost of many economic evaluations in low- and middle-income countries, interest has also been generated in pooling data and the results of previously published studies.

A review of published literature demonstrated that very few economic evaluations of communicable disease interventions in low- and middle-income countries were published during 1984-1997.[35] Although the situation has improved since then, much remains to be done, including with regard to the development of tools for comparing cost-effectiveness measures across health interventions.

(b) Need for comparative data

Why is it necessary to compare a wide variety of health interventions? Policy-makers are concerned with two questions requiring evidence on costs and effects:

- *Do the resources currently devoted to health achieve as much as they could?* To answer this question, the costs and effects of all interventions currently employed must be compared with the costs and effects of alternative interventions. Reallocating resources from inefficient to efficient interventions can substantially increase population health with no change in costs.
- *When additional resources become available, how can these be best used?* This type of analysis is critical for ensuring that, as societies become wealthier, additional resources are well used. But it is pointless asking this type of question if the current mix of interventions is inefficient; both questions need to be asked together.

(c) Developing tools for generalized cost-effectiveness analysis

In order to tackle the difficulties stated above, WHO has initiated the WHO-CHOICE project (CHO*osing Interventions that are Cost-Effective*). WHO-CHOICE is an 'aid to policy' which provides information on intervention costs and effects. The aim is to improve health systems performance. Health systems with very similar levels of health expenditure per capita show wide variations in population health outcomes. This is partly explained by variation in non-health system factors, such as the level of education of the population. But it is also due to the fact that some systems devote resources to expensive interventions with little impact on population health, while low-cost interventions with potentially greater benefits are not fully implemented.

WHO seeks to provide the evidence decision-makers need to set priorities and improve the performance of their health systems. WHO's Global Programme on Evidence for Health Policy has contributed to this question in the following way:

- developing tools and methods for generalized cost-effectiveness analysis;
- assembling regional databases on the costs, impact on population health, and cost-effectiveness of key health interventions.

The Project is currently assembling regional databases on the cost and effectiveness of

[35] Walker D and Fox-Rushby J. "Economic evaluation of communicable disease interventions in developing countries: a critical review of the published literature" in *Health Economics* 2000; 9(8): 681-698.

approximately 500 preventive, promotive, curative and rehabilitative health interventions using a standardized methodology. Regional databases containing raw data on costs and effects are being developed for analysts from different countries to use and, if required, to modify the basic assumptions to make them consistent with their own settings. Completed examples of the use of CHOICE are available for over 250 interventions.[36]

Section 6

Comparison of outputs of priority-setting exercises

This section reviews the recommendations made over the last 14 years by different international bodies regarding the priority areas for research into diseases/conditions and risk factors, which show a large consensus on the priority diseases and determinants to be studied at the global level. These are typically the high-burden diseases receiving very little research funding, which are easily identifiable.

In order to correct the 10/90 gap, more investments are needed for research into these diseases. There are two ways to accomplish this. One is to focus research investments on disease-specific interventions (such as medicines, vaccines and diagnostic tools) and disease-specific policies. A second approach is to focus on cross-cutting factors which influence the burden represented by these diseases, such as poverty, malnutrition, population pressure, inequity and inefficiency of health services, behavioural factors, corruption or lack of health research capacity. Both approaches (diseases and risk factors) are essential and their interaction is vital if health research is to be effective and efficient.

Insert 4.10 offers an overview of the global recommendations made by different international committees over the past 14 years on priority diseases for health research, while Insert 4.11 summarizes the priority risk factors which need to be addressed.

Beyond this, it is also essential to establish what the research priorities are within each of these priority areas. This issue is dealt with in chapter 9, which reviews the actions undertaken in the past two years by specific disease networks and partnerships in addressing specific risk factors.

[36] Available at www.who.int/evidence/cea

Section 7

Conclusions

In summary:

- The failure in practically all countries to establish a process for priority setting based on the burden of diseases and their causes has led to a situation in which only about 10% of health research funds from public and private sources are devoted to the diseases that account for 90% of the world's health burden.
- This extreme imbalance in research funding has a tremendous economic and social cost for individuals, countries and the world as a whole.
- To make matters worse, even the 10% of research funds allocated to 90% of the world's health problems are not used as effectively as they should be and need to be better prioritized.
- The prioritization of health research should take place at the local, national and global levels, as resources are invested in health research, in one form or another, at all three levels. The three levels should be linked in an iterative process and involve all stakeholders.
- The priority-setting process is a subjective process. In order to make the results as objective as possible, it is essential (i) to adopt a priority-setting process which is as transparent and as participatory as possible and (ii) to apply a methodology which is as scientific as possible.
- A number of processes and methodologies for the prioritization of health research were developed in the 1990s (in particular ENHR, the Five-Step Process and the Visual Health Information Profile).
- The CAM is an attempt to combine the main advantages of these methods. It incorporates both the economic and institutional dimensions of priority setting in health research.
- The prioritization process in health research should encompass all factors affecting people's health, i.e. not only basic, biomedical, clinical and laboratory research, but also health systems, demography, social and behavioural sciences, economics, management, macroeconomic policies, and sectors other than health having a large impact on health in the country.
- Priority setting is a long-term effort. The information will inevitably be partial in the first exercises, probably even sketchy in some cases, but the tool should demonstrate its usefulness at an early stage by highlighting the most important gaps in the information needed to make the best possible use of the limited resources available for health research, so as to have the largest impact possible on people's health (i.e. the largest number of healthy life-years saved) for a given research budget.

Insert 4.10

Key recommendations for health research regarding diseases/conditions over the past 14 years

Health research priorities	Commission Report (1990)	Ad Hoc Committee (1996) [1]	ACHR (1997)	ENHR Projects (1999)[2]	International Conference (2000) [3]	Fogarty International Center (2001)	Global Forum (2002)
Tropical diseases (malaria, schistosomiasis, leprosy)	•	•	•	•	The International Conference 2000 focused on the need to improve health research systems to deal with nationally prevailing diseases	•	•
TB-HIV	•	•	•	•		•	•
Childhood diseases (diarrhoeal diseases and respiratory diseases)	•	•	•	•		•	•
Sexually transmitted infections	•	•	•	•			•
Dengue				•		•	•
Maternal mortality	•	•	•	•		•	•
Cancer/diabetes			•	•		•	•
Cardiovascular diseases	•	•	•	•			•
Mental/neurological diseases	•	•	•	•		•	•
Violence and injuries	•	•	•	•			•
Chronic degenerative diseases	•	•	•				

[1] Recommended establishment of a programme to review health systems, NCDs and capacity development.
[2] See ENHR projects (Indonesia, Tanzania and South Africa) reported in *The 10/90 Report on Health Research 2000*, Global Forum for Health Research, 2000 (pages 22-26).
[3] See chapter 3 for recommendations at the national, regional and global levels.

Insert 4.11

Key recommendations for health research regarding risk factors over the past 14 years

Health research priorities	Commission Report (1990)	Ad Hoc Committee (1996) [1]	ACHR (1997)	ENHR Projects (1999)[2]	International Conference (2000) [3]	Fogarty International Center (2001)	Global Forum (2002)
Health policies and systems	•	•	•	•	•	•	•
Health information systems	•	•	•			•	•
Gender and socioeconomic inequalities	•	•	•	•	•	•	•
Health equity				•	•		•
Health cost and financing	•	•	•			•	•
Capacity building for health policies	•	•			•	•	•
Health behaviour research				•	•	•	•
Health impact of development of other sectors	•		•	•	•		•
Sustainable health research linked to development	•		•	•	•		
Environmental degradation			•			•	•
Child nutrition research	•	•	•				•
Food security			•	•			
Formal education			•	•	•		•
Education by health sector	•		•	•	•		•
Food and water management			•	•			•
Research on social justice				•	•		
Occupational health				•			•
Reproduction and contraception	•	•			•	•	•
Population dynamics	•		•			•	•

[1] Recommended establishment of a programme to review health systems, NCDs and capacity development.

[2] Recommendations depend on each country situation. See ENHR projects (Indonesia, Tanzania and South Africa) reported in *The 10/90 Report on Health Research 2000*, Global Forum for Health Research, 2000 (pages 22-26).

[3] See chapter 3 for recommendations at the national, regional and global levels.