Chapter 1

Introduction

Four major challenges confront human health at the end of the 20th century:

- First, the world's poorest regions are still suffering a heavy—and largely avoidable—toll of premature death and disability from childhood infectious diseases, malnutrition and poor reproductive health. While progress against these old, familiar conditions has been spectacular in recent decades, they still account for more than one-third of the entire global burden of disease.
- Second, all populations are threatened by continually evolving microbes at a time of spreading antimicrobial resistance and greater human mobility. Particular threats include the TB bacterium *Mycobacterium tuberculosis*, pneumococcus, the malaria parasite *Plasmodium falciparum* and the human immunodeficiency virus.
- Third, epidemics of noncommunicable diseases and injuries are fast emerging in the middle-income and low-income countries as their populations age and their exposure to certain risk factors, such as tobacco, increases.
- Fourth, governments are struggling to meet a rising demand for health services in the face of spiralling costs. Yet their task is being hampered by lack of information to guide their policies for disease prevention and treatment. The shortage of data affects both the health sector—which in many countries is pressing ahead with health system reform without knowing how best to provide equitable and efficient services—and other sectors of the economy such as education or employment, whose influences on health may be profound.

Daunting as these challenges appear, there are good reasons to believe that research and development can deliver information and tools that will greatly strengthen the response to them. But, since resources are limited, priorities must be set. Governments and all others who invest in health R&D, such as international organizations and private foundations, must decide how their investments—or how their policies that affect private sector investments—can be put to work most efficiently to bring the greatest possible improvements to human health.

This Report is intended to assist them. It explores how they might inform decisions about resource allocation through a comparatively simple, rational process that takes into account the size of the disease burden linked with a given health problem, the state of the current knowledge base about the problem, the promise of the R&D effort—including the likelihood of developing an intervention that is more cost-effective than any existing ones—and the level of existing R&D investment into the problem. Where a health problem is not restricted to one specific condition but has a broad impact on overall population health—for example, inefficiencies or inequities in a health system—then other measures, such as the percentage of national product consumed by health care, are suggested as means to gauge its severity and assist informed judgement about priorities.

The Report provides much new information on global health status and trends. It contains a major reassessment of current levels of disease burden, new projections of disease burden to 2020 and assessments of the burden attributable to a number of risk factors for disease. It also contains data on current levels of R&D spending; and for selected conditions, analyses of the cost-effectiveness of interventions under development or under consideration for R&D investment. In addition, it provides information on scientists' judgements about development opportunities and strategic research needs. The Committee has identified priorities and suggested some key choices ahead. Our Report points to areas where international efforts in R&D could have a high payoff and proposes limited but important changes in the institutional arrangements for health R&D, including those that affect the private sector that could help to redirect highly constrained resources to bear the greatest fruit.

1.1 The background to this Report

This study was initiated in response to several recent requests for a broad-based review of needs and opportunities for R&D in the health sector. It builds on the World Bank's *World development report 1993: investing in health* (World Bank 1993). The packages of interventions for public health and disease control that were identified by that report—on the basis of disease burden and intervention cost-effectiveness—reasonably reflect the minimum potential of today's technology, and the analysis of health systems and health policy provides an appropriate starting point for country-based plans of action. The World Bank report suggests an approach to assessing priorities for R&D—using information on disease burden, existing interventions and ongoing efforts—that foreshadows the assessments reported here.

The study also draws on the important contributions of the WHO Advisory Committee on Health Research (ACHR) and the strategic orientations, both global and regional, given by the ACHR system. The ACHR's fore-

runner, the Advisory Committee on Medical Research, first suggested criteria for setting WHO's research priorities two decades ago. This Report builds on the ACHR's more recent discussions of a *Health research strategy for health for all by the year 2000* (Advisory Committee on Health Research 1986) and the Technical Discussions on health research at the 43rd World Health Assembly. The report of those discussions states that the setting of priorities for R&D requires "a multidimensional consideration: of the scale and urgency of various problems, of the solutions that are possible or likely to emerge from research as practicable and affordable measures, of possible benefits or detriments to other sectors, and of the different consequential returns achieved by the various possible choices of priorities" (Davies & Mansourian 1992). The report adds that "global interdependence implies that methodological research can be of benefit for all. The search for new objective methods of resource allocation, of determining and ranking priorities, constitutes research of a strategic nature. Strategic decisions are those which derive from a global understanding of a given problem". The present study starts from similar principles.

The Committee also builds on the work of the Commission on Health Research for Development whose report *Health research: essential link to equity in development* (Commission on Health Research for Development 1990) has influenced debate for the past five years. The Commission identified a "gross mismatch" between health needs and research investment in developing countries and found that many countries neglect the research needed to inform decisions on health policy. To fill the gap, the Commission argued for research at the national level for each country to understand its own problems, make the best use of limited resources, improve health policy and management, foster innovation and experimentation, and provide the foundation for a stronger voice from developing countries. In so doing, it developed the concept of Essential National Health Research (see Box 1.1). A growing number of countries are adopting ENHR strategies, facilitated by the Council on Health Research for Development, a nongovernmental body established in 1993.

The Commission argued that national research priorities should be set by: targeting major causes of mortality; taking account also of morbidity; considering the potential effectiveness of interventions that would emerge from the research; taking account of the percep-

Box 1.1 Definitions and explanations of terms used in this Report

Types of health research

Health research: a process for obtaining systematic knowledge and technology that can be used to improve the health of individuals or groups.

Health research provides basic information on the state of health and disease of the population; it aims to develop tools to prevent and cure illness and mitigate its effects; and it attempts to devise better approaches to health care for the individual and the community (Advisory Committee on Health Research 1993). Information about health needs may consist of measurements of conditions, measurements of the relative importance of various risk factors for ill-health, and analysis of the sources of inefficiency in health services which have a direct impact on health.

Health research embraces different types of activity, ranging from fundamental research—whose primary purpose is to advance knowledge—to development and evaluation research—whose primary purpose is to solve specific problems relating to health care and its delivery (see Box Figure 1.1.1).

Each stage of research is to some extent dependent upon others, and a linear model of the different stages of research is unhelpful in understanding the process. The diagonal line in Box Figure 1.1.1 seeks to stress the interrelatedness of each stage and the fact that there is likely to be substantial movement back and forth between stages. Nevertheless, it is generally true that the proportion of the defined research objective that seeks to change practice rather than to advance knowledge will increase with the spread of the dark section towards the left side of the bar.

Fundamental research: research whose purpose is principally to increase knowledge about questions of scientific significance.

Strategic research: research whose purpose is primarily to increase knowledge and understanding of a health problem, with a view eventually to solving or reducing the impact of the problem through further development and evaluation.

The relative importance of the knowledge-gaining component and the problem-solving component will vary depending on the type of project and the nature of the problem. Importantly, the definition of strategic research adopted by this Report *is not purely biomedical but encompasses also the work of behavioural scientists, epidemiologists, demographers and health policy scientists.* Specific examples of strategic research within each discipline might include sequencing the genome of an important pathogen, analysing what proportion of the burden of a given disease can be attributed to a specific risk factor in a specific population, and analysing what effects the decentralization of health services have on the coverage of a given service within a given population.

Development outcomes: products, interventions and policy instruments

Products. These encompass five basic groups of health related material products: drugs, vaccines, equipment including tools for public health, prostheses, and diagnostics.

Interventions. These may be combinations of products, algorithms, information or policies that reduce the risk, duration or severity of an adverse health condition. They may be usefully subdivided as either:

a. ***Public health interventions***—those that are sought of or directed towards entire populations or subgroups, including immunization, mass chemoprophylaxis such as the addition of iodine or medications to salt or the fluoridation of water, and nutritional interventions, such as encouraging women to take folic acid supplements before and after conception;

or

b. ***Personal health service interventions***—those that are provided at facilities and usually to individuals; these include inpatient and outpatient medical treatments, screening and rehabilitation.

Instruments of government policy. These encourage or discourage specific health interventions, e.g. pricing and/or taxing policies on tobacco, pricing policies for health services, essential drugs lists, policies for paying health workers according to the type and range of services they offer.

The health sciences

Biomedical sciences: includes all strategic biological, medical and clinical research, and biomedical product development and evaluation.

Population sciences: includes epidemiology, demography and the behavioural sciences. This category is *not* intended to denote solely that part of health research concerned with fertility, family planning and population control.

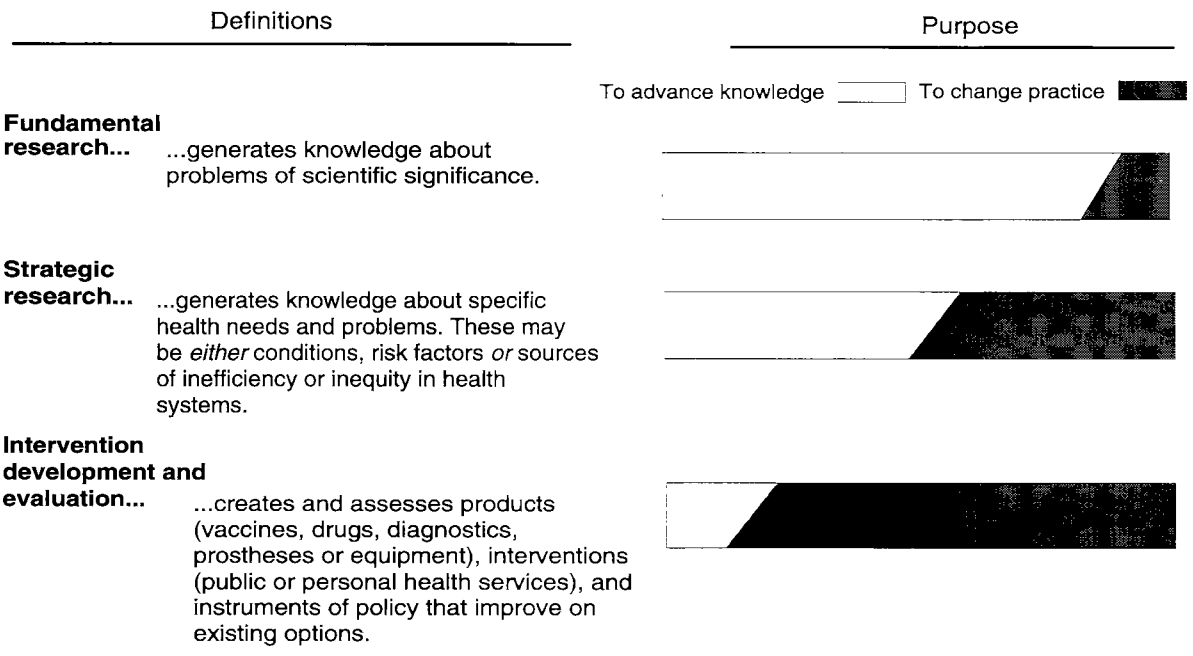
Health policy sciences: includes health policy research, health systems research and health services research.

It is understood that different traditions and institutional cultures may use some of the above terms in other senses than those adopted in this Report.

Essential national health research (ENHR)

This concept, first set out by the Commission on Health Research for Development (1990), aims to achieve equity in health and development. It holds that each developing country should establish and strengthen an appropriate health research base to "understand its own problems; improve health policy and management; enhance the effectiveness of limited resources; foster innovation and experimentation; and provide the foundation for a stronger developing country voice in setting international priorities".

Box Figure 1.1.1 Definitions and purpose of R&D



tions of need held by populations as well as the needs determined by "scientific" analysis; taking account of current R&D efforts; and considering research not only into specific diseases but also into broader health issues. While the Commission recognized the need for some international efforts, its emphasis was on national-level research, with international agendas emerging through consensus between countries.

Our Report emphasizes global priorities, and therefore complements the work of the Commission. However, if assessment is based on rational and quantitative methods, it is likely that global priorities will have much in common with those of individual nations and regional groups. There is already some evidence that such shared concerns are emerging: individual countries' agendas for ENHR identify many priorities similar to those discussed in this Report, including the major childhood infections, problems related to the demand for, and supply of, health services, and problems related to major risk factors for disease such as poor sanitation (Council on Health Research for Development 1995). It is worth stressing, however, that global priorities reach beyond the sum of national ones. For example, the cost of developing an HIV vaccine might be expected to deter any single low-income country from making it a priority. Yet a global assessment of priorities might conclude that the effort was worthwhile because many countries would benefit. Hence, it is essential to complement national assessments with a global one.

1.2 Scope and focus

The focus of this Report is on the needs of people who live in low-income or middle-income countries, since they make up four-fifths of the world's population and suffer most of its ill-health. But the Report's scope is global: in an increasingly connected planet where populations and economies are more and more interdependent, no region can consider itself immune to the problems of others.

Because the scope of this Report is necessarily broad, the Committee's basic assumptions and definitions must be made explicit. First, we should clarify what we mean by *health*. Health has been defined as "a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity" and this definition has also been interpreted as "the ability to lead a socially and economically productive life" (World Health Organization 1978). In the Committee's view, the most important and most practical contribution that the health sector can make to advancing that broad vision of improved health is to reduce the burden of disease and disability. We therefore focus on developing and utilizing quantitative measures of disease burden and the relative cost-effectiveness of different interventions intended to reduce that burden.

We should stress, however, that as a Committee we do not view health as a matter for the health sector alone. It is clear that factors outside the health sector, such as income level and access to education, strongly influence population health. Our Report seeks to advance an agenda for assessing and quantifying those influences so that governments will be able to assess the desirability of devising multisectoral, integrated policies for health—as some, indeed, are already doing.

It is equally important to clarify what the Report means by *health research*. As the definition in Box 1.1 shows, research for health is a process for obtaining knowledge or technologies that can be used to improve human health. Because it involves human subjects, its conduct must always meet ethical standards, and this Committee endorses the guidelines set by the Council for International Organizations of Medical Sciences for that purpose (CIOMS 1993).

Health research encompasses a wide range of activities from fundamental research to product evaluation. Among previous attempts to subdivide the phases of the scientific research process in history, Francis Bacon's 17th-century distinction may be considered among the most useful; he divided "experiments for light" from "experiments for fruit" (*Instauratio Magna*, discussed in Webster 1975). For the purposes of our analysis, we have subdivided the process into three phases: fundamental research, strategic research, and intervention development and evaluation. As Box 1.1 shows, the purpose of fundamental research is mainly "for light"—to increase knowledge—while strategic research seeks knowledge specifically to solve health problems, and intervention development and evaluation put greater emphasis on finding "fruit"—to change practice.

In the Committee's view, these phases are interdependent and equally valuable. However, while we stress in Chapter 2 that fundamental research is the vital base for all other R&D activities, we have excluded it from our assessment of *priorities for resource allocation*. Our task was to consider priorities for R&D to address the practical health problems of populations. We have therefore focused on strategic research and intervention development and evaluation. Fundamental research is driven by many scientific considerations other than the measurement of need and opportunity, and it is therefore beyond the scope of this Report to judge priorities within it.

We have also subdivided the activities of health research into broad disciplinary groupings, to reflect the different levels at which human health problems must be analysed, from the sub-individual level of cells and molecules to the institutional level of health policies. Our three groupings of disciplines (defined in Box 1.1) are: biomedical sciences, population sciences, and health policy sciences. Each is to some extent dependent on the others for the information that sets their respective research agendas on particular health problems. In the case of malaria research, for example, biomedical researchers have studied the immune response of individuals to malaria parasites at the molecular level and have used the knowledge to develop candidate vaccines. Population scientists (epidemiologists) work with their bio-

medical colleagues to carry out trials of the vaccines and other interventions, such as insecticide-impregnated bednets. Sociobehavioural researchers, meanwhile, study the factors that determine whether people use bednets or other protective devices or not, economists study the pricing and policy factors that determine whether people should be asked to buy their own bednets or have them provided free, and health policy researchers study the advantages and disadvantages of different approaches to organizing the prevention and treatment of malaria.

We have sought to determine the balance of disciplinary effort that is most relevant for each of the four identified health challenges. Table 1.1 provides suggestive results; they are of interest not for being a specific guide to disciplinary priority but, rather, for indicating the need for a broad mix.

In our assessments of current resource allocation we have usually considered health R&D as a segment within the health sector, rather than health R&D as a segment within all R&D. This is because other components of the health sector such as disease control, health promotion and clinical services are intimately linked with strategic research and intervention development. None the less, individual countries conducting analyses of investment in health R&D may consider it appropriate to look at resources in the overall R&D context as well as in the health sector.

1.3 Approach and methods

The Committee has taken a comparatively simple approach to assessing needs and opportunities for research and development. In thinking about the claims on R&D resources that a particular problem might make, there are clearly certain criteria to consider. Is the problem big? (The world lost 70 times as many years of healthy life from TB as from lymphatic filariasis in 1990.) Do we already have good and cost-effective tools for dealing with the problem? (The availability of multidrug therapy—MDT—for leprosy weakens the case for investing in development of a leprosy vaccine.) Is the science base good? If so, one might proceed rapidly to product development and testing (as with the candidate conjugate pneumococcal vaccines); if not, strategic research to develop the knowledge base might be required (as with HIV vaccines). Are the high-income countries already spending a lot on the problem? (R&D money available to low-income and middle-income countries could add little to what is already being spent by rich countries to study atherogenesis or to develop new drugs for controlling hypertension or hyperlipidemia.)

In the case of problems that cut across specific diseases or risk factors—such as the rising costs of health care—we again suggest measuring the scale of the problem, for example in terms of the percentage of GDP consumed; assessing the reasons for the persistence of the problem through the informed judgement of experts; assessing the extent of existing knowledge about the problem; and the probability of developing policies or interventions that will provide cost-effective solutions to it.

Few would disagree that decisions about resource allocation within health R&D should, in some way, take the above considerations into account. Yet the Committee has been struck by how often these considerations are ignored: R&D money goes to diseases of little epidemiological significance while major killers, such as TB, are neglected; attention goes to marginal improvements in already good products while major opportunities are missed (e.g. work on heat-stable polio vaccine continues while countries with heavy disease burdens from infections such as *Haemophilus influenzae B* or pneumococcus must wait for trials of available vaccines). This Report argues, simply, that investors in R&D should attempt to take these factors into account as quantitatively, explicitly and systematically as possible. The degree to which this is possible will vary and the Committee considers its approach to be part of an ongoing process. The knowledge that the process yields can only inform—not determine—resource allocation decisions. Even where quantitative information is excellent, the approach should not be prescriptive.

This Report contains summaries of the assessments of disease burden for 1990 and projected for 2020 (Annex 1) and the burden attributable to selected risk factors (Annex 2). The full data from which these summaries are drawn, including separate assessments of mortality, years of life lost and years lived with disability, are published in the companion volumes to this Report (Murray & Lopez 1996 and forthcoming). In general, the Committee has used the disability-adjusted life

Table 1.1 R&D to address major health challenges: the role of different disciplines

	Disciplines		
Broad health challenge	**Biomedical science**	**Population sciences**	**Health policy sciences**
Childhood infections, malnutrition and poor reproductive health	++	++	++++
Evolving microbial threats	++++	++	++
Noncommunicable diseases and injuries	+	++++	+++
Informing health policy	-	++++	++++

Note: The estimated importance of each discipline ranges from the unimportant ('-') to extremely important ('++++').

Box 1.2 Measuring the burden of disease

This Report uses the disability-adjusted life year (DALY) as its main unit of currency for measuring the burden of disease. Unlike traditional mortality statistics, the DALY allows researchers and health policy-makers to assess the nonfatal consequences of ill-health and injuries and can thus reveal the extent of health problems that mortality statistics fail to capture. For example, the number of *deaths* from psychiatric and neurological diseases in 1990 was about 1% of the world total. Measured in terms of disability-adjusted life years, however, this group of diseases accounted for more than 10% of the total global disease burden (Annex 1).

Each DALY indicates the loss of a year's healthy life—that is, the time lived with a disability or the time lost through premature death. Years of life lost through premature death are calculated as the difference between the actual age at death and the age to which a person could have expected to live at birth in an advanced industrialized country—that is, 82.5 for women and 80 for men. Disability is assessed in terms of its expected duration and its severity. The total number of DALYs in a population in any given year indicates that population's disease burden: the higher the total, the greater the burden. The advantage of this currency is that, as a single indicator, it provides a comparable measure of the outcome of health interventions—in terms of DALYs averted—for a wide range of health problems and diseases.

The value choices incorporated into the DALY continue to be debated (see, for example, Morrow & Bryant 1995). An extensive discussion of these issues is contained in the companion volumes to this Report (Murray & Lopez 1996 and forthcoming), which present disease burden estimates in detail and also include sensitivity analyses. The Committee took the decision to use the DALY as its main indicator of disease burden for four reasons. First, the reality is that decision-makers allocate resources in part on the basis of aggregated measures of disease burden, implicitly if not explicitly. Second, it is important to have a unifying measure that enables assessment of both the burden of disease and the cost-effectiveness of different interventions. Third, the DALY has been developed through collaboration between different sectors and has helped to strengthen the foundations for a multisectoral approach to health which, the Committee believes, should continue. Fourth, the explicit nature of the assumptions underlying the DALY enables them to be debated and modified.

By 1995 some 28 countries were using the DALY in some form to assist them in the measurement of population health needs.

year (DALY) to measure disease burden and assess health need (see Box 1.2). In addition, wherever possible, we have considered other indicators, such as the percentage of GDP consumed by health care in individual countries and the level of R&D investment into particular health problems. Our methods are set out below. We suggest five steps to inform decision-making about the allocation of R&D resources to and within a problem area (e.g. TB or malnutrition or tobacco use).

1. Calculate the burden of the condition or risk factor

We have used the DALY as our main unit. Annexes 1 and 2 provide details of how burdens are calculated for conditions and risk factors respectively.

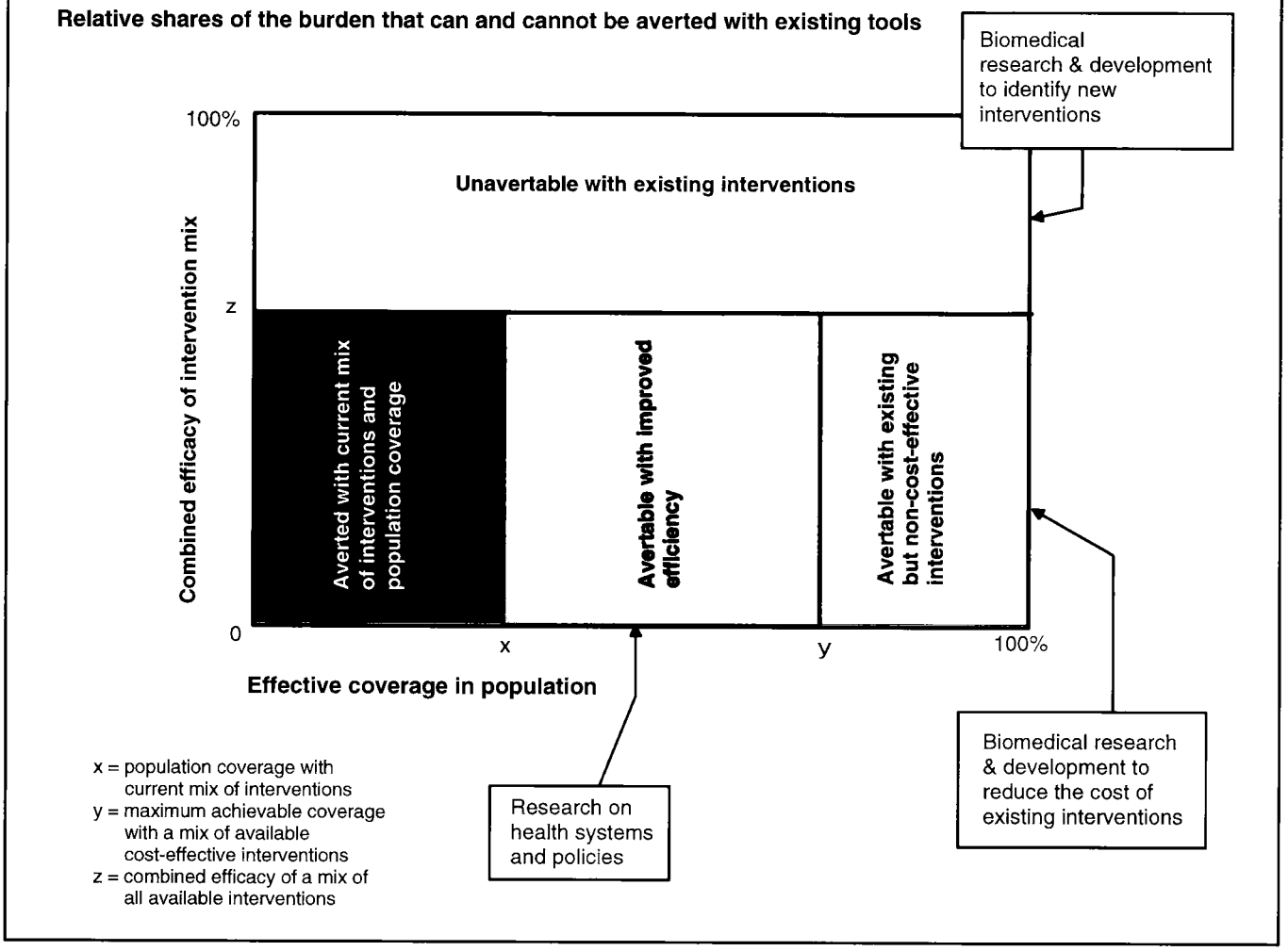
2. Identify the reasons why the disease burden persists

This requires an analysis, essentially, of whether the problem persists mainly because of (a) a lack of knowledge about the disease and its determinants, (b) a lack of tools, or (c) failure to use the existing tools efficiently. Of course, more than one factor is likely in each case. Where possible, this analysis can be quantitative. Figure 1.1 indicates the analytical approach applied. Using data on the efficacy of the available cost-effective interventions, and consulting the judgement of field experts on the proportion of the population receiving effective interventions, it is possible to estimate:

- what portion of the total burden of each disease or condition is now being averted;
- what could be averted now with better use of existing cost-effective interventions;
- what could be averted now, but only with interventions that are not cost-effective; and
- what cannot be averted with existing interventions but requires new ones.

The analysis is intended to identify where the greatest needs lie, and thereby guide assessment of the priorities for different types of research. The unit of currency employed for this analysis is, once again, the disability-adjusted life year. While such analyses are not intended to suggest that some spurious precision can be achieved in the analysis of need, they do indicate a sense of the *relative* distribution of the effort required.

Figure 1.1 Analysing the burden of a health problem to identify research needs



The whole square in Figure 1.1 represents the total estimated disease burden (in DALYs) from a given condition, such as diarrhoeal disease, globally or for a particular region. The horizontal axis represents the extent to which effective treatment is reaching the population—that is, how far into the population a mix of interventions is penetrating. The vertical axis represents the combined efficacy of this mix. The subdivisions within that square represent different portions of the burden: (1) that which is being averted now by the existing mix of cost-effective interventions among the people that the intervention is reaching, (2) that which could be averted if the existing interventions were used more efficiently, (3) that which could be averted with existing tools, but not cost-effectively, and (4) that which is not avertable with existing interventions. Calculations of the relative share occupied by each subdivision can help to spell out the priorities for research. For example, where it is calculated that a large portion of the total burden of a certain disease cannot be averted with the existing cost-effective tools, then there is a strong case for R&D to develop new ones. Where it is calculated that a large portion of the burden could be averted if existing tools were used more efficiently, there is a strong case for research into the needs and behaviours of users and the behaviour of providers, to learn how coverage could be increased and efficiency maximized. The methods used to conduct this form of analysis are described in more detail in Annex 1.

3. Judge the adequacy of the current knowledge base

This undertaking relies on the subjective judgement of informed scientists. If the knowledge base is adequate to support development of specific interventions, then the estimated cost-effectiveness of those interventions relative to those currently available can be assessed. The desirability of an intervention will then depend on its cost, the estimated probability of success and the ex-

tent to which it is better than available alternatives. If the knowledge base does not yet allow the development of new interventions—judged to be attractive in the way indicated—there is a suggestion that strategic research is desirable to strengthen the base. Clearly, the analysis will sometimes conclude that multiple approaches are desirable—particularly if the relevant disease burden is large.

4. Assess the promise of the R&D effort

This can be divided into two subsections:

a. ***The expected cost-effectiveness of the potential intervention.*** Provided certain data are available, calculations of the likely cost-effectiveness (in dollars per DALY averted) of a desired intervention can be undertaken and the results compared with the cost-effectiveness of existing interventions. Thus, for example, as we discuss in Chapters 3 and 4, a malaria vaccine could be highly attractive compared with other available preventive strategies while, by contrast, a schistosomiasis vaccine would be unlikely at present to compete with the available interventions. A broad guide to what counts as cost-effective is shown in Table 1.2; in essence, anything that costs less than US$ 25 to US$ 30 per DALY averted in low-income countries is highly attractive, and anything that costs less than US$ 150 is attractive. In middle-income countries, interventions that cost less than US$ 100 per DALY averted are highly attractive and those that cost less than US$ 500 attractive.

While there are undoubted uncertainties in the assessment of intervention cost-effectiveness, these should be kept in perspective. The range of cost-effectiveness is extremely large: some interventions in low-income countries cost less than US$ 15 per DALY averted while in industrialized countries specialized treatments for myocardial infarction may cost well above US$ 10 000 per DALY averted (Mark et al. 1995).

b. ***The probability of successful development.*** In most instances, there will be an ongoing R&D effort with one or several tools in the pipeline. The probability of success will depend in part on the knowledge base that underlies the development of the tools. For example, a candidate drug's probability of success is likely to be higher if the drug target is known to be essential to the organism, and if the mechanism of action is understood. Obviously, the closer the product is to application, the higher its chances of success, the lower will be the required investment and the shorter the time required before completion.

5. Finally, assess the adequacy of the current level of effort

Annex 5 reports the Committee's attempts to describe ongoing levels of resource allocation to R&D into particular health problems. We find that some important health problems receive extraordinarily little R&D investment. While the amount of funding devoted to a health problem cannot and should not be expected to be directly proportionate to the scale of the health problem, the particularly severe mismatches that have emerged from this study indicate a misjudgement of priorities. In light of what is now being spent, and of the attractiveness of development and strategic research possibilities identified in step (3), judgements about appropriate changes in the level or composition of resources allocated to the problem area can be made. A shortage of available data makes this effort a difficult one; additional attention is required on an ongoing basis.

The Committee's approach builds on earlier efforts to inform resource allocation in a number of specific ways. First, we explicitly consider disease burden and the burden attributable to selected risk factors, using a unit of measure that incorporates morbidity as well as mortality. Previous discussions have in practice considered mortality only, and none has attempted to quantify the burden attributable to risk factors. Second, we have attempted explicit analyses of the reasons for the persis-

Table 1.2 Good buys: examples of attractive health interventions in low-income and middle-income countries

	Attractive interventions (US$ per DALY averted)	Highly attractive interventions (US$ per DALY averted)
Low-income countries	**<150** Primary prevention programmes to reduce STD transmission through behaviour change	**<25** Measles immunization; breast-feeding promotion; targeted mass anthelminthics; smoking prevention or cessation programmes; treatment of pneumonias with antibiotics
Middle-income countries	**<500** Treatments with medication for schizophrenia and bipolar affective disorder; secondary prevention of stroke or angina by behaviour change and appropriate medication	**<100** Improved antenatal care; use of oral rehydration solutions; promotion of improved weaning practices

Source: Jamison 1993

tence of disease burden in selected areas, where previous discussions have left these analyses implicit. Third, we have made a limited number of estimates of the cost-effectiveness of desired interventions, where earlier efforts have made no such explicit estimates.

The Committee views this systematic approach to informing decision-making as a way of informing judgement—not replacing it. Our experience in applying the approach suggests that neglecting one or more of the above steps is frequent and distorts resource allocation; hence our conclusion about the desirability of more generally adopting a systematic approach. So far, the Committee has been able to apply the process with full rigour only to selected health problems and for others, where good data are not available, has relied more heavily on expert judgement and qualitative analysis. As such our work has made only a start, and further advances will require a continuing effort. It is hoped that this Report will help to stimulate a wider and ongoing systematic process.

Table 1.3 illustrates, with examples, the approach taken by the Committee. The first two examples show conditions where, in our view, the information clearly points to the need for R&D investment. The third example (leprosy) shows a condition where, in our view, R&D investment in a vaccine is less easy to justify.

Table 1.3 Steps to inform resource allocation: selected examples

Condition or risk factor	Need	Opportunity: promise of R&D effort					Investment requirement
	Disease burden (rank, of 96 causes)	Primary reasons for persistence of burden	Current knowledge base/R&D capacity	Desired intervention/ estimated likely cost-effectiveness (in US$)	Probability of success	Current effort, additional cost (in US$)/ time frame	Conclusion
Pneumonia	High (1)	Failure to use existing tools efficiently	Good	Package for integrated management of the sick child: Very high (<US$ 50 per DALY gained)	High	Current investment relatively small; required further costs and time frame: modest (US$ 15 million over 3 years)	High priority for investment
Malaria	High (11)	Lack of tools	Moderate to good	Malaria vaccine: Very high (<US$ 30 per DALY gained and <US$ 15 in some circumstances)	High	Current investment relatively small; required further costs and time frame: moderate (US$ 50 million over 10 years)	High priority for investment
Leprosy	Low (95)	Failure to use existing tools efficiently	Good	Leprosy vaccine: Low (US$ 2 453 per DALY gained compared with <US$ 50 for MDT treatment based on passive case finding and treatment, or US$ 42–US$ 2 700 based on active case finding	Moderate	Not assessed	Low priority for investment