

Chapter 3

An unfinished agenda: improving maternal and child health

The world's poorest populations live under the shadow of a group of old enemies which, despite decades of progress and an arsenal of weapons to prevent and treat them, still kill more than 12 million children and almost half a million women a year. They are responsible for more than half of the disease burden in sub-Saharan Africa, almost half of it in India and—even though they are virtually unknown in the rich countries—more than a third of the entire global burden (Figure 3.1). They are:

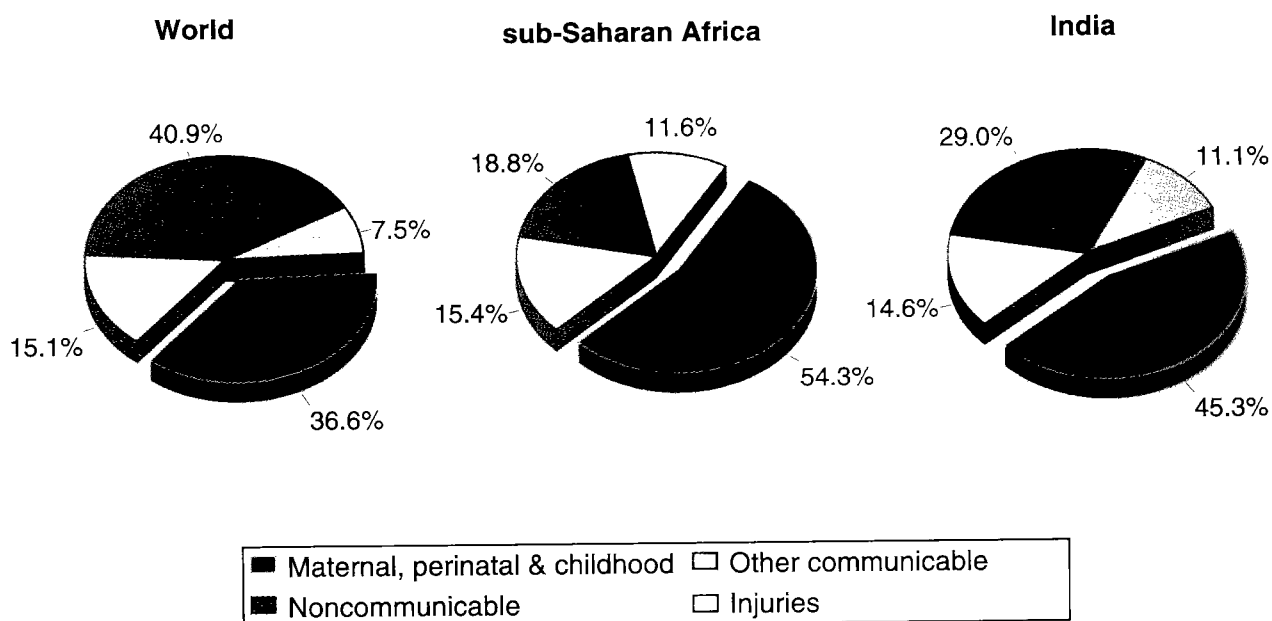
- the communicable diseases of childhood—such as pneumonia, diarrhoeal diseases, malaria, measles and the other vaccine-preventable infections, and intestinal parasitic infestations;
- malnutrition; and
- poor reproductive health—the consequences of un-

wanted pregnancy and the complications of pregnancy, childbirth and the first week of life. These conditions make up only a subset of the massively important cluster of reproductive health needs, which we return to elsewhere in the Report.

In this chapter, the first of four focusing on the major health challenges identified in this Report, we ask how research and development can tackle this group of conditions. We discuss them as a group because they often occur together, because the reasons for their persistence are largely shared, and because efforts to address them must overlap.

Poverty increases people's vulnerability to most diseases, but its link with this group of conditions is particularly strong. The childhood infections, malnutrition,

Figure 3.1 Traditional enemies: percentage of the burden of disease attributable to maternal, perinatal and childhood conditions (in DALYs), 1990



Source: Annex 1

and maternal and perinatal conditions are borne almost exclusively by poor populations. Not only is poverty a predisposing factor for these conditions, it is also a consequence of them. As incomes have risen and health technologies have improved, there has been significant progress against them, but that progress has not gone far enough. As long as they persist, hundreds of millions will be trapped in a cycle of underdevelopment, prevented from reaching their potential at school, in the workplace, in the household and thus in the economy.

The persistence of these old foes in the face of effective means to avoid or control them—such as vaccines, drugs and algorithms for safe care in pregnancy and delivery—must be blamed in large part on inaction. Governments have failed to invest in the health of poor people by providing essential, responsive and equitable health services, and the pharmaceutical industry has too few incentives to develop promising new candidate vaccines, drugs or other products for their needs. But action is not all that is required. Many of the existing interventions fall short of their potential today because no one knows how to make the best use of them. Operational research is needed to make existing interventions more responsive to people's needs and to increase their effectiveness. And, where existing tools are inadequate, new ones need to be developed.

The case for renewed effort is strong on humanitarian grounds alone. But there is also a strong economic rationale for pursuing greater equity. Most of the existing interventions against childhood diseases and maternal conditions are, in principle, highly cost-effective and, in poor countries where these conditions are highly prevalent, the potential health gain from using them properly is massive. All can be delivered for less than US\$ 50 per year of healthy life that they gain, and some for less than US\$ 30 (Bobadilla et al. 1994). In recent years, attention has focused on the idea of putting interventions together into *packages*. Briefly, this means grouping services to make the best use of patients' and carers' time, treating an individual instead of the individual's diagnosis, bringing prevention and treatment activities together, and reducing the costs of providing the services by sharing resources. Health workers and operational research teams have shown, for example, that it makes good sense to examine a mother and her newborn baby together, rather than make them both attend a clinic twice. Or that, when a child is likely to be affected by several conditions at once, it makes sense to diagnose and treat them together rather than separately. Some packages, such as the group of vaccines delivered by the Expanded Programme on Immunization (EPI), are already well established. Others, such as a package for the care of sick children, have been developed and are ready for implementation. Still others, however, are little more than theoretical concepts.

According to health economists' estimates, developed with data from low-income countries, a set of these packages of essential services, including family planning, immunization, the care of sick children, school health programmes, and the care of women in pregnancy and

childbirth, could be delivered for less than US\$ 12 per head per year. Together, put to best use, these packages could lift around one-third of the burden of premature mortality and disability from the populations of low-income countries. Figure 3.2 shows the potential impact of the essential packages on total disease burden in both low-income and middle-income countries.

The incentive for making these packages of essential interventions work is therefore exceptionally high. As yet, however, few have been evaluated in real populations, although efforts are now underway to do so, for example in Tanzania (Box 3.1). A key question for research is to establish *how* to achieve this effective use of packages. In the following sections, we investigate the health needs of children and mothers in low-income countries in more detail, and discuss how research and development could improve existing interventions and produce new ones where needed.

3.1 Responding to children's needs

3.1.1 The magnitude of the burden

More than a quarter of the entire global disease burden is caused by conditions that primarily affect children in low-income populations (Table 3.1).

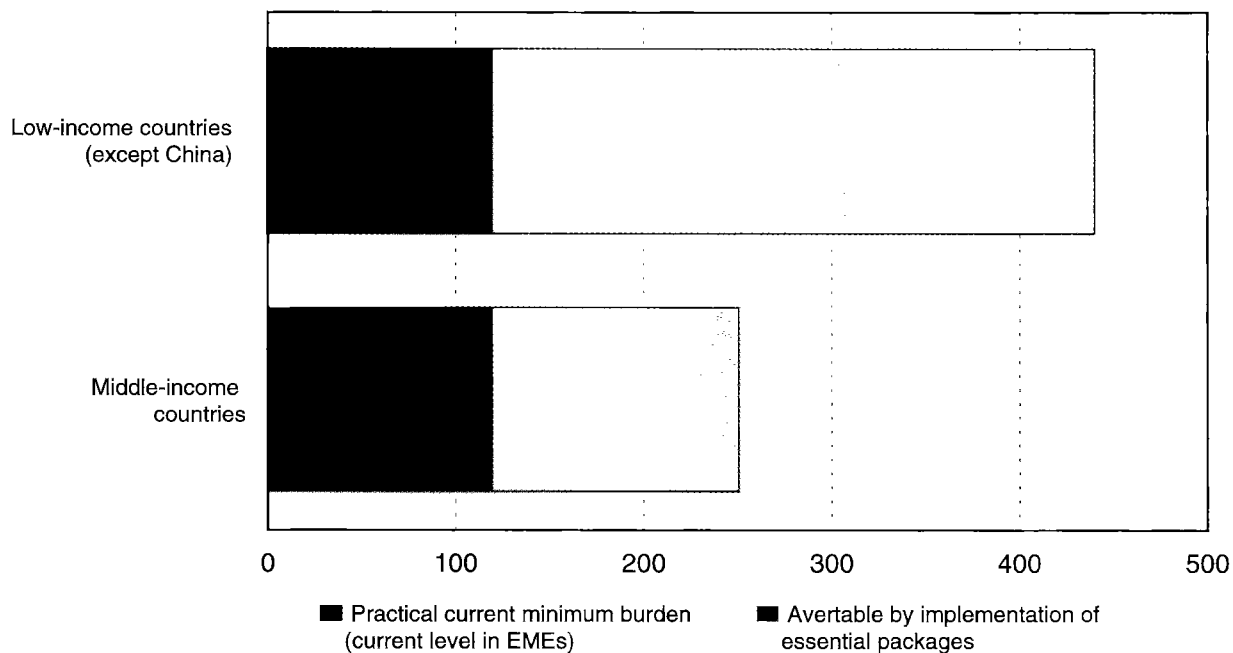
Of these conditions, pneumonia, diarrhoeal disease, malnutrition, measles and malaria are dominant. Together, these five conditions are responsible for seven out of every ten deaths among under-fives in low-income countries and the vast majority of the disease burden. As Figure 3.3 shows, they frequently overlap and interact with each other.

Pneumonia, the most frequently suffered disease worldwide, kills four million children under the age of five every year and ranks first among all causes of disease burden. Disease-specific mortality rates from pneumonia are between 10 and 50 times higher in low-income countries than in the established market economies (Stansfield & Shepard 1993). Most deaths are in children under the age of two years and more than 60% are caused by two bacteria, *Streptococcus pneumoniae* and *Haemophilus influenzae*, with the remainder caused by a variety of bacteria and viruses including respiratory syncytial virus and adenovirus. Pneumonia can also be a complication of infection with measles virus or with pertussis. Children are most vulnerable to die of pneumonia if they are poor, undernourished, weighed less than average at birth, are not breast-fed and live in crowded homes. Indoor air pollution from cooking stoves may be an additional risk. Children whose mothers received an adequate education are less likely to die than those whose mothers are uneducated.

Diarrhoeal disease kills another three million under-fives and ranks second among all causes of disease burden worldwide. There are three broad types of diar-

Figure 3.2 Much to gain: the potential impact of the essential packages

Total disease burden per 1000 population, 1990



The two horizontal bars show, for low-income and middle-income countries respectively, the total disease burden per 1000 people in 1990, measured in years of healthy life lost (DALYs). The black segment shows the lowest level of burden that could practically be achieved if all countries had as little ill-health as the established market economies. The grey segment, to the right, shows the amount of the total burden that could be removed if the essential packages were fully implemented.

rhoeal disease: acute watery diarrhoea, persistent diarrhoea—lasting more than 14 days—and dysentery. About half of all deaths are caused by acute watery diarrhoea, with rotavirus the single biggest cause. Babies who are not breast-fed are eight or more times more likely to die of diarrhoeal disease than breast-fed babies. In addition, low birth weight, undernourishment and lack of maternal education all increase children's vulnerability. Unsafe water and sanitation, and poor personal hygiene, are important risk factors for diarrhoeal disease (Table 3.2). It should be noted, however, that diarrhoeal disease is not the only consequence of unsafe water and poor sanitation. These risk factors also increase children's vulnerability to waterborne parasites and other pathogens, such as polio virus, and poorly drained areas also provide opportunities for disease-bearing mosquitos to breed.

Malaria is a major threat to health in sub-Saharan Africa, where it accounts for almost a tenth of the total burden. Worldwide, the disease currently accounts for just over 2% of the burden. Children whose immunity to the malaria parasite has not yet developed are more lia-

ble to suffer severe and complicated malaria than adults, and 90% of deaths from the disease are among the young. Malaria is discussed in more detail in the following chapter, but is included here because its epidemiology, diagnosis and treatment are closely linked with the other major childhood killers.

The vaccine-preventable childhood infections—polio, diphtheria, pertussis, tetanus and measles—together still account for about 5% of the global burden and 10% of the burden in under-fives. Half of this is due to measles virus, which is linked with the deaths of about one million children a year and ranks as the eighth greatest cause of disease burden worldwide. Measles is most likely to kill undernourished, underweight children and is a particular threat in populations suffering from enforced migration and famine. Every year, half a million babies die of neonatal tetanus because their mothers are not immunized with tetanus toxoid, and more than 110 000 children are still crippled by polio virus.

Helminth infestations. Every year, between 170 million and 400 million children become infected with

Box 3.1 The Tanzanian Essential Health Intervention Project

The development of a common currency for measuring the global burden of disease and the cost-effectiveness of interventions has, in principle, enabled countries to establish health intervention priorities. However, the adoption and implementation of an essential package of health interventions entails some difficulties, such as a health system's capacity to effectively plan and implement the package, and the availability of the information needed in the planning process. To assess the feasibility and impact of such an approach at district level, Canada's International Development Research Centre (IDRC) supported the creation of the Essential Health Interventions Project (EHIP). It is EHIP's hypothesis that health intervention prioritization and resource allocation should be made on the basis of burden-of-disease and cost-effectiveness analysis carried out at the district level. EHIP has identified several steps as necessary for achieving this end:

- assess "the District Health Management Teams' capacity to establish priorities and plan the allocation of resources according to local estimates of burden of disease and knowledge of cost-effectiveness";
- determine the extent to which district health plans can be translated into effective delivery of and use of the essential health interventions;
- assess the cost as well as impact of the essential health intervention package on the burden of disease.

In an effort to promote the implementation of EHIP, the International Development Research Centre and the Tanzanian Ministry of Health organized a 12-day workshop in summer 1995 in Morogoro, Tanzania, with rep-

resentatives from WHO, the World Bank, and from the districts of Morogoro Rural and Rufiji, where the project will be implemented. The objectives were: to give all participants a basic understanding of the project's objectives; to identify potentially cost-effective essential packages based on disease burden data currently available in Morogoro and Rufiji; and to develop and plan activities for the first year of the project.

Six interventions were costed: the Integrated Management of the Sick Child, the Mother-Baby package, EPI-Plus (that is, an augmented form of the Expanded Programme on Immunization with selected additions of antigens and micronutrients), STD control, impregnated bednets, and tuberculosis management. The simulations provided some comparisons of costs between districts and at the national level.

The research component of the project aims at investigating supply and demand aspects of the health system. It hopes to determine the current health system capacity and to identify those areas that need capacity-building. Its two main components are health system research and demographic and epidemiological research. The research component of Tanzania's EHIP aims at strengthening the districts' information base so as to assist the District Health Management Teams establish priorities and plan the allocation of resources based on local burden of disease estimations, cost-effectiveness, system capacity, and community preferences.

The EHIP steering committee is chaired by the IDRC and includes representatives from Tanzania and several international donors. However, the IDRC is committed to establishing full intellectual partnership with the recipient country and leaves all in-country management and planning to the host country.

one or more of three common types of intestinal nematodes: giant roundworms, hookworms and whipworms. Schistosomiasis, caused by trematodes, affects almost 100 million school-aged children each year and onchocerciasis, caused by nematodes, also affects children. Unsafe water and poor sanitation are of course risk factors for waterborne parasites. The combined burden from these parasites is comparatively small at around 1% of the total, but their impact on children is profound. Not only do worms cause anaemia and reduce growth, they also affect cognition, reducing the usefulness of precious time in school. Intestinal helminths also contribute to malnutrition.

Malnutrition is a massive, and in some respects neglected, health problem. Its causes are complex and its name misleading. In fact, this condition results not only from inadequate dietary intake, but also from repeated infections and parasitic infestations (see Box 3.2).

Malnutrition is usually identified by indicators of reduced growth, such as low weight for height or low weight for age, and by specific micronutrient deficiencies. As many as one-third of children under the age of five in developing countries are underweight, with the prevalence reaching almost 60% in South Asia. Malnutrition affects not only physical development but also cognitive performance and educability.

More than 40% of women of reproductive age in developing countries are regarded as underweight, again with the greatest concentration by far in South Asian countries. Women who are underweight when they become pregnant are more likely to give birth to underweight infants, and underweight infants are themselves at greatly increased risk of death in childhood. It now appears that they may also face higher-than-average risks of certain noncommunicable diseases in later life, at least in some circumstances.

Some 13.8 million children have reduced eyesight be-

Table 3.1 The burden of childhood disease

Condition	Burden (as % of total DALYs), 1990		
	World	Sub-Saharan Africa	India
Childhood communicable diseases			
Lower respiratory tract infections (pneumonia)	8.2	10.2	11.4
Diarrhoeal diseases	7.2	10.9	10.2
Vaccine-preventable childhood infections*	5.2	10.3	6.4
Malaria	2.3	9.2	0.4
Bacterial meningitis and meningococcaemia	0.5	0.3	0.5
Intestinal nematodes	0.4	0.2	0.3
Malnutrition (direct effects only)	3.7	3.2	4.2
Total burden from these conditions	27.5	44.3	33.4

*Diseases preventable with the vaccines currently available through the Expanded Programme on Immunization: diphtheria, pertussis, tetanus, polio, measles.

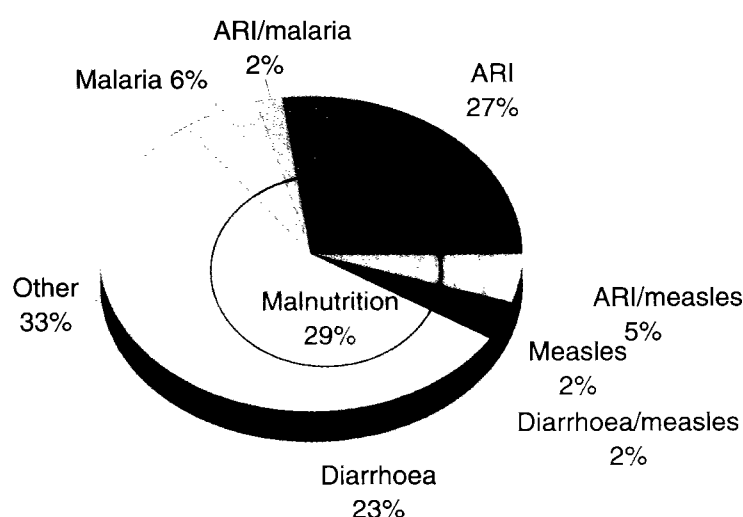
Source: Annex 1

cause of vitamin A deficiency, of whom up to half a million lose their sight every year. More than 25 million people are mentally retarded as a result of iodine deficiency. Iron-deficiency anaemia affects about four in every ten women of reproductive age in developing countries.

The complex and interactive relationship between inadequate food intake and infection in causing malnutrition is of tremendous importance to public health. But its significance is often underestimated because

traditional mortality statistics usually attribute deaths to one cause only and those involving infectious diseases are usually described in terms of the infection only. Similarly, the burden of disease that can be *directly* attributed to malnutrition—estimated to be about 3.7% of the global total—underestimates its overall impact on health. Since malnutrition predisposes people to infections and may produce long-term disability, it is a powerful risk factor and the *indirect* cause of

Figure 3.3 Distribution of 12 million deaths among children less than 5 years old in all developing countries, 1993



Notes: 1. Although less than 4% of deaths under age five are directly attributable to malnutrition (i.e. to being underweight or short for age or anaemic, etc.) a much larger percentage of deaths are associated with malnutrition in the sense that they occur in malnourished children and may, in part, be caused by their malnutrition. This figure points to 29% of deaths associated with malnutrition; recent studies and ongoing work suggest that the association is higher still.

2. Much of malnutrition is itself caused by the infections indicated; hence *inadequate food intake* would be associated with a (perhaps substantially) smaller percentage of deaths.

Source: Modified from material provided by the WHO Division of Diarrhoeal and Acute Respiratory Disease Control

Table 3.2 The burden of disease avoidable if access to safe water and sanitation were universal

Region	Disease burden attributable to unsafe water and sanitation (as % of total DALYs), 1990
Established market economies	0.1
Former socialist economies	0.2
India	9.5
China	2.0
Other Asia and islands	7.4
Sub-Saharan Africa	10.1
Latin America and Caribbean	5.3
Middle Eastern crescent	8.8
World	6.8
EME and FSE	0.1
Developing countries	7.6

Source: Annex 2

a much greater burden. Almost one-sixth of the entire global burden in 1990 can be attributed to malnutrition; in sub-Saharan Africa, the proportion is as much

as one-third and in India, more than one-fifth (Table 3.3).

3.1.2 Current R&D investment

Research spending has been assessed for the two main childhood killer diseases—pneumonia and diarrhoeal diseases. The results indicate clearly the broad mismatch between activity and need. In 1992, total funding for *all* health research worldwide—from basic science to health policy research—reached almost US\$ 56 billion. But assessments based on annual averages for three years from 1990 to 1992 indicate that each year just US\$ 32 million was spent on R&D on diarrhoeal diseases relevant to the needs of low-income and middle-income countries. This is far below a tenth of one per cent of the 1992 world total. R&D expenditure on acute respiratory infections relevant to the needs of low-income and middle-income countries was estimated at between US\$ 48 million and US\$ 68 million (Annex 5). These amounts are insignificant compared with the size of the global burden from these conditions. And, even though the research financed by these investments was directed at low-income and middle-income countries, the outcomes of that research have often been enjoyed disproportion-

Box 3.2 Malnutrition: why hunger is only half the story

The search for solutions to the global problem of malnutrition begins with a better understanding of the relationship between its two contributing factors—inadequate food intake and infection—and their relative importance in different populations.

The dietary component of malnutrition takes several forms. An inadequate overall intake of food results in a condition frequently called protein-energy malnutrition (PEM), which is usually measured in terms of growth failure in children and underweight in adults. A number of specific micronutrient deficiencies—most importantly vitamin A, iodine and iron—also contribute to malnutrition. Other micronutrients, such as zinc, potassium, sodium, magnesium and phosphate may be important but full data are not available. In reality, micronutrient deficiencies may also contribute to growth failure alongside PEM.

Children who are sick tend to lose their appetite, or have food withheld from them by well-meaning carers. When they do eat, their absorption of nutrients may be impaired, their energy requirements increased, and symptoms of diarrhoeal disease may lead to direct loss of nutrients. In turn, inadequate dietary intake adversely affects mucosal immunity and increases children's susceptibility to infections. As understanding of this interaction has grown, researchers have established that it is not merely additive, but synergistic and multiplicative: as a child loses weight, the risk of death climbs not in a

simple additive fashion but more and more steeply. If two children begin life with the same birth weight and are exposed to the same frequency of infectious diseases, but one is better fed and cared for, the better-fed one will suffer shorter overall periods of illness and will recover and regain weight more rapidly afterwards. The less well-fed and less cared-for child will be ill for longer periods, lose more weight, and will take longer to regain it. This child is more and more likely to die.

Children who are starving clearly need more food to grow. But for children whose diet is barely adequate, the treatment of infection may be as important as getting more food. Treatment for infectious and parasitic diseases has been shown to have an important effect on weight and growth, and, in the absence of diarrhoea, there is little difference in the growth of children up to the age of three years, despite significant differences in energy intake (World Bank 1993). Mass chemotherapy to reduce intestinal worm infestation has been shown to lead to significant weight gain in a number of different populations.

Understanding the conditions under which malnutrition can be less expensively addressed through control of infection than through increasing nutrient intake is a clear research priority: resource constraints and efficiency considerations typically preclude the possibility of proceeding with a range of approaches.

Table 3.3 The burden of disease that could be avoided if malnutrition were eliminated

Region	Disease burden attributable to malnutrition (as % of total DALYs), 1990
Established market economies	0.0
Former socialist economies	0.0
India	22.4
China	5.4
Other Asia and islands	14.5
Sub-Saharan Africa	32.7
Latin America and Caribbean	5.2
Middle Eastern crescent	11.0
World	15.9
EME and FSE	0.0
Developing countries	18.0

Source: Annex 2

ately by the populations of the industrialized countries—for example, vaccines and drugs designed to protect business travellers and holidaymakers.

Our findings underscore the degree to which researchers—and those who fund them—have neglected two of today's most important global health problems. While the relationship between the size of a health problem and the amount of R&D investment cannot be expected to be proportionate, a mismatch of this degree strongly suggests a serious misjudgement of priorities and the need for reallocation of resources.

3.1.3 Assessment of research needs

A key step towards assessing needs and opportunities for R&D on this unfinished agenda is to analyse the reasons *why* poor maternal and child health persist in a population. As we set out in Chapter 1, we have identified three broad reasons to explain the persistence of a disease in a population: (a) a lack of knowledge about the disease and its determinants, (b) a lack of tools and (c) failure to use the existing tools efficiently. This tripartite analysis is a means of guiding decisions about the *types* of research and development that are most likely to pay off and the probable balance of effort that should be devoted to each of them. For example, a lack of knowledge about the disease calls primarily for strategic biomedical and epidemiological research. Lack of tools calls for biomedical research and development, and may also require the development of instruments of policy (such as essential drugs lists, pricing policies and the like) by health economists and other health policy researchers. Failure to use the existing tools efficiently calls for research and policy development to achieve either or both of the following: (1) greater *technical* efficiency, obtained through behavioural research to understand the reasons for current failures and operational research to improve the delivery of services; and/or (2) greater *allocative* efficiency, obtained by targeting resources to the problem.

Here, we assess the relative importance of the three

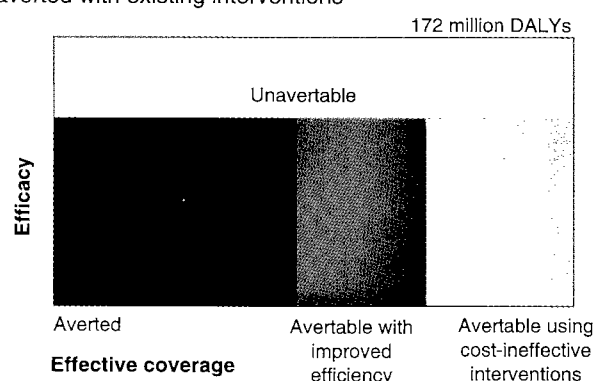
reasons for the persistence of the major childhood diseases. In the case of the two most significant diseases, pneumonia and diarrhoea, we have conducted quantitative analyses.

Pneumonia. The causes of lower respiratory tract infection are generally understood and the existing interventions—primarily case management with antimicrobials—are generally effective. In low-income countries, options for preventing infections are much more limited: vaccines against the two principal microbial agents, *S. pneumoniae* and *H. influenzae*, are not available. Recently, antibiotic-resistant strains of *S. pneumoniae* have emerged and, if these become widespread, control prospects could be worsened—a situation we discuss in Chapter 4. At present, however, it appears that pneumonia's persistence in the low-income countries is due to a combination of reasons (b), i.e. lack of tools, and (c) failure to use the existing tools efficiently in the population at risk.

We have further analysed the pneumonia disease burden to quantify the relative importance of each of the three reasons for its persistence. As set out in Chapter 1, the Committee used published data on the efficacy of the mix of currently available existing interventions, together with estimates provided by specialists in each field of the approximate proportion of the population that receives these interventions. These data were used to assess what proportion of the burden could be averted with better use of the existing cost-effective interventions, what proportion could be averted only with interventions that are not cost-effective, and what proportion cannot be averted now but requires new interventions (Figure 3.4). The relative size of each of these subdivisions of the burden aids decision-making about the broad types of research that are most appropriate to tackle the remaining burden.

Figure 3.4 Analysing the burden of pneumonia to identify research needs

Relative shares of the burden that can and cannot be averted with existing interventions



Note: The total DALY figure represents the number for this condition in 1990 plus an estimate of the number then averted through existing interventions.

As Figure 3.4 shows, around one-fifth of the remaining burden of pneumonia could probably be removed by more efficient use of the existing tools—for example, by making appropriate case management widely available and reducing the *inappropriate* use of antimicrobials. About another one-fifth could be averted today only with approaches that are not yet cost-effective, such as treatment with expensive antimicrobials or in tertiary facilities. Beyond these avertable parts of the remaining burden, more than a quarter of the total cannot be averted by any existing approaches.

Diarrhoeal disease is rarely fatal in the industrialized countries. Its causes, like those of pneumonia, are well understood, and effective treatments exist. In ideal conditions, oral rehydration therapy (ORT) can successfully treat 90% of cases of acute watery diarrhoea, which accounts for about half of all deaths from diarrhoeal disease. ORT could substantially reduce the disease burden if more health workers used it instead of mistakenly prescribing inappropriate antimicrobials and other drugs, and if more mothers and other carers knew when and how to use it. However, some additional tools would help: for example, there is so far no licensed vaccine against rotavirus, the principal causative agent of this form of diarrhoea in low-income countries. The burden that persists in low-income countries therefore appears to be due once again to (b) a lack of tools and (c) failure to use the existing tools efficiently.

As with pneumonia, we have analysed the burden due to acute watery diarrhoea in an attempt to quantify the relative importance of these reasons. Whereas in the case of pneumonia the results were split between the need for more efficient use of existing tools and the need for more tools, the results for this form of diarrhoeal disease show a different balance. Figure 3.5 shows that more than half of the remaining burden could be lifted

now with more efficient use of existing tools—for example, through better use of ORT.

However, acute watery diarrhoea accounts for only half the total burden of diarrhoeal disease. Persistent diarrhoea requires careful dietary management, while dysentery must be treated with an effective antibiotic. Most cases of dysentery are caused by *Shigella* bacteria and as yet there are no effective vaccines to protect against these extremely common infections. Worryingly, an increasing number of strains of *S. dysenteriae* are becoming resistant to antimicrobials and the need for effective vaccines is becoming more and more pressing. Thus, while the broad reasons for persistence of the disease burden still lie mainly in a failure to use existing tools efficiently, new tools are also needed in some areas.

Malaria is a more complex problem. There are some important gaps in researchers' understanding of the disease process and an undoubted shortage of tools—subjects to which we return in the next chapter. However, among the principal victims of the disease—young children in rural sub-Saharan Africa—there is little doubt that case-fatality rates could be substantially lowered today with more efficient use of the existing tools, for example, through more rapid diagnosis and appropriate treatment with the affordable, first-line antimalarials.

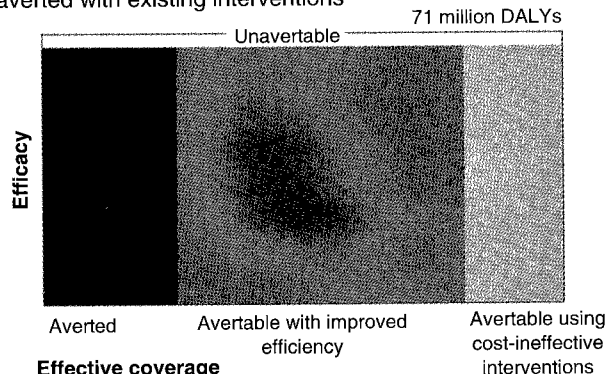
The vaccine-preventable childhood infections.

The impact of immunization on children's health has been dramatic. As a result of the Expanded Programme on Immunization, vaccines against measles, diphtheria, pertussis, tetanus and polio averted almost 3 million deaths and 138 million cases of disease in low-income and middle-income countries during 1994. When the Programme began work in the 1970s, only some 5% of children in these countries were immunized. Twenty years later about 80% of infants under the age of 12 months are being immunized against polio, diphtheria, pertussis and tetanus, and about the same percentage of infants under the age of 2 are being immunized against measles. Without these efforts, the burden of disease among under-fives would be 23% greater than it is today.

But the Programme has not yet reached its potential. Immunization coverage is still relatively low in sub-Saharan Africa—around 54% on average. In some countries, coverage is falling and in 18 countries is below 50%. The vaccine-preventable childhood infections remain, primarily, not because of a lack of understanding of the disease processes or their causes, but because of a failure to extend coverage to these groups. In practice, coverage of 100% is unlikely to be achievable, but a target of 90% has been set. Reasons for the failure to reach 90% to date are essentially due to (c) failure to use the existing tools efficiently. Among the inefficiencies are inadequate resources, administrative failures, failure to target those least likely to be immunized and most likely to become infected, missed opportunities to immunize children through health workers' misjudgements, and failure to engage with local communities. In addition,

Figure 3.5 Analysing disease burden of acute watery diarrhoea to assess research needs

Relative shares of the burden that can and cannot be averted with existing interventions



Note: The total DALY figure represents the number for this condition in 1990 plus an estimate of the number then averted through existing interventions.

there are technical failures in the service, including breakdown in the cold chain and problems with poor-quality vaccines.

But there are also some areas of need where new tools are desirable. A significant proportion of deaths from these infections occurs in very young babies below the age at which vaccines are recommended. Alternative approaches, such as immunizing pregnant women to enable them to transmit passive immunity to their newborn infants, should be explored. In addition, there are important diseases, such as hepatitis B, for which vaccines of proven efficacy exist, but which are not yet incorporated into the EPI in many countries.

Helminth infestations remain a source of disease and disability even though mass chemotherapy has proven to be effective and among the most cost-effective interventions available. Failures in the design and administration of programmes, and particularly failure to target those at greatest risk, including school-age children, account for much of the burden. High reinfection rates are an additional problem. However, the burden that remains can be attributed mainly to (c) failure to use existing interventions efficiently.

Malnutrition. This condition persists in part for the obvious reason that too many people have an inadequate food intake, but also for less obvious reasons. First, the existing interventions have not been used as well as they might. For example, the efficacy of vitamin A supplementation is clearly established and the success of breast-feeding promotion programmes has been demonstrated in a range of settings, but these interventions do not reach all those who might benefit from them. Secondly, a significant part of the burden may remain because of important gaps in the knowledge base. For example, the relative contributions of interventions to control infection and inadequate dietary intake in different epidemiological environments are not known. Likewise determinants of the relative efficacy of interventions to increase *quality* of dietary energy intake (through increased proportions of protein and fat) relative to *quantity* of intake remain to be well understood. These are some of the reasons why the wide variation in rates of underweight between different populations (for example, between South Asia and sub-Saharan Africa) are not fully explained. The importance of certain micro-

nutrients such as zinc remains unclear, and the impact of low weight in utero and in infancy for adult health in low-income environments has not been fully assessed. Thus, in clear contrast to the other childhood conditions, malnutrition appears to persist at least in part because of reason (a), lack of knowledge of the disease process and its determinants.

Table 3.4 summarizes the above assessments and points towards broad priorities for R&D.

For pneumonia, diarrhoeal disease, the vaccine-preventable infections and helminth infestation, we conclude that the knowledge base is adequate to proceed with the development and evaluation of interventions. Efforts should, in our view, focus mainly on making existing interventions more efficient in the populations at risk through behavioural and operational R&D. For malaria, some new knowledge is needed, but the primary requirement in the currently vulnerable population is again more efficient use of existing interventions. In the case of malnutrition, even though better food supplies and more efficient use of the existing interventions to control infection and enhance micronutrient intake are of course desirable, more knowledge is also needed, suggesting that strategic epidemiological and biomedical research are priorities. In parallel, however, efforts to increase the efficiency of existing interventions should be maintained with equal intensity.

3.1.4 Opportunities for intervention development and evaluation

As set out in Chapter 1, the process of assessing opportunities for developing and evaluating interventions should consist of specifying the nature of the desired interventions, estimating their probable cost-effectiveness relative to existing approaches, and then further assessing how much it is likely to cost to develop them, how long it will take, and how likely they are to succeed. Obviously, the process can indicate interventions that are *unlikely* to be cost-effective as well as those that are attractive. (For example, the Committee has calculated that in the current epidemiological situation, development of a vaccine against one parasite—*Schistosoma mansoni*—is not likely to be a profitable investment of R&D funds as long as the drug praziquantel remains active against the par-

Table 3.4 Broad reasons for the persistence of disease burden from the five major childhood killers

Condition/risk factor	Inadequate knowledge of disease process and causes		Inadequate tools	Failure to use existing tools efficiently
Pneumonia			++ +	+++
Diarrhoeal disease			++	++++
Vaccine-preventable childhood infections			++	++++
Malaria	+		++	+++
Malnutrition	+++			+++
Helminth infestations			+	++++

Note: The estimated rating ranges from little importance ('+') to extremely important ('++++'). A blank means not significant.

asite, *unless* the vaccine were to give exceptionally long-lasting protection [Supplementary paper 2].) The extent to which this type of assessment can be quantified, and how much it will, or should, continue to rely on subjective judgement, are matters for debate.

In the Committee's view, a selected small group of desirable interventions could dramatically reduce disease burden among children in low-income countries if they were applied widely. We therefore conclude that R&D should focus on them. We discuss them here, with information on their likely cost-effectiveness, the probability of their success and the necessary costs and time frames for development where available. Our selection has been informed by review of the available data, consultation and informed judgement. An ongoing effort will be needed to make the process systematic, and this list can be no more than a preliminary step.

The desired interventions are of two distinct types: packages of essential interventions, and tools to improve the content of those packages.

Highly attractive packages

- *Refine, implement and evaluate the package for the Integrated Management of the Sick Child*

Since pneumonia, diarrhoeal disease, malaria, measles and malnutrition share many common risk factors and may be found together in the same child at the same time, researchers have argued that they may be most effectively addressed as a group rather than singly. A package of clinical services for sick children, known as the Integrated Management of the Sick Child (IMSC), has already been developed by research organizations including WHO. So far, guidelines for outpatient care have been completed but their effectiveness needs to be evaluated in the field. In addition, further guidelines for inpatient care have yet to be developed. In the view of the Committee, the enormous potential of the package to reduce disease burden, and its outstanding cost-effectiveness, are solid grounds for investing substantially in operational research to evaluate the outpatient component of the package and to develop the inpatient component in specific settings.

In the current package, treatment guidelines for outpatients have been developed to cover the most common potentially fatal conditions, enabling health

workers to focus on the whole child rather than on specific diseases. The health worker assesses every child for a set of signs and symptoms, including cough or difficulty in breathing, diarrhoea, fever, and ear problems, and assesses the child's nutrition and immunization status. Depending on the findings, the health worker can then allocate the child either for urgent referral, or specific medical treatment and advice, or simple advice for home treatment. The guidelines for the IMSC are printed in wallcharts and booklets for use in health care settings. Health workers are trained in their use.

Properly implemented, this package could, in principle, reduce the global burden of disease by more than any other (World Bank 1993). Like other packages, it is likely to be more cost-effective than the sum of the separate services that it contains when these are given singly because, in principle, it exploits the shared use of inputs and reduces the cost to patients of obtaining services. As yet, however, the potential of this package has not been met—otherwise the burden from these conditions would not be as great as it is now. The key to maximizing the effectiveness of the package may lie in operational research.

Table 3.5 summarizes the existing estimates of cost-effectiveness of the package in different settings. This kind of information can help to clarify how, and in what settings, this desired intervention is most likely to pay off, and where it is not worth developing. The IMSC has been estimated to cost less than US\$ 50 for every DALY averted in low-income countries. By comparison, in middle-income countries, where child mortality rates are relatively low, this intervention is still cost-effective but less so than in low-income countries, at US\$ 50 to US\$ 100 per DALY averted (Bobadilla et al. 1994). This suggests that the package would not be cost-effective in countries where child mortality is very low, and that efforts should focus on its implementation and refinement in low-income countries.

The development of the IMSC represents a highly attractive investment to research investors. Not only is its potential to reduce disease burden exceptionally high, it is also at an advanced stage of development. It is judged that the R&D needed to develop and evaluate the package in different settings can be achieved in a relatively short time, probably under five years,

Table 3.5 Comparisons of the likely cost-effectiveness of the package for Integrated Management of the Sick Child in different settings

Setting	Cost/ beneficiary (US\$)	Cost / capita (US\$)	DALYs averted per 1 000 population	Effectiveness*	Cost / DALY (US\$)
Low-income countries	9	1.6	184	0.25	30-50
Middle-income countries	8	1.1	21	0.25	50-100

*Calculated by multiplying efficacy, diagnostic accuracy (when applicable) and compliance.

Source: Bobadilla et al. 1994:175

and at a cost of about US\$ 15 million. Investment and effort should be focused on these tasks, including assessments of the cost-effectiveness of the package in different local settings.

- *Evaluate an immunization package augmented by additional important immunogens and selected micronutrients*

The Expanded Programme on Immunization is highly successful. However, at least two existing interventions, vitamin A supplementation and hepatitis B vaccination, could in principle be added to the existing schedule for marginal cost and potentially significant health gain. Limited experience is already being accumulated in some countries under the name EPI-Plus. The Committee views this as an attractive opportunity for wider development and evaluation.

It has been calculated that an augmented EPI that includes hepatitis B vaccine, yellow fever vaccine and micronutrient supplementation with vitamin A, and iodine where required, could be delivered for no more than US\$ 17 per DALY averted in low-income countries (World Bank 1993). In middle-income countries, the cost would be slightly higher, at between US\$ 30 and US\$ 50 per DALY averted, but still a very good “buy” for health. The opportunity to develop and evaluate such an augmented programme is excellent: costs are likely to be low and the time needed for development is probably less than five years. Some limited trials to assess the safety of administering vitamin A at the same time as immunization should be incorporated.

In addition, as we discussed earlier, alternative approaches to preventing severe infectious diseases (such as pneumonia) during the first three months of life should be investigated. Possibilities include the immunization of pregnant women, or women of child-bearing age, to protect newborn infants through the transfer of antibodies from mother to child, as currently practised for the prevention of neonatal tetanus.

Packages for further investigation

Work should also continue on evaluating the potential of packages for which little information is currently available, but which appear to merit R&D investment because they are expected to provide cost-effective ways of reducing disease burden. For example:

- *A Healthy Schoolchild package*

This would focus on reducing the levels of helminth infestation—including those that cause schistosomiasis and onchocerciasis—in children of school age. Although the disease burden from these helminths is comparatively low, the cost-effectiveness of existing interventions is exceptionally high. Mass chemotherapy delivered annually to schoolchildren is

estimated to cost less than US\$ 25 per DALY averted in low-income countries. By reducing the burden of helminth infestation, governments may be able to invest in their countries’ human capital by improving children’s cognitive performance and educability. Additionally, some micronutrient supplementation might be feasible.

- *A Healthy House package*

Improved shelter, safe drinking water and proper sanitation together form the pillars of preventive child health programmes. A package of interventions might emerge from collaboration between the health sector and others (e.g. municipal engineering departments, community groups) to design and modify the *physical* environment of homes for maximum health, for example through demonstrating latrine construction, water source protection and the provision of soap, and interventions to reduce indoor air pollution, as well as reimpregnation of bednets and some other modest vector control activities. Much is known about the risks of unsafe water and poor sanitation and shelter, but appropriate technologies for reducing those risks need to be identified at national and local level. These might include small-scale water disinfection systems, further improvements in latrine design and cost-effective approaches to providing proper shelter. If this R&D were to pay off in making homes safer, households could see significant reductions in diarrhoeal disease and other childhood infections.

Tools to improve package content

- *Develop and promote wider use of insecticide-impregnated bednets*

Bednets, used properly, have been shown capable of reducing child deaths from all causes by one-quarter in areas where mortality is high. If a programme of bednet use is to be worth developing, however, it is desirable to demonstrate that it can at least compete with or supersede existing interventions. Comparative cost-effectiveness estimates for bednets and another existing preventive intervention against malaria, chemoprophylaxis, have been performed for this Report. In this case, there are data from The Gambia for at least some of the intervention types compared and additional studies in Burkina Faso, Ghana and Kenya. Analyses based on those data show that in a high-mortality area, impregnated bednets would be much more cost-effective than chemoprophylaxis, buying years of healthy life for approximately half the price of chemoprophylaxis. Obviously, the cost-effectiveness depends on a number of factors, such as how dependably householders use bednets as intended. A range of different scenarios are set out in greater detail in Supplementary paper 2. As the sum-

Box 3.3 Best buys for R&D for child health

Strategic research

- Understand the relative importance, in different environments, of increased nutrient intake and controls on infectious disease as means to reduce malnutrition.

Package development and evaluation

- Evaluate and refine the package for the Integrated Management of the Sick Child.

New tools to improve package content

- Evaluate the efficacy and optimal dosage of candidate rotavirus vaccine in low-income countries.
- Evaluate the efficacy of candidate conjugate pneumococcal vaccine and existing Hib vaccine in low-income countries.
- Develop and evaluate ways to increase efficiency in the Expanded Programme on Immunization by simplifying delivery and maximizing use of opportunities for immunization.
- Evaluate promotion of insecticide-impregnated bednets, possibly for inclusion in a future Healthy House package.

mary data presented here show, however, the cost-effectiveness remains surprisingly high even in far from optimal conditions (see Table 3.6).

The payoff from developing this intervention in high-mortality settings is clearly great. It is considered that development work in assessing the actual efficacy and cost-effectiveness of selected different kinds of programmes could proceed in under five years and for very modest costs.

- *Complete trials in low-income countries of appropriate vaccine against rotavirus*

The analysis of research needs for acute watery diarrhoea suggested that existing interventions,

such as oral rehydration therapy, could remove much more of the burden of diarrhoeal disease than they currently do. However, in the judgement of public health researchers, the existing mix of interventions is unlikely to eliminate the problem even under optimal conditions. A further desirable intervention, in the view of the Committee, is to complete trials of candidate rotavirus vaccines in low-income countries. A vaccine which gives 80% protection against severe rotavirus diarrhoea in trials in the United States has so far shown much lower efficacy in developing countries. Trials at higher doses are currently under way. A key requirement for further R&D is to establish, in addition to safety and efficacy, the optimal dose and the potential for delivering the vaccine within the Expanded Programme on Immunization. If 80% efficacy were achieved, the estimated cost-effectiveness would be exceptionally high: around US\$ 10 per DALY averted. Since more than one candidate vaccine is already in advanced development, and others based on equally promising approaches are under earlier stages of development, the likely payoff is high, the time frame short and the investment requirement relatively low.

Clearly, a vaccine against *Shigella dysenteriae* is also highly desirable and becoming more urgent with the spread of antibiotic-resistant strains. However, rotavirus vaccines are at a more advanced stage of development and therefore, according to the criteria adopted by the Committee, they are a more promising R&D investment at this time.

- *Complete trials in low-income countries of existing appropriate vaccines against Haemophilus influenzae and Streptococcus pneumoniae*

Since the licensing of conjugate vaccines for *H. influenzae* in the United States and many northern European countries, the infection has all but disappeared as a public health problem in those countries. The high efficacy of Hib vaccines appears to have been confirmed in Chile, and a trial in The Gambia is now nearing completion, with results expected in late 1996. Although cost-effectiveness estimates in low-income countries are not yet available, the Committee considers this intervention is likely to be cost-effective in areas where child mortality from pneumonia is high. Trials should be continued and if the vaccine's

Table 3.6 Comparisons of the likely cost-effectiveness of two malaria interventions
(Cohort analysis, 10 000 newborns)

Option	Cost (US\$)	DALYs averted	Cost per DALY (US\$)
Impregnated nets (government distribution, 50% compliance)	143 000	10 400	14
Chemoprophylaxis (government distribution)	79 000	2 800	28

Source: Supplementary paper 2. Based on cohort of 10 000, followed from birth to age 5, West Africa model life tables. Cost of nets US\$ 9.77; costs of government bednet programme including insecticide and reimpregnation, and costs of chemoprophylaxis programme, taken from Picard et al. 1993. Assume 2 children sleeping under each net. Further assumptions (e.g. on efficacy of each intervention) detailed in Supplementary paper 2.

efficacy is confirmed, further studies should investigate the potential cost-effectiveness of delivering it as part of the EPI in a range of different countries.

New conjugate vaccines for *S. pneumoniae* are currently under development and trials in low-income countries are expected soon. A more detailed discussion of these vaccines can be found in Chapter 4.

- *Increase the efficiency of the Expanded Programme on Immunization*

The vaccines given within the EPI are among the most cost-effective of all interventions. Measles vaccine buys years of healthy life for less than US\$ 10. Polio, diphtheria, pertussis and tetanus together cost less than US\$ 25 for each DALY averted. If health workers made use of all opportunities for immunizing children, and if the delivery of vaccines were made simpler, this already excellent set of interventions could be made even more cost-effective. At present, five contacts are required between health worker and child. If there were only one (i.e., if all immunization requirements could be met at once), costs could be cut by as much as 70% (World Bank 1993). Steps towards improving the technical content of the package could include reducing the number of doses of vaccine required (and ensuring that any new antigens incorporated into the programme can be given at the same time as those already incorporated). In the longer term, the possibility of potential "one-shot" vaccines and other initiatives deserves investigation. Although the time frame and costs of such activities are more difficult to estimate, the expected payoff in reducing costs of the EPI programme are so great that a relatively large investment is merited.

3.2 Achieving safe motherhood

In traditional public health circles, women are often discussed only in relation to their role as reproducers. Women are more than mothers, however, and have the right to good health in their own right—including the right to *avoid* unwanted children. However, the particular risks that many women face through their reproductive role form a major barrier to their overall health. In the Committee's view, R&D that results in better reproductive health for women will enhance their health overall. While each chapter of the Report is concerned equally with men and women and their risks for all types of disease, in this section we focus on women's reproductive health needs.

Good reproductive health is about more than avoiding disease. According to the definition adopted by WHO, it is also about the ability to have a safe, responsible and fulfilling sex life and the freedom to decide if, when and how often to have children (Khanna, Van Look & Griffin 1994). Among the necessary conditions for this good reproductive health are the right of men and wom-

en to learn about and obtain safe, effective, affordable and acceptable methods of family planning, and the right of women to have appropriate health services to enable them to go through a safe pregnancy and birth. Yet all too few women in the poorest countries find these services within their reach. The immediate consequences are unacceptably high rates of unwanted pregnancies, unsafe abortions, complications of pregnancy and delivery, and infants dying in the first week of life. In the longer term, children born to women in these circumstances also suffer poorer health. In addition, HIV/AIDS and other STDs are important causes of poor reproductive health: they are discussed in the next chapter.

3.2.1 The magnitude of the burden

Only some of the effects of poor reproductive health can be quantified in terms of disease burden, death or other measures of mortality and morbidity. These include the number of women who die in delivery, the number of babies who die in the first week of life, deaths resulting from ectopic pregnancy and deaths resulting from unsafe abortions. Excess fertility may result, indirectly, in a measurable burden of ill-health to children: those who are born either too soon after an older sibling, or into a family where there are already more children than can be reasonably fed, cared for and educated, are at greater risk for a number of diseases. It is much more difficult, though, to quantify the impact of other distressing outcomes of poor reproductive health. For example, women may become permanently incontinent as a result of a bad delivery, or may suffer fistulae in the reproductive tract that not only interfere with sexual intercourse but bring social stigma. Equally, it is difficult to quantify the benefits to couples of contraception that not only "averts a birth" but also improves quality of life for the entire household. Table 3.7 summarizes the burden of those conditions that can be measured in terms of DALYs.

Excess fertility. An estimated 120 million fecund women are not using contraception even though they want to avoid becoming pregnant. Surveys within individual countries suggest that most women want smaller families than the current average family size in their country, even though in some countries, particularly in sub-Saharan Africa, the gap between desired and actual family size is small. In addition, an estimated 300 million couples are not satisfied with the methods of contraception available to them. In part because of this dissatisfaction, many couples stop using their contraceptive method or do not use it properly. Up to 30 million unintended conceptions occur every year among people using contraception.

In the poorest countries, the capacity of the services is inadequate to meet need. In many sub-Saharan African countries, for example, family planning services are able to meet less than a third of the potential demand. As well as desiring fewer children, many couples want to

space their births better. Evidence suggests that babies born within 24 months of an older sibling are more likely to suffer ill-health or to die before they reach five years of age.

Unwanted pregnancies not only carry heavy emotional and practical costs to women and their families; they may also be dangerous and impose a heavy economic burden on the population as a whole. Worldwide, it is estimated that 25 million of the 55 million abortions performed each year are done under unsafe conditions. The complications kill some 70 000 women. A study in Tanzania found that symptoms diagnosed as likely to be due to the complications of abortion were the most common reasons for admission to gynaecological wards.

Complications of pregnancy and childbirth.

Having a baby carries risks in the healthiest populations, but the difference in the degree of risk to women in developed and developing countries is among the starkest of the global gaps in health. In the established market economies, there are just 7 maternal deaths for every 100 000 births. In low-income countries there are more than 500. Girls and young women are at particularly high risk. Maternal complications include haemorrhage, sepsis, hypertensive disorders of pregnancy, eclampsia and obstructed labour. The death of a woman puts her surviving children at risk, too: such children are 50% more likely to die before they reach age five than had their mother lived.

Perinatal complications, which are inextricably linked to those affecting the mother, include birth asphyxia, birth injuries, sepsis and prematurity. In the assessments conducted for this Report, this category also includes low birth weight. Perinatal complications can also include a number of communicable diseases acquired during pregnancy or delivery, including STDs, neonatal tetanus and hepatitis.

Together, maternal and perinatal conditions account for 9% of the global total, and about 12% of the total in India and in the Middle Eastern crescent.

3.2.2 Assessment of research needs

Couples—and women and girls outside stable relationships—continue to suffer all these effects of poor reproductive health despite the existence of a number of methods of contraception and effective algorithms for the management of safe pregnancy, childbirth and care of infants in the first week of life. As above, we have analysed the reasons for the persistence of the burden as a step towards identifying the probable balance of R&D that is likely to bring results. We have analysed each condition separately.

Excess fertility. Inefficient use of the existing tools is a major part of the problem. Too few women who want contraceptives have access to them, either because of shortages of supplies or inadequate services. Many women and girls lack access to information about how to avoid pregnancy and many health workers lack the training to meet their needs. In addition, the available range of methods for family planning offers couples inadequate choice. In particular, there is much unmet demand for a wide choice of long-term methods, postcoital methods for both emergency and regular use, and male methods.

These reasons point to two overall types of R&D: research aimed at improving the efficiency of existing services in family planning, and the development of new and acceptable methods of contraception. The need for new knowledge is relatively small, except in two areas. Behavioural strategic research is needed to better understand perceived needs in different communities. Secondly, some strategic biomedical research is required, both into mechanisms of spermatogenesis, sperm maturation and fertilization that would lay the foundations for developing a wider choice of male contraceptives, and also into mechanisms of implantation which would lay the foundation for developing postcoital methods for emergency and regular use.

In general, however, the knowledge base is adequate to enable most of the relevant intervention opportunities to be assessed. Some selected interventions are discussed below, in section 3.2.3.

Table 3.7 The burden of maternal and perinatal ill-health

Condition	Burden (as % of total DALYs), 1990		
	World	Sub-Saharan Africa	India
Maternal conditions (obstructed labour, abortion, maternal sepsis, maternal haemorrhage, hypertensive disorders of pregnancy)	2.2	3.2	2.6
Perinatal conditions (birth asphyxia, birth trauma, low birth weight)	6.7	6.5	8.8

Note: A background paper to this Report (Jamison, Jamison & Shibuya, forthcoming) presents an alternative methodology for constructing DALYs that would add in DALYs from late fetal death but have the overall effect of markedly *reducing* DALYs arising from perinatal conditions relative to maternal conditions.

Source: Annex 1

Maternal and perinatal complications. The gap between maternal mortality rates in the industrialized countries and in the low-income countries indicates that knowledge about how to deliver a baby is not the problem. Once again, inefficiencies in the use of existing interventions, such as algorithms for the early detection of complications of pregnancy and for safe delivery, must be held to account. Essential obstetric services, such as a referral plan for home deliveries, are also lacking in many communities. In addition, there is a shortage of *appropriate* tools to facilitate safe and convenient obstetric practice in low-income populations.

Table 3.8 summarizes the discussion above.

As with the childhood conditions, the Committee concludes that the predominant effort in R&D should therefore be directed at operational research to develop, evaluate and improve the efficiency of the existing interventions for family planning and maternal health in low-income populations. In addition, a significant amount of effort needs to be devoted to the development of new tools.

3.2.3 Opportunities for intervention development and evaluation

As before, the Committee has identified a small number of key interventions that have the potential to reduce disease burden and improve the quality of life for millions of women and their families.

- *Develop and evaluate a package of services for mother and infant for antenatal care, delivery and the first week of life: the "Mother-Baby package"*

For safe motherhood, the priority is to develop existing services into an integrated form that can reach all who need them at the highest level of quality possible. The World Bank has estimated that the extension of prenatal, delivery and postpartum care to 80% of the world's population would reduce by 40% the burden of disease associated with unsafe childbirth. In low-income countries the cost-effectiveness of such a package is expected to be high at between US\$ 30 and US\$ 50 per DALY averted (Bobadilla et al. 1994). However, although WHO has identified the desirable contents of such a package, their cost and effectiveness in different administrative environments remains to be evaluated. And while researchers have good overall knowledge of what constitutes good, es-

Box 3.4 Best buys for R&D on maternal and perinatal health

Package development and evaluation

- Develop, evaluate and refine the Mother-Baby package for pregnancy, delivery and neonatal care.
- Evaluate the implementation of a range of family planning packages offering a wide choice of methods.

New tools to improve package content

- Develop new contraceptive methods, particularly to widen the choice of long-term but reversible methods, postcoital methods for regular and emergency use, and methods for men.

sential care in the delivery and the postpartum period there is much less understanding of the types, and degree, of intervention that are essential in antenatal care. Indeed, research in the EMEs is only now evaluating the outcomes of different programmes of antenatal care and has only recently established which obstetric practices benefit patients and which do not.

The Mother-Baby package which is now being developed by WHO incorporates the provision of information and services for family planning, antenatal care, including the diagnosis and treatment of STDs, and the detection of any pregnancy complications; the ensuring that all birth attendants have the necessary skills, knowledge and equipment to perform a clean and safe delivery and to give essential postpartum care to mother and baby; and the provision of essential obstetric care for all high-risk cases and emergencies. Properly implemented, the package could avert about half of the maternal deaths that occur each year (World Health Organization 1995). Communities should be involved in developing, implementing and evaluating the services provided.

Among the R&D priorities identified by WHO for the development of the package are: studies of the delivery of services to women and girls with the aim of identifying targets for improvements in the quality of care; the assessment of appropriate technologies,

Table 3.8 Broad reasons for the persistence of the burden of poor reproductive health

Condition	Inadequate knowledge of the physiological processes	Inadequate tools	Failure to use existing tools efficiently
Excess fertility	+	+++	++
Maternal complications		+	+++++
Perinatal complications		+	+++++

Note: The estimated rating ranges from little importance ('+') to extremely important ('+++++'). A blank means not significant.

such as a simple partograph, that can be used to monitor labour outside the hospital environment or the adaptation of simple sterile pre-loaded injection capsules to enable health workers to give oxytocin in stage III of labour, with the aim of reducing postpartum haemorrhage and minimizing the risk of sepsis; and ultimately, the development of guidelines for health workers. The expected costs and time frame of developing the package are moderate.

- *Evaluate the practical implementation of alternative family planning packages, particularly those offering a wider choice of contraceptive methods*

A package of existing family planning interventions, including information on sexual health, access to contraceptive methods and regular monitoring where appropriate, can be delivered for US\$ 20 to US\$ 30 per DALY averted in low-income countries. Since good reproductive health has wider benefits to women and families, however, this assessment may underestimate the value of such services to human well-being and economic development. To improve the availability and choice of family planning, development and evaluation of services are needed, not only at the level of policies to increase the availability of contraceptives themselves, but also to make improvements in the interactions between service providers and clients. Efforts should focus on developing acceptable and effective services for particularly vulnerable groups, including teenage girls. Once again, local communities' views should be made central to this research.

R&D efforts are needed both for developing male methods of contraception and for better and more acceptable female methods. The aim should be to increase the choice of cost-effective options to people in *low-income countries*, particularly for those who want long-term but reversible contraception. The cost-effectiveness of such interventions is difficult to estimate because the benefits they bring go much further than simply averting disease burden. However, it is likely that the development of methods that are accessible and acceptable would prove an excellent investment, given that inadequate choice or dissatisfaction with a particular method has been shown to lead to reduced use and thus increased risk of excess fertility. There is a strong case, therefore, for continued investment in the development of products already at advanced stages of development, such as postcoital contraceptive methods for regular as well as emergency use, and alternative injectables with reduced side-effects.

3.3 Chapter summary and recommendations

The infectious diseases of childhood, malnutrition and poor reproductive health are massive burdens on the people of low-income countries and thus on global health. They account for well over one-third of total disease burden, and more than half of the burden in sub-Saharan Africa. A set of packages of existing essential health interventions, such as the package for the Integrated Management of the Sick Child, could in principle avert more than one-third of the burden of ill-health among children in low-income countries for less than US\$ 12 per head per year. R&D efforts on this unfinished agenda should concentrate on developing and evaluating certain packages of essential services in low-income countries to increase the efficiency of existing interventions. This will involve mainly operational research and behavioural studies. In addition, a lesser, but significant, degree of investment is needed to develop new tools to improve the content of some packages. This will call for primarily biomedical research. Finally, the health sector must assess the potential for collaboration with other sectors such as education and agriculture in reducing risks and enabling people to take greater control of their health.

Recommendations

1. Investors should increase resources for developing and evaluating selected essential packages of interventions, such as the package for the Integrated Management of the Sick Child and the Mother-Baby package, in low-income countries, as potentially highly cost-effective means to achieve massive gains in the health of the poor.
2. A significant portion of the burden of childhood infectious diseases and poor maternal and perinatal health still cannot be addressed by existing tools. New tools are needed—for example, vaccines against certain respiratory and diarrhoeal infections, and a wider choice of contraceptive methods. Current efforts, both in strategic research and in new product development, are inadequate to deal with these challenges. Investment in these areas now holds the promise not only of improving health but also of reducing costs.