Chapter 4

Cost-Effective Strategies for the Excess Burden of Disease in Developing Countries

Many of the diseases and health conditions that account for a large part of the disease burden in low- and middle-income countries are far less common in high-income countries. These burdens are primarily associated with infectious diseases, reproductive health, and childhood illnesses. Just eight diseases and conditions account for 29 percent of all deaths in low- and middle-income countries: TB, HIV/AIDS, diarrheal diseases, vaccine-preventable diseases of childhood, malaria, respiratory infections, maternal conditions, and neonatal deaths.

Approximately 17.6 million people in low- and middle-income countries die each year from communicable diseases and maternal and neonatal conditions. Both the occurrence of and the death rates from such diseases and conditions are far lower in all high-income countries. This is due in part to greater wealth, better general living conditions, and different climatic and environmental factors, but also to the use of cost-effective health interventions. Many of the diseases that account for the largest differences in health status between low- and middle-income countries and high-income countries are also diseases for which cost-effective strategies are known, available, and feasible.

If low- and middle-income countries achieved the same rates of death from these diseases as high-income countries, the number of deaths would fall from 17.6 million to 3.0 million per year. The difference, some 14 million deaths, represents a measure of the excess burden of ill-health in low- and middle-income countries. Applying known and cost-effective measures to these diseases could substantially reduce many needless deaths.

A number of cost-effective measures for addressing communicable diseases and maternal and neonatal conditions were already known when the first edition of *Disease Control Priorities in Developing*

Countries (Jamison and others 1993) was published. ORT had been proven cost-effective for reducing case fatalities associated with childhood diarrhea. Prenatal care and skilled birth attendance, immunization against tetanus and hygienic care of a newborn's umbilical cord, immunization against childhood illnesses, and the DOTS strategy for controlling TB were also known, cost-effective measures for addressing this excess burden of disease. *DCP2* presents information confirming many of these earlier findings, but also surveys new evidence concerning, for example, the emergence of drug-resistant strains of malaria, TB, and HIV and the large concentration of childhood deaths that occur in the first 28 days of life.

This chapter can discuss only a selection of the diseases covered in *DCP2* that constitute the excess disease burden in low- and middle-income countries. (For a complete list of communicable diseases and maternal and neonatal conditions that are covered in *DCP2* see chapter 1, box 1.1, and the appendix.) Moreover, the following accounts can highlight only a few of the findings for each of the diseases included. For a fuller and more complete account, refer to the associated *DCP2* chapters as referenced in this chapter.

INFECTIOUS AND COMMUNICABLE DISEASES

"Infectious diseases account for less than 2 percent of deaths in high-income countries, but . . . 21 percent of deaths in low- and middle-income countries."

Infectious diseases account for less than 2 percent of deaths in high-income countries, but are responsible for 21 percent of deaths in low- and middle-income countries. Infectious diseases reveal a glaring difference in health status between rich and poor countries precisely because cost-effective interventions are available to prevent and treat so many of them.

Infectious diseases pose a range of challenges. Some are transmitted directly from one person to another, others through contact with insects or other animals. The human body's immune system readily resists some, whereas others, including auto-immune diseases, attack and weaken the immune system itself. Some present visible and obvious symptoms in a short time, while others are harbored for years before becoming active. Infectious diseases also vary in their virulence, infectiousness, and duration, and the infectious agents of some develop resistance to medications more rapidly than others.

Three communicable diseases, HIV/AIDS, TB, and malaria, account for about 10 percent of the deaths in low- and middle-income

countries. Looking at just these three diseases suggests the immense variety of infectious diseases and demonstrates why strategies for dealing with them must be so different. HIV/AIDS is transmitted primarily through sexual contact, TB through inhaling infectious droplets in the air, and malaria exclusively from mosquito bites. HIV/AIDS attacks the body's immune system, while TB primarily attacks the lungs and malaria impairs the bloodstream and can attack the brain, liver, and other organs. Untreated HIV/AIDS is almost invariably lethal, and TB and malaria can also be fatal.

Another 10 percent of deaths in low- and middle-income countries are attributed to other diseases caused by infectious or communicable agents. For many of these diseases, such as pertussis, tetanus, and diphtheria, vaccines are available and universal coverage is practicable. Nevertheless, millions of children remain unvaccinated and consequently risk illness or death. Infections also cause diarrheal diseases that lead to needless deaths when children are not given proper treatment and die from dehydration.

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HIV/AIDS

HIV has spread worldwide in a short time, but is disproportionately concentrated in low-income countries.[1] In 2004, some 2.9 million deaths attributed to AIDS occurred in the low- and middle-income countries, compared with an estimated 22,000 in the high-income countries. Sub-Saharan Africa is the region most affected by the epidemic. With only 10 percent of the world's population, it nonetheless accounts for 66 percent of all HIV cases and more than 75 percent of AIDS-related deaths. Countries in East Asia and the Pacific do not have prevalence rates as high as those in Sub-Saharan Africa, but their populations are large and prevalence is rising. In 2004, approximately 505,000 AIDS-related deaths occurred in this region, representing about 17 percent of all AIDS-related deaths.

When the disease was first identified in the early 1980s, most of those living with HIV/AIDS were men. The proportion of women affected by the epidemic has steadily grown: by 2004, women and girls accounted for nearly 50 percent of all people living with HIV/AIDS, and in Sub-Saharan Africa, women and girls represent 57 percent of those infected.

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[1] This section is based on *DCP2*, chapters 17 and 18.

HIV is transmitted primarily through sexual intercourse, which accounts for approximately 80 percent of all infections. HIV is also transmitted via exposure to infected blood and from mother to child during childbirth or breastfeeding. Efforts to reverse the epidemic are founded on preventive strategies. For sexual transmission and exposure to infected blood, such measures include educating people about infection and how it is transmitted, encouraging condom use and decreased sexual contact with concurrent partners, screening blood that will be used for transfusions, establishing needle exchanges for injecting drug users, and promoting universal access to clean needles in health care settings. Antiretroviral drugs can be used to halt mother-to-child transmission (MTCT) during birth; perinatal transmission can also be reduced by limiting the duration of breastfeeding and preventing mixed feeding. Epidemic control strategies must also include treatment regimens using antiretroviral therapy (ART), which can extend lives and improve the quality of life for people living with AIDS.

In spite of these efforts, global attempts have not proved sufficient to control the spread of the pandemic or to extend the lives of the majority of those infected. The desired level of success has not yet been achieved for several reasons. Most people who could benefit from available control strategies (including treatment) do not have access to them. Modeling of the epidemic has determined that existing interventions could prevent 63 percent of all infections projected to occur between 2002 and 2010. However, as of now, fewer than one in five people at high risk of infection had access to the most basic prevention services, including condoms, AIDS education, MTCT prevention, voluntary counseling and testing (VCT), and harm reduction programs. Furthermore, care for those infected with HIV has historically been limited in developing country settings, and coverage of ART has been unavailable to most people living in resource-scare countries (notable exceptions include Argentina, Brazil, and Mexico). In short, national programs have lacked the means to undertake a comprehensive approach to HIV/AIDS.

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Another enormous barrier to developing appropriate control strategies is lack of data about how to best implement packages of existing interventions at appropriate scale to maximize the effect of care interventions and to protect the human rights of people affected by the epidemic. During the past decade, governments and NGOs have accumulated limited but valuable experience with preventive and treatment strategies in a wide range of settings, making it possible to identify and

emulate general principles of success. Nevertheless, the epidemic has continued to spread, but much less quickly in countries—including Brazil, Mexico, Senegal, Thailand, and Uganda—where national policies have taken the AIDS epidemic seriously and implemented national programs to control the disease (see box 4.1 and box 4.2). These successful programs had several features in common, including high-level political leadership, active engagement of civil society and religious leaders, population-based programs designed to change social norms, condom promotion, surveillance and control of sexually transmitted infections (STIs), programs to combat stigma and discrimination, and interventions targeting key "bridge" populations.

Perhaps the greatest challenge to effective global control of HIV/AIDS, however, is the lack of reliable evidence to guide the selection of prevention and care interventions for specific areas or populations. In the same way that global policy makers increasingly recognize the need for rigorous evaluation of development programs to ensure their success and eliminate waste, the need for reliable scientific evaluations of AIDS control programs is equally paramount for the same reasons. Lack of data on both the effectiveness and the cost of interventions to guide informed policy-making means that the current allocation of resources for HIV/AIDS prevention is seldom evidence-based.

Nevertheless, in spite of the paucity of rigorous data on effectiveness and costs of various control strategies, action is required. Guidelines

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Box 4.1 Uganda HIV/AIDS Epidemic

Like many countries in Sub-Saharan Africa, Uganda experienced a rapid increase in HIV incidence and a generalization of the epidemic in the late 1980s and early 1990s. By 1991, overall HIV prevalence was 21 percent (Low-Beer and Stoneburner 2003); however, the trajectory of Uganda's epidemic has differed markedly from that of its neighbors. By 2001, overall HIV prevalence had fallen to 5 percent, with dramatic decreases in incidence among key populations, such as soldiers, pregnant women, and young women (USAID 2002). Critical components of Uganda's HIV prevention program include the following:

- strong political support, especially from President Yoweri Museveni
- interventions to empower women and girls
- a strong focus on youths
- active efforts to fight stigma and discrimination
- emphasis on open communication about HIV/AIDS
- engagement of the religious leadership and faith-based organizations
- creation of Africa's first confidential VCT interventions
- emphasis on STI control and prevention.

Source: DCP2, chapter 18, box 18.5.

Box 4.2 Thailand's 100 Percent Condom Program

Thailand's HIV prevalence, fueled primarily by high rates of commercial sex work and low levels of condom use, began to rise rapidly in the late 1980s. Beginning in 1989, the Thai government initiated a nationwide condom distribution and education campaign focusing on commercial sex workers and their clients, to ensure 100 percent condom use in all commercial sex encounters. Elements thought to contribute to the program's success include the following:

- government-mandated 100 percent condom use in commercial sex establishments
- mass condom promotion advertising campaign
- education in commercial sex workplaces
- government-distributed condoms
- STI testing and treatment
- surveillance and tracking of infections to points of origin
- strong political and financial commitment
- active involvement of provincial and local governments.

Despite this unprecedented success, evidence indicates that enforcement of the 100 Percent Condom Program is not as strong today as when it was initially implemented. A recent study in Bangkok found that 89 percent of sex workers used condoms, a decline from 96 percent in 2000 (UNDP 2004).

Source: DCP2, chapter 18, box 18.4.

have been developed for selecting appropriate prevention and treatment strategies based on the epidemiological profile of a country (the characterization of individual epidemics, based on the prevalence of infection in particular key populations, such as sex workers, men who have sex with men, or intravenous drug users, and in the general population) and the unique political, cultural, and economic context.

These categories are listed in table 4.1, "Epidemic Profiles" (with the generalized epidemic category further subdivided into low and high categories). These categories can be used to develop prevention guidelines.

In countries where the prevalence of HIV infection is low, prompt, effective action is still imperative. Data collection is critical to evaluate the progress of the epidemic and guide public policy. Mapping key populations to learn about behaviors associated with infection and tracking the infection rate can provide valuable information for taking appropriate and timely actions. Basic knowledge about how HIV is transmitted and how to obtain and use condoms should be conveyed through limited mass media campaigns and school programs. Such information, education, and communication (IEC) activities should respond to prevailing attitudes toward sexual activity, as these will shape how people perceive educational materials. Public policies

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Table 4.1 Epidemic Profiles

	Highest Prevalence in a key population (sex workers, drug injectors, MSMs)	Prevalence in the general population	WHO Regions
Low level	< 5%	< 1%	Middle East and North Africa
Concentrated	> 5%	< 1%	East Asia and the Pacific, Europe and Central Asia, Latin America and the Caribbean, South Asia
Generalized low	≥ 5%	1–10%	Sub-Saharan Africa
Generalized high	≥ 5%	≥ 10%	Sub-Saharan Africa

Source: UNAIDS 1997.

should also ensure that condoms are readily available through existing channels, such as pharmacies, clinics, and food stores. In addition, health facilities should screen all blood products to be used for transfusions and use sterile needles for all injections, because the rate of virus transmission through such means is high. Furthermore, because the infection spreads so rapidly among intravenous drug users, prevention programs are needed for this key population even where the infection is relatively unknown.

In countries with a concentrated epidemic, additional measures are needed. Programs aimed at preventing transmission among key populations at especially high risk of contracting or transmitting infection are of particular importance, including VCT for individuals and peer-based programs that educate individuals at risk, promote safe behaviors, and distribute condoms. Screening and treatment for STIs should be promoted, and pregnant women who fit a high-risk profile should be offered HIV screening and treatment, both to benefit them and to reduce the likelihood of mother-to-child transmission.

In a generalized low-level epidemic, such as in Tanzania, the emphasis on targeted interventions must be maintained or even strengthened, but interventions for broader populations must also be aggressively implemented. These prevention priorities should include surveillance of STIs, risk behaviors, and HIV infections in the entire population, with a particular focus on young people; extension of mass media IEC beyond basic education; routine voluntary and confidential HIV testing and STI screening and treatment promoted beyond key populations; subsidized and social marketing of condoms and strengthened distribution to ensure universal access; offering of HIV

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screening to all pregnant women; and broadening of peer approaches and targeted IEC to include all populations with higher rates of STIs and risk behavior.

In a generalized high-level epidemic, such as in Botswana and Zimbabwe, the epidemic is a national emergency that calls for the most vigorous possible public action. Routine HIV testing and STI screening and treatment should be promoted universally. Innovative mass strategies for reaching large numbers of people with information, screening, and condoms should be developed—for example, at workplaces, transit venues, political rallies, schools and universities, and military camps, and via youth brigades, workers' unions, and farmers' movements. Free distribution of condoms in all possible venues is imperative. VCT should be promoted for all couples initiating sexual relations. The poverty, education and social status of women, important factors in all epidemics, should be overriding concerns. Priority action should be taken to alter gender norms and reduce the economic, social, and legal restrictions on girls and women.

In addition to these preventive strategies, appropriate strategies for care and treatment are needed. Researchers have developed new therapies for treating HIV/AIDS, some of them easier to administer and less toxic than their predecessors. Treatment is also becoming a reality for many living in resource-constrained countries as the prices of antiretroviral drugs have dropped significantly because of international negotiations with and political pressure on drug companies, the manufacture of generics, and changes to international trade policy to allow compulsory licensing of pharmaceutical products in cases of emergency and to ease importation of generics. As ART becomes more widely available, HIV resistance to a number of antiretroviral drug regimes has emerged, frequently requiring patients to switch from first-line to second-line drugs that are more costly and have more problematic side effects.

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The lives of people infected with HIV/AIDS can also be greatly improved and prolonged through psychosocial support, treatment of opportunistic infections, ART, and palliative care, which includes not only end of life and pain control, but also the psychological, social and spiritual problems of patients and their families. End-of-life care can be provided in numerous settings, ranging from hospitals and hospices to individuals' homes. Many inexpensive measures to treat pain,[2] diarrhea, nausea, and skin conditions[3] in infected individuals are available

[2] See *DCP2*, chapter 52.
[3] See *DCP2*, chapter 37.

and can improve patients' quality of life. Micronutrient supplements, which only cost US$15 a year, can increase body weight, reduce HIV viral load, improve CD4 counts, and reduce opportunistic infections in infected individuals. Despite the wide range of interventions to treat symptoms in people living with HIV/AIDS and their low cost, the need for palliative care for such people is far from being met.

Mass education campaigns can reduce the stigma of HIV infection and enable individuals to remain involved in their communities. Direct psychosocial support can also make a substantial difference. Studies in South Africa and Thailand have demonstrated that access to mental health services and counseling contribute significantly to patients' quality of life and, in some cases, was even associated with reduced mortality.

Diagnosing, treating, and managing life-threatening opportunistic infections (OIs) remains one of the most important aspects of caring for patients with HIV. When HIV begins to weaken patients' immune systems, which tends to occur five to seven years after infection, bacteria, fungi, viruses, and even cancers that would otherwise be held in check become active and damaging. Some infections such as pneumonia, tuberculosis[4] and oral and esophageal candidiasis are relatively easy to diagnose and cost-effective to treat, while others, such as cytomegalovirus, and *Mycobacterium avium* complex, are difficult to diagnose and costly to treat. In the latter case, ART, which reduces the viral load of HIV, thereby improving the immune system, may be more cost-effective than treating the actual infection. Certain OIs are cost-effective to prevent, and simple prophylaxis, such as co-trimoxazole to prevent *Pneumocystis jiroveci* pneumonia, positively influences survival. However, prophylaxis of OIs is underused in low- and middle-income countries, and unfortunately the benefit is short-lived, as it does not halt the relentless erosion of the immune system in infected individuals. The only way to halt the progression of disease in these individuals is to interrupt viral replication through ART.

The prospects for treating people infected with HIV with antiretroviral drugs in low- and middle-income countries have improved, but ART continues to be a costly and complex challenge. The cost of ART in some developing countries has fallen from US$15,000 per year per patient to less than US$150 per year. This lower price brings it within

[4] See *DCP2,* chapter 16.

reach of many middle-income countries, but is still a substantial burden for low-income countries, where annual public health expenditures are often less than US$20 per person per year. WHO and the Joint United Nations Programme on HIV/AIDS estimate that only about 7 percent of the nearly 6 million people in need of treatment receive it and that the number of people requiring ART increases by 8,000 each day.

DCP2 (chapter 18) describes the various regimens available for first-line treatment of HIV/AIDS when drug resistance is not encountered and for second- or third-line therapies when resistance is encountered. The preferred first-line medications in developing countries are dictated by differential efficacy of a number of combinations, as well as pricing and patent concerns. Nearly all highly active ART has some side effects, ranging from the fairly simple to treat (for example, anemia, with iron supplementation) to the more complex (lipodystropy and cardiovascular disease).

To achieve the full benefit of ART, adherence must be nearly perfect (in excess of 90 percent); in cases of suboptimal adherence, resistance can develop in as little as two weeks. Experiences with ART in Haiti and Uganda have shown that programs to implement directly-observed treatment can achieve high drug adherence rates in low-income countries, sometimes higher than in wealthy countries. Nevertheless, high adherence cannot be taken for granted, as studies in India, Mexico, and Senegal have shown poor adherence rates, demonstrating the need for more research on effective intervention to increase adherence.

Confronting the HIV epidemic requires appreciation of the myriad interconnections between technology, economics, politics, and behavior. When political leaders and celebrities endorse public campaigns to raise awareness and normalize public discussion of HIV, then technical and behavioral approaches gain wider acceptance. When technical developments make screening more accurate, cheaper, and easier, then voluntary counseling and testing can be better targeted and more effective. When generic competition reduces the cost of drugs, when international assistance is available for their purchase, and when social programs encourage adherence to drug regimes, then ART becomes more cost-effective and financially feasible.

"Much more research is needed on the cost-effectiveness of interventions to combat HIV/AIDS . . ."

Much more research is needed on the cost-effectiveness of interventions to combat HIV/AIDS, and figures in *DCP2* chapter 18 should be interpreted with the recognition that interventions and their costs are changing rapidly. *DCP2* chapter 2 reports that diagnosing and

treating STIs cost about US$57 per DALY averted, while blood and needle safety programs cost about US$84 per DALY averted. Treatment of OIs costs about US$150 per DALY averted and preventing and treating coinfection with TB costs about US$120 per DALY averted. The cost-effectiveness of ART is difficult to estimate, because it depends on the price of drugs, the prevalence of drug-resistant strains, the costs of diagnostics, and the effectiveness of the health system in delivering the drugs appropriately. While ART is not likely to be as cost-effective as these other interventions, treatment is an important component of an overall national strategy to combat and control HIV and cannot be ignored. Whether it can be effectively extended in hard-hit low-income countries is a major test for the affected countries themselves and for the international community.

The greatest research challenges in care and treatment for developing countries do not revolve around new drug development but rather around how to adapt care and treatment strategies to low-income, low-technology, low-human resource capacity settings in ways that maximize adherence; minimize toxicity, monitoring, and cost; and maximize the prolongation of high-quality life from ART—all without damaging the existing and often fragile health care infrastructures.

The synergy between prevention and treatment must be considered when struggling to allocate limited resources. Although preventing HIV/AIDS is often more cost-effective than treating it, decisions for allocating public funds are complicated by interactions between prevention and treatment. Making treatment available can remove some of the stigma and fear associated with AIDS and make those who are currently infected easier to contact and counsel so as to prevent future transmission. Treatment may also decrease infectiousness. However, there are concerns that the availability of treatment may reduce inhibitions and lead to increased risky behavior (as has been documented in the United States, Canada, and Europe). Poor adherence to treatment may also encourage drug resistance, while increased longevity as a result of treatment could expose more partners. The net effect of the interaction of prevention and treatment is likely to differ from one country to the next, and further study and monitoring of the interrelationships are imperative.

Controlling HIV/AIDS requires strategies and policies that address both prevention and treatment with limited resources. Much has been learned about the disease itself, the specific interventions and strategies,

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the interaction of prevention and treatment, and the larger contextual interconnections. *DCP2* presents the accumulated experience and evaluations conducted to date that permit policy makers to select appropriate strategies.

Tuberculosis

TB remains the second largest cause of death from an infectious agent in the world, even though drugs to cure the disease have been available for 50 years.[5] TB is high on the international public health agenda because of this enormous burden, because of the increase in TB cases associated with HIV infection and drug resistance, and because the internationally recommended TB control strategy known as DOTS has come to be recognized as one of the most cost-effective of all health interventions.

The resurgence of TB in high-income countries in the 1980s surprised public health officials, but effective public responses halted its spread and reduced the incidence in Western and Central Europe, Latin America and the Caribbean, and the Middle East and North Africa. TB has continued to spread and kill, however, wherever social conditions have deteriorated, public health measures are weak, and HIV/AIDS is prevalent. Thus the incidence of TB has been increasing in Eastern Europe, primarily in the former Soviet republics, since the political upheavals at the end of the 1980s and in Sub-Saharan Africa since the mid 1980s. By 2003, an estimated 8.8 million new cases of TB worldwide occurred annually. The highest incidence rate, 345 per 100,000 population per year, is in Sub-Saharan Africa, but the most populous countries of Asia—Bangladesh, China, India, Indonesia, and Pakistan—account for half of the world's cases of TB. Epidemiologists estimate that these upward trends can be reversed if 70 percent of cases are detected and 85 percent of those detected are cured. Reaching this target is necessary if the internationally sanctioned MDG of halving prevalence and death rates by 2015 is to be achieved.[6]

Interventions for controlling TB include preventing infection by means of vaccination, treating latent infections, and treating active disease. About 80 percent of infants worldwide currently receive a live attenuated vaccine, Bacille Calmette-Guérin (BCG). While the vaccine

[5] This section is based on *DCP2*, chapter 16.

[6] In 2000, the Group of Eight nations met in Okinawa, Japan, and informally set targets for reducing TB cases and deaths by 2010. The United Nations MDGs set targets for halving the number of cases and deaths by 2015 relative to their levels in 1990, and WHO is monitoring progress toward these targets.

is protective against meningitis and miliary TB in children, it has low efficacy against pulmonary TB in adults. Vaccination is still cost-effective in places with a high incidence, but is often discontinued in low-incidence countries, because the risk of infection is low and the immune response to the vaccine makes tuberculin skin tests less effective for disease surveillance purposes.

Identifying and treating active cases is currently the primary and most effective measure to control TB. The cornerstone of this approach is the DOTS strategy. DOTS entails diagnosis with a positive sputum sample, short-course treatment with effective case management, regular drug supplies, and systematic monitoring to evaluate outcomes for every patient. Effective case management includes regular supervision by a health worker or community volunteer to assure that the patient is actually taking the medication. The additional cost of monitoring patients and ensuring their adherence to the drug regimen even after symptoms have stopped has proven cost-effective because of its impact on cure rates, consequently both slowing the epidemic and limiting the development of drug resistance.

In all regions except Europe and Central Asia, DOTS costs between US$5 and US$50 per DALY averted. Under certain circumstances, DOTS can save money as well as prevent new cases and deaths. Treating people who have multidrug-resistant strains or are also infected with HIV/AIDS is less cost-effective, because treatment costs are higher and both efficacy and expected benefits are lower. Nevertheless, treating patients with multidrug-resistant TB costs relatively little for the likely gains in healthy life, typically less than US$400 per DALY averted. Treating people with latent infections, that is, people who are infected with TB but are not symptomatic, is the least cost-effective, at US$5,500 to US$26,000 per DALY averted, when TB is endemic (relatively stable) and HIV prevalence is low. However, during a TB epidemic among HIV-infected individuals, providing treatment for latent infection among those who have not yet developed active disease could cost less than US$100 per DALY averted in low-income countries. BCG vaccination is also cost-effective at US$40 to US$170 per DALY averted.

Research could provide a better range of interventions in the future, whether by improving the DOTS approach; tightening the link between private providers, who in many settings are the first to see TB patients, and the public sector; improving the understanding of risk factors; refining diagnostics; or actively seeking cases. Developing a low-cost vaccine that would be more effective than BCG in protecting

adults against pulmonary TB would revolutionize the control of TB by shifting the emphasis from treatment to prevention. Until that time, DOTS or other treatment regimens will play the central role.

Success in controlling TB is closely related to the capacity of local health systems to maintain an effective system for identifying cases, beginning treatment, and assuring adherence. The cost is not unmanageable at the global level. In 2005, the high-burden countries that account for about 80 percent of global cases spent only US$1.2 billion, of which about US$200 million came from international donors. Continued international financial assistance is critical to ensuring that TB control can be maintained in the world's poorest countries, where the challenge of TB control is aligned with the challenge of building and implementing effective public health programs.

Malaria

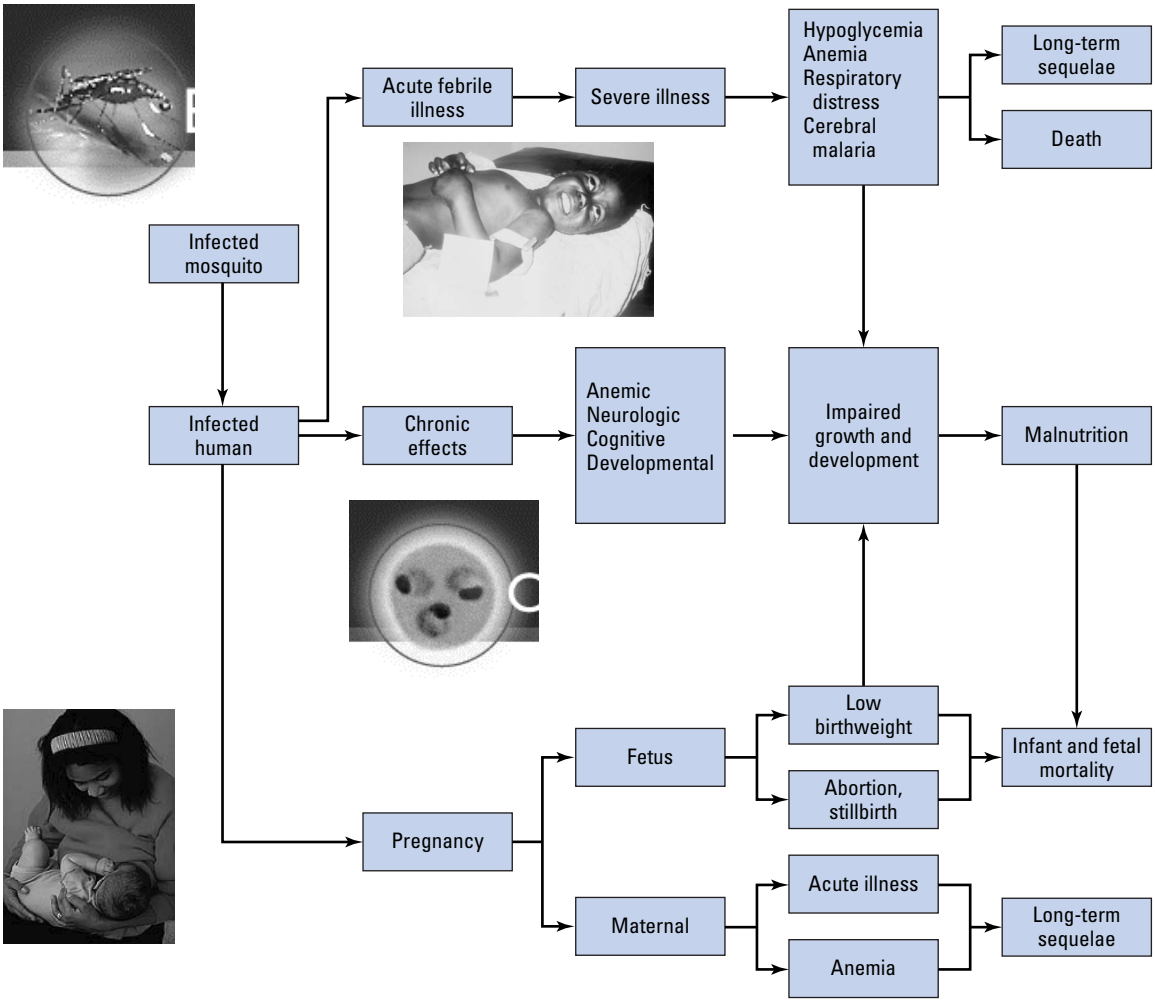
Malaria is directly responsible for about 2 percent of all deaths in the world each year (an estimated 1.2 million deaths) and almost 3 percent of global DALYs.[7] In Sub-Saharan Africa, malaria accounts for a large share of the disease burden, causing about 9 percent of all deaths and 10 percent of all DALYs. The share in other regions is much lower, approximately 1 percent, but still accounts for a significant number of deaths and disabilities.

More than 3 billion people live in areas where malaria is present. Many countries outside Africa have successfully controlled the disease through a combination of preventive measures and treatment strategies. For those countries most afflicted by malaria, the implementation of such programs has been obstructed by the emergence and spread of drug-resistant strains of the parasite and of the vectors and hindered by the weakness of public health infrastructure.

Four species of malaria parasites infect human beings. *Plasmodium vivax* and *P. falciparum* are the most common, and the latter is the most dangerous. Virtually all deaths are caused by *P. falciparum,* which predominates in Haiti, Papua New Guinea, and Sub-Saharan Africa. *P. vivax* is more common in Central America and South Asia. The parasite is carried by mosquitoes, whose ability to reproduce and spread the parasite is strongly influenced by climate. Infestations occur when people are bitten by mosquitoes carrying the parasite. The incidence rate therefore depends on the number of bites per person that transmit the

[7] This section is based on *DCP2,* chapter 21.

Figure 4.1 Malaria Ecology and Burden: Clinical Manifestations



Source: Breman, Alilio, and Mills 2004.

parasite, or the entomological inoculation rate. This ranges from less than 1 bite per person per year in Latin America and Southeast Asia to more than 300 in parts of tropical Africa (figure 4.1).

Correctly treated, uncomplicated malaria has a mortality rate of only 0.1 percent. When the disease is left untreated and affects vital organs, mortality rises steeply. Coma may occur, in which case the likelihood of death is about 20 percent in adults and 15 percent in children. Cerebral malaria can lead to convulsions, neurological damage, and death. Malaria infections also lead to anemia that can be mild, moderate, or severe.

In addition, malaria has a significant impact on other health conditions. Women contracting malaria during pregnancy are more likely to develop anemia and bear children with low birthweight who are then at greater risk of disease, disability, or even death. About 3.7 percent of maternal deaths, or 5,300 deaths per year, are the result of malaria-related conditions. Estimates show that between 190,000 and 934,000 children die each year when malaria contributes to the development of anemia. Being ill with malaria has a variety of other consequences. One study in Africa estimated that 13 to 15 percent of school absenteeism was due to malaria in children (Holding and Kitsao-Wekulo 2004). Studies in The Gambia and Kenya showed that children who were protected by insecticide-treated bednets grew faster than those left unprotected.

Drug use and vector controls are the main antimalaria strategies and interventions for controlling malaria. Others aim at killing mosquitoes, preventing bites, blocking the development of the disease, or treating the disease itself. Environmental methods to kill the mosquitoes that spread malaria include eliminating breeding sites and spraying insecticides. Other efforts to kill mosquitoes or prevent bites include indoor residual spraying and the use of insecticide-treated bednets. A range of drugs work prophylactically and are taken by travelers to malaria-ridden areas and pregnant women. Finding drugs to treat the disease has become more of a challenge because of the emergence of drug-resistant strains of malaria globally.

The effectiveness and feasibility of some interventions depend heavily on whether malarial transmission is unstable (low, erratic, or focal) or stable (frequent, intense, and year round). Where malarial transmission is unstable, protective immunity is not acquired. Where malarial transmission is stable, survivors develop some immunity, and by adulthood, malarial infections are commonly asymptomatic.

In areas with unstable transmission, focused programs that eliminate breeding sites through judicious use of insecticides or through changes in construction practices may be feasible and effective, while in areas with stable transmission, identifying and controlling all potential breeding sites is generally infeasible. In unstable transmission areas, prophylaxis for pregnant women or intermittent preventive therapy will be most effective only during localized temporary epidemics. In stable transmission areas, however, more general use of intermittent preventive therapy can be extremely effective.

Many places have successfully used insecticide-treated nets (ITNs) to reduce transmission. ITNs have been associated with reductions in child

mortality by 18 percent and reductions in malarial episodes by as much as 50 percent in different parts of Africa. The impact of ITNs is related not only to the technical effectiveness of the nets and the duration and efficacy of the insecticide used, but to the social and cultural acceptance of their use and to their affordability. China, Tanzania, and Vietnam have successfully promoted the use of ITNs and achieved substantial control of malaria in many places. Strategies to encourage ITN use have included social marketing in Kenya and Malawi; assisted commercial sector development in Mali, Senegal, and Tanzania; free generalized distribution in Togo; and vouchers for highly subsidized ITNs distributed to pregnant women in Tanzania.

Treatment programs have traditionally relied on relatively inexpensive drugs, principally chloroquine. The key to success is timely detection and treatment. In South Africa, where 83 percent of the population live within 10 kilometers of a health clinic, health professionals play a central role. In countries like Burkina Faso, Ethiopia, and Uganda, where health clinics are much less accessible, reducing mortality and morbidity through treatment has required training mothers and community health workers to dispense treatment based on presumptive diagnoses.

In many areas, strains of the parasite resistant to chloroquine and sulfadoxine-pyrimethamine are now common. Fortunately, researchers have developed a new array of drugs, including artemisinin combination therapy (ACT), which costs more than traditional first-line drugs but is cost-effective in areas where drug-resistant strains are highly prevalent.

Health education and counseling are also significant for controlling malaria. They improve the timeliness of treatment by helping people identify the disease and seek appropriate care. They also promote better and more regular use of ITNs and encourage re-treatment of nets with insecticide as required. In addition, they further improve adherence to treatments, thereby reducing transmission of the parasite and the development of drug resistance.

Most of the malarial interventions available are quite cost-effective. Almost all of them cost less than US$150 per DALY averted and many of them can be implemented at a cost of less than US$10 per DALY. *DCP2* estimates that ITNs cost between US$11 and US$17 per DALY averted, depending on the type of insecticide and the frequency of re-treatments required; indoor residual spraying costs between US$5 and US$18 per DALY averted; and intermittent preventive treatment for pregnant women costs US$13 to US$35 per DALY averted.

Among drug treatments, chloroquine remains the most cost-effective treatment as long as chloroquine resistance is less than about 35 percent. When the prevalence of resistance increases beyond this level, ACT becomes more cost-effective. Sulfadoxine-pyrimethamine can be more cost-effective than chloroquine and ACT, but sulfadoxine-pyrimethamine resistance appears to emerge fairly quickly, and ACT is more cost-effective than sulfadoxine-pyrimethamine when sulfadoxine-pyrimethamine–resistance surpasses approximately 12 percent.

While malaria interventions are cost-effective, their feasibility depends on the availability of financial resources and health infrastructure and local epidemiological conditions. The total cost of a program to promote ITN use for children is about US$2.80 per capita per year, and a program for indoor residual spraying would cost about US$4 per capita per year. While these costs may seem low by many standards, they are prohibitive for countries where malaria is endemic, because the entire public budgets for all health expenditures in such countries range between US$2 and US$10 per capita per year. Breaking the financial constraints for these cost-effective programs requires substantial external assistance.

Research for a vaccine against malaria has long been under way, and should be further encouraged, but developing such a vaccine will require many more years. In the meantime, research is also needed to improve patient care, including easier, cheaper home management and evaluation of alternative delivery systems; prevention, such as intermittent treatment and increased ITN use; technologies, such as insecticides and antiparasitic effector molecules using genomics; and field evaluations of transgenic methods for interrupting malaria transmission.

Such research into new forms of intervention, together with the implementation of known and cost-effective prevention and treatment strategies, will permit successful control of this disease. Since the greatest burden of malaria is concentrated in countries where high transmission rates are combined with limited resources and weak health systems, control of malaria also undoubtedly requires expanded international assistance.

Vaccine-Preventable Diseases

Illnesses for which relatively inexpensive and highly effective vaccines are available account for a significant portion of the disease burden in

developing countries.[8] *DCP2* (chapter 20) discusses TB, diphtheria, tetanus, pertussis, polio, measles, rubella, Hib, hepatitis B, yellow fever, meningococcal disease, and Japanese encephalitis. Vaccines are also available or are being developed for two causes of diarrheal disease: rotavirus and cholera (*DCP2,* chapter 19).

Vaccine-preventable diseases are quite varied. Some vaccine-preventable diseases are bacterial and others are viral; some are found primarily in human beings, while others readily thrive in other species as well; some have high fatality rates, while others are debilitating; some are concentrated in particular regions, while others are widespread; and some are spread through respiratory contact, while others are transmitted through insect bites or contact with infected fecal matter or blood. Despite this variability, vaccine-preventable diseases generally share two important characteristics: people can be infected without signs or symptoms (with the exception of tetanus) and vaccine-induced immunity is generally lifelong (with the exception of pertussis).

Countries that immunize a large share of their populations against these illnesses have eliminated most of the mortality and morbidity associated with them. Regions with lower vaccination coverage continue to have thousands of deaths that would be relatively easy to avert. In 2001, seven vaccine-preventable diseases—measles, hepatitis B, Hib, pertussis, tetanus, yellow fever, and diphtheria—caused more than 2.3 million deaths, primarily in Africa and Asia. Some 80 percent of all deaths from yellow fever occur in Africa, as do 59 percent of deaths from measles, 58 percent of deaths from pertussis, and 41 percent of deaths from tetanus. East Asia and the Pacific faces the largest burden of deaths from hepatitis B and its associated conditions and accounts for 62 percent of all such deaths. South Asia also has high mortality from these diseases, especially tetanus and measles.

In recent decades, a number of global initiatives have sought to expand the coverage of vaccines. Since 1974, WHO's Expanded Program on Immunization (EPI) has provided guidance and support for expanding coverage by standardizing immunization schedules, promoting safe injection technologies, improving the stocking and availability of vaccines, and protecting vaccines' potency through cold chain management. Its Reaching Every District strategy aims at having 80 percent of children in each country receive three doses of diphtheria-pertussis-tetanus vaccine. In 2000, international agencies, bilateral donors, private foundations,

[8] This section is based on *DCP2,* chapters 16, 19, 20, 25, and 27.

NGOs, and pharmaceutical companies collaborated in launching the Global Alliance for Vaccines and Immunization (GAVI). Since that time, GAVI has raised more than US$1.3 billion to strengthen immunization systems; introduce new or underutilized vaccines, such as those for Hib, hepatitis B, and yellow fever; and support safe injection practices. In addition, major research efforts are aimed at developing new vaccines and delivery methods.

Once a vaccine is available, the most important aspect of designing immunization programs is organizing the logistics of vaccinating people. In most developing countries, children are brought to fixed health facilities to receive injections or to take oral vaccines. A substantial number of vaccines are also delivered through outreach, that is, mobile strategies in which health care workers travel to homes and villages. Immunization campaigns that focus on specific antigens are another approach. The most famous immunization campaigns have focused on smallpox, which was declared completely eradicated in 1980, and polio, which is now found in only a handful of countries (*DCP2,* chapter 8).

Vaccination is generally very cost-effective. In the best of cases, vaccines are relatively inexpensive and a single dose leads to lifetime immunity. Whenever such an intervention is available for a widespread and potentially fatal infection, it is likely to be cost-effective.

The mix of delivery strategies, the price of key inputs (the vaccine itself plus labor, transportation, and cold storage), and the overall scale of the program all affect costs. Recurrent costs represent some 80 percent of the costs associated with delivering vaccines through fixed health facilities and 92 percent of the costs of immunization campaigns. The cost per fully immunized child for the six original EPI vaccines—TB, diphtheria, pertussis, tetanus, polio, and measles—is approximately US$20. Investigators estimate that the incremental cost of replacing oral polio vaccine with injectable polio vaccine and adding new antigens for hepatitis B, yellow fever, Hib, measles, rubella, Japanese encephalitis, and meningoccocal disease to existing programs is between US$1 and US$16 per person.

Cost-effectiveness is influenced not only by differences in prices and strategies but also by existing levels of immunization coverage. The cost per death averted from successfully vaccinating children against the six original EPI diseases is US$205 per death averted in South Asia and Sub-Saharan Africa, and US$3,540 per death averted in Europe and Central Asia, with the relatively high coverage rates in the latter region being largely responsible for the difference. Nevertheless, even at

US$3,450 per death averted, vaccination is still highly cost-effective in Europe and Central Asia and compares favorably with many other uses of public money.

Future progress in controlling vaccine-preventable diseases depends on addressing financial and logistical constraints in low-income countries. Even though immunization programs are relatively inexpensive, the financial resources of many low-income countries are so constrained that even inexpensive programs account for substantial shares of available funding. On average, immunization programs account for 6 percent of government health expenditures in developing countries. However, among the world's lowest-income countries, expanding the coverage of traditional antigens, introducing new vaccines, and improving vaccine quality and safety could consume as much as 20 percent of a government's health budget in the absence of substantial foreign assistance.

The financial burden may be reduced through research and development into vaccines that require fewer doses and are cheaper to produce, easier to transport and store, and safer to administer. The development of new delivery strategies could also make a substantial difference to universalizing immunization coverage in low-income countries.

Diarrheal Diseases

Diarrheal disease is one of the top five preventable killers of children under five years old in developing countries.[9] It is most dangerous for the young, with about 90 percent of deaths from diarrhea occurring in small children. However, even though children in developing countries still experience an average of 3.2 episodes of diarrhea each year, the number of deaths appears to have fallen significantly from an estimated 4 million to 6 million deaths in 1979 to an average of 2.6 million per year in the 1990s, with the bulk of the improvement attributable to effective public health interventions (see, for example, the discussion on using ORT in the Arab Republic of Egypt in *DCP2,* chapter 8).

Dozens of viruses, bacteria, protozoa, and helminths cause diarrheal disease. Some of these agents rely almost exclusively on human hosts, whereas others also infect animals. They are generally acquired through fecal-oral transmission, often through the ingestion of contaminated water or unwashed foods. Infection by such agents causes severe bouts of diarrhea, compromises the body's immune system, weakens its ability to draw nourishment from food, and can lead to serious and

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[9] This section is based on *DCP2,* chapters 19 and 41.

rapid dehydration. Severe watery acute diarrhea, caused mostly by rotavirus, enterotoxigenic *Escherichia coli,* and *vibrio cholerae,* causes rapid dehydration and can lead to death. Persistent diarrhea is associated with malnutrition, and even though it accounts for a relatively small share of diarrheal cases, it is three times more likely to be fatal than watery diarrhea. Bloody diarrhea is often associated with intestinal damage and nutritional deterioration, some dehydration, and fevers.

The strategies for reducing the burden of diarrheal disease have not changed substantially since the first edition of *Disease Control Priorities in Developing Countries* (Jamison and others 1993) with the exception of some advances in vaccine technologies. Better and more hygienic feeding practices, immunization, improved water and sanitation, and better case management are the major interventions available for preventing and treating diarrheal disease.

Better and more hygienic feeding starts with programs that promote exclusive breastfeeding during a child's first six months of life. This reduces the likelihood that a child will ingest contaminated food or water during infancy and strengthens the child's immune system through the ingestion of beneficial elements in the mother's milk. Such programs include hospital policies that encourage breastfeeding, counseling and education from peers and health workers, mass media and community education campaigns, and mothers' support groups.[10]

"Some 800,000 lives per year could be saved by more hygienic food storage and preparation and by promoting education, providing good nutrition, and ensuring adequate weight gain."

Better feeding practices once a child is six months old can also be encouraged and effective. Some 800,000 lives per year could be saved by more hygienic food storage and preparation and by promoting education, providing good nutrition, and ensuring adequate weight gain. Researchers have also shown that vitamin A and zinc supplementation have beneficial effects on diarrhea: both are associated with reducing the frequency of severe diarrhea, and zinc supplementation also reduces the incidence of diarrhea.

Rotavirus immunization could prevent some 440,000 deaths per year from this common infection. Developing a safe and effective vaccine for cholera has also proven difficult, and it can usually be controlled through effective public health programs. Only Vietnam routinely deploys cholera vaccine. Other countries have decided that ORT is so

[10] The one important qualification to this approach is concern about mother to child transmission of HIV. The best practice in such cases would be safe replacement feeding for the child of an HIV-positive mother. However, when a mother's HIV status is unknown in countries with high HIV prevalence, a decision has to be made that balances the risks of HIV transmission against the likely benefits of exclusive breastfeeding (*DCP2,* chapter 19).

inexpensive and so effective in preventing deaths from cholera that the costs and risks of immunization are not worthwhile. Measles compromises the immune system and can thereby lead to acute diarrhea. By reducing the occurrence of measles, vaccines could reduce 6 to 26 percent of diarrheal deaths among children under five.

Another way to reduce diarrheal disease is by providing clean water and sanitation, because estimates indicate that contaminated water causes 90 percent of diarrheal cases among children. Nevertheless, *DCP2* (chapter 41, p. 778), notes that "domestic hygiene—particularly food and hand hygiene—is the principal determinant of endemic diarrheal disease rates and not drinking water quality." Rather than quality, the quantity, continuity, and convenience of water services is what reduces the incidence of diarrhea by encouraging more hygienic behavior with regard to personal care and food preparation.

Investment infrastructure for water and sanitation can be expensive relative to other preventive measures and case treatment. Nevertheless, water service has many health benefits beyond reducing diarrheal disease. When water service is associated with better personal hygiene, it interrupts the transmission of skin and eye infections such as trachoma from one person to the next; reduces the incidence of water-based illnesses such as schistosomiasis and guinea worm; and reduces exposure to water-related insect vectors responsible for dengue, malaria, and trypanosomiasis.

The most important benefit people popularly associate with water and sanitation services is greater convenience other than the effects on health. The savings in time and labor can be substantial, given that women and children in particular spend an average of more than an hour each day in rural East Africa and more than two hours each day in several Asian countries obtaining and hauling water. Surveys also show that people in developing countries value improved sanitation less for health reasons than for reasons of comfort, prestige, and safety.

". . . women and children . . . spend an average of more than an hour each day in rural East Africa and more than two hours each day in several Asian countries obtaining and hauling water."

In public policy debates, the health benefits of water and sanitation can best be viewed as an additional benefit conferred by water and sanitation investments that are justified for other reasons. Public health policy still has a role to play in regulating water quality, but public health authorities may be justified in expanding their regulatory authority to consider the quantity and continuity of water service given services' important influence on hygienic behaviors that reduce the incidence of disease.

When diarrhea prevention fails, simple and low-cost techniques are available for managing most cases. ORT, which consists of the oral

". . . where basic water and sanitation are not available, hygiene is poor, and ORT is not widely used, public health interventions aimed at preventing diarrheal diseases are extremely cost-effective."

administration of fluids containing simple salts and sugars, is inexpensive, can be administered by family members with limited training, and is highly effective at reducing the severity of many diarrheal diseases and averting death. After its introduction in the 1980s, many countries rapidly expanded the use of ORT to reach 33 percent of children with diarrhea in the Philippines, 35 percent in Brazil, 50 percent in Egypt, and 81 percent in Mexico. Zinc supplementation for children with diarrheal disease also helps reduce the severity of the illness. For bloody diarrhea, treatment with antimicrobial drugs is indicated, but as with so many other diseases, resistance to first-line antimicrobials is spreading and making these drugs less effective.

In places where basic water and sanitation are not available, hygiene is poor, and ORT is not widely used, public health interventions aimed at preventing diarrheal diseases are extremely cost-effective. Promoting exclusive breastfeeding, measles immunization, ORT, and hygiene costs less than US$5 per DALY averted; promoting better sanitation through public policy costs about US$11 per DALY averted; investing in and maintaining hand pumps for water costs about US$94 per DALY averted; house connections for potable water cost about US$223 per DALY averted; and construction and promotion of basic sanitation facilities costs more than US$270 per DALY averted (*DCP2,* chapter 41).

Factors that encourage the transmission and development of diarrheal diseases are prevalent among people living in poverty. Impoverished people are more likely to be undernourished, to lack clean water and sanitary means of disposing of human waste, to cohabit with animals that harbor and transmit human pathogens, and to lack access to proper means of food storage such as refrigeration. Nevertheless, progress against diarrheal diseases can be made despite poverty. Effective programs can encourage such healthful behaviors as exclusive breastfeeding and personal hygiene; improve environmental conditions through the provision of safe water and sanitation; and train caregivers to recognize symptoms, especially of the more dangerous forms of diarrhea, and apply relatively simple treatments.

". . . progress against diarrheal diseases can be made despite poverty."

MATERNAL AND NEONATAL HEALTH

Along with infectious diseases, maternal and neonatal conditions account for a substantial part of the health gap between rich and poor countries; for example, more than 99 percent of maternal deaths occur

in the developing world. This differential represents the largest single disparity in public health statistics between low-income and high-income countries. Overall, the average lifetime risk of maternal death is 1 in 4,000 in high-income countries, 1 in 61 in middle-income countries, and 1 in 17 in the lowest-income countries.

Death rates during the neonatal period (from birth to 28 days old) also reveal vast differences between rich and poor countries. Only 1 percent of all neonatal deaths occur in high-income countries, where the neonatal mortality rate averages 4 per 1,000 live births. In low-income countries, the average is about 33 per 1,000 live births. The majority of neonatal deaths occur in South Asia because of its sizable population; however, 20 of the countries with the highest neonatal mortality rates are in Sub-Saharan Africa. The highest rates are found in countries where civil wars and political instability have exacerbated poverty, such as Ethiopia, Liberia, and Sierra Leone. In these countries, neonatal mortality rates exceed 50 per 1,000 live births.

International agreements have recognized the importance of reducing maternal and child mortality in low- and middle-income countries. Indeed, two of the eight MDGs address these issues: the fourth goal calls for reducing mortality among children under five by two-thirds and the fifth calls for reducing the maternal mortality ratio by three-fourths, both by 2015. *DCP2* stresses that neonatal deaths account for 40 percent of all deaths of children under five, that the first week of life is when 75 percent of these neonatal deaths occur, and that 50 percent of maternal deaths occur in the first week after childbirth.

The maternal and infant mortality rates in a particular country may reveal more about the state of its health system than any other figures. Achieving low maternal and infant mortality rates requires an integrated and well-functioning health care delivery system that reaches communities with education and counseling, helps people avoid unwanted pregnancies, promotes good nutrition, screens for risks, assists healthy births, and responds to obstetric emergencies effectively.

The health sector alone, however, is unlikely to achieve or sustain maternal health improvements in many countries without concomitant social changes to increase girls' education; reduce gender biases in employment and pay; and confront imbalances in bargaining power within the household that affect women's access to nutrition, domestic workload, and physical safety. Nonetheless, the primary focus of *DCP2* is health sector interventions, and it shows that many cost-effective

". . . more than 99 percent of maternal deaths occur in the developing world. This differential represents the largest single disparity in public health statistics between low-income and high-income countries."

". . . neonatal deaths account for 40 percent of all deaths of children under five, . . ."

interventions to prevent unwanted pregnancies, to make pregnancy and childbirth safer, and to improve neonatal health are available.

"... 210 million pregnancies occur each year, of which 60 million end in an abortion or with the death of the mother or baby."

Family Planning

Globally, an estimated 210 million pregnancies occur each year, of which 60 million end in an abortion or with the death of the mother or baby.[11] Twenty-five percent of all pregnancies, about 52.5 million, end in abortions. More than 500,000 maternal deaths and 4 million neonatal deaths occur annually, but mortality is only one possible negative outcome. Every year, more than 54 million women also suffer from diseases or complications during pregnancy and childbirth. Indeed, conditions associated with maternity represent between 12 and 30 percent of the disease burden among women age 15 to 44 in developing countries. Reproductive health conditions are a major source of the difference in the disease burden between men and women, with women generally leading longer but less healthy lives.

Although pregnancy and childbirth are natural parts of a healthy life, they do entail risks. Women with high blood pressure, heart disease, malaria, anemia, TB, hepatitis, STIs, or HIV/AIDS face substantial risks during pregnancy. Providing appropriate screening, counseling, and contraception services is particularly important for these women. Unwanted pregnancies also have negative consequences. Data are patchy and regional variations are large, but estimates indicate that family planning programs could prevent between 20 and 40 percent of all infant deaths by preventing births among adolescents and older women and permitting intervals of three to five years between pregnancies.

Family planning can reduce unwanted pregnancies and help couples achieve their desired family size. Access to effective contraception is key. The unmet need for contraception is defined as the number of women who wish to avoid pregnancy but are not using contraception. The unmet need for contraception is highest in Sub-Saharan Africa, where an estimated 19.4 percent of women would like to avoid becoming pregnant but are not using any contraceptive. Major obstacles to meeting the need for contraception include lack of knowledge, health concerns, and social disapproval. With some variation across countries and contexts, these factors are more significant than contraceptive supply, availability, or cost. In countries where demand for contraception is mostly satisfied, such as Brazil, Colombia, and Vietnam, there are

"... family planning programs could prevent between 20 and 40 percent of all infant deaths ..."

[11] This section is based on *DCP2,* chapter 57.

lower fertility rates and lower maternal mortality. By contrast, in Sub-Saharan Africa, the share of women with unmet needs sometimes exceeds the share of women who are using contraception.

When women have unwanted pregnancies, many will seek an abortion whether or not it is legal or socially acceptable. In 1995, an estimated 35.5 million abortions were performed in developing countries. Most legal abortions take place in China and elsewhere in Asia, but because of population size and high fertility rates, the bulk of illegal abortions also occur in Asia. In countries where abortion is illegal, it is far riskier. Each year, unsafe abortions cause some 80,000 deaths, accounting for about 13 percent of the disease burden among women of reproductive age. The mortality rate for unsafe abortions ranges from 100 to 600 per 100,000 procedures, compared with a mortality rate for safe abortions of only 0.6 deaths per 100,000 procedures. Many of those who survive an unsafe abortion suffer from disabilities.

"Each year, unsafe abortions cause some 80,000 deaths, accounting for about 13 percent of the disease burden among women of reproductive age."

Contraception for those who wish to avoid a pregnancy can be permanent, long-term, or temporary. Permanent methods involve sterilization for women or men. This is the most popular and effective method of contraception: the 187 million sterilized women worldwide account for 34 percent of all contraceptive practices. Male sterilization by means of vasectomy is a simpler and safer procedure than female sterilization, but is less common. Nevertheless, the estimated 40 to 50 million sterilized men worldwide account for 8 percent of contraceptive practices. Intrauterine devices are the second most common method of contraception, used by 150 million women worldwide. These devices are long-term methods of contraception, as they are inserted in the uterus and prevent pregnancy until they are removed.

Temporary methods include pills, skin implants, and injectable products that alter a woman's hormone cycle to prevent conception. Although these methods are safe and effective, they can also cause irregular bleeding, a problem for women in societies that bar or restrict women from certain activities during menstruation. WHO estimates that 10 to 30 percent of women abandon these contraceptive methods for this reason. Other temporary methods include barriers, the most common of which are condoms. Unlike other forms of contraception, condoms are unique in providing protection against STIs. Male condoms account for about 4 percent of contraceptive use among couples of reproductive age. Strategies for meeting the demand for contraceptive services include education and outreach, subsidies, free distribution, and measures to facilitate or encourage sterilization

"The cost of family planning programs is between US$5,000 and US$35,000 per maternal death averted, between US$1,300 and US$5,000 per infant death averted. . . . "

(box 4.3). Social marketing refers to a variety of strategies that adopt traditional commercial marketing techniques to promote socially beneficial behaviors, products, and services. Typically such programs will promote products, such as condoms, through the mass media. They will also repackage the products and promote them in ways that are effective within a particular culture and context. Sometimes governments will partner with commercial manufacturers to market existing brands. Social marketing programs have expanded contraceptive sales and use in many countries.

The cost of family planning programs is between US$5,000 and US$35,000 per maternal death averted, between US$1,300 and US$5,000 per infant death averted, and after including other health impacts along with averted deaths, between US$30 and US$60 per DALY averted. Interventions appear to be more cost-effective in South Asia and Sub-Saharan Africa than in East Asia and the Pacific. Cost-effectiveness within regions also varies by as much as two orders of magnitude because of differences in fertility rates, risks of mortality, and existing contraceptive prevalence rates.

Overall, the evidence is strong enough to show that family planning is cost-effective, but not strong enough to show which programs are the most cost-effective. The cost of contraception is not usually a major barrier to acceptance. Rather, social mores and health concerns are larger obstacles. Proximity to services and availability of supplies are also relevant. To be effective, programs need to ascertain local obstructions to family planning and then design an appropriate response.

Maternal Conditions

Family planning reduces the disease burden associated with pregnancy by averting unwanted pregnancies.[12] For women who are pregnant, a variety of maternal conditions (understood to occur in the period from conception to 42 days postpartum) can lead to death or disability even though pregnancy and childbirth are not inherently pathological. Providing care during normal, healthy pregnancy and childbirth while ensuring a state of readiness to deal with potential health problems is the goal of safe motherhood programs.

Of the 210 million pregnancies worldwide each year, some 500,000 end in maternal death, and each year more than 54 million women suffer from diseases or complications related to pregnancy and childbirth.

[12] This section is based on *DCP2,* chapter 26.

Box 4.3 The Bangladesh Success Story

In the mid 1970s, an average Bangladeshi woman had more than six children, which—in combination with poor nutrition and lack of access to quality health services—jeopardized the health of both the woman and her children. Beyond the health impact of this situation, high fertility and rapid population growth represented major constraints to the country's economic development and social progress.

The Bangladeshi family planning program, initiated to reach demographic goals, had four elements. The first element was the deployment of young, married women who were hired as outreach workers and trained to conduct home visits with women, offering contraceptive services and information. The number of these outreach workers, referred to as family welfare assistants, eventually reached about 25,000 in the public sector and another 12,000 in NGOs. The program also recruited 4,500 male outreach workers.

Each family welfare assistant was expected to cover three to five villages, or 850 rural women, visiting each household once every two months (Hossain and Phillips 1996). The program's reach was dramatic: family welfare assistants contacted virtually all Bangladeshi women at least once and reached more than one-third every six months. The family welfare assistants were well-recognized village visitors and constituted the main link between the government program and rural women.

A second element of the program was the provision of as wide a range of methods as possible to meet a variety of reproductive needs. This so-called cafeteria approach offered temporary methods as well as sterilization services for individuals with two living children where the youngest child was at least two years old (Rob and Cernada 1992). A well-managed distribution system provided family planning commodities to outreach workers to support their work.

A third element of the program was the family planning clinics established in rural areas to which outreach workers could refer clients who wished to use long-term or permanent methods such as sterilization. Eventually, about 4,000 government facilities and 200 NGO clinics were established.

A fourth element was the information, education, and communication activities that were intended to change norms about family size and provide information about contraceptive options. State-of-the-art use of mass media proved to be particularly effective.

As a result of the program, virtually all women in Bangladesh are aware of modern family planning methods. Contraceptive use by married women increased from 8 percent in the mid 1970s to about 50 percent in 2000, and fertility decreased from more than 6.0 children per woman in 1975 to about 3.3 in 2000. Even though social and economic improvements have played a major role in increasing the demand for contraception, investigators have shown that the provision of services and information has had an independent effect on attitudes and behavior.

The program is estimated to cost about US$100 million to US$150 million per year, with about one-half to two-thirds of the funding coming from external donors. Cost-effectiveness has been estimated at about US$13 to US$18 per birth averted, a standard measure for family planning programs.

Despite its achievements, the Bangladesh family planning program is far from perfect. Since about 1995, declines in fertility have slowed greatly. Many observers have noted opportunities to increase the program's efficiency, to respond more effectively to women's needs, and to better link family planning and health. Nevertheless, Bangladesh has done something few other countries at its level of social and economic development have been able to accomplish: it has complemented efforts to change attitudes about

(Continued on the following page.)

Box 4.3 (*Continued*)

family size with the provision of family planning services to realize a sustained and dramatic decrease in fertility. Although the original motivation for the program was to achieve demographic aims, the government was able to create a program that responded to couples' needs rather than employing coercive measures.

Source: Authors.

Thirteen countries—Afghanistan, Angola, Bangladesh, China, Democratic Republic of Congo, Ethiopia, India, Indonesia, Kenya, Nigeria, Pakistan, Tanzania, and Uganda—account for 70 percent of all maternal deaths because of varying effects of population size, low incomes, and poor health care. Together South Asia and Sub-Saharan Africa account for 74 percent of the global burden of maternal conditions. Complications experienced by mothers also lead directly to many stillbirths and neonatal deaths each year, and several studies have shown that the survival prospects for a baby whose mother dies are low.

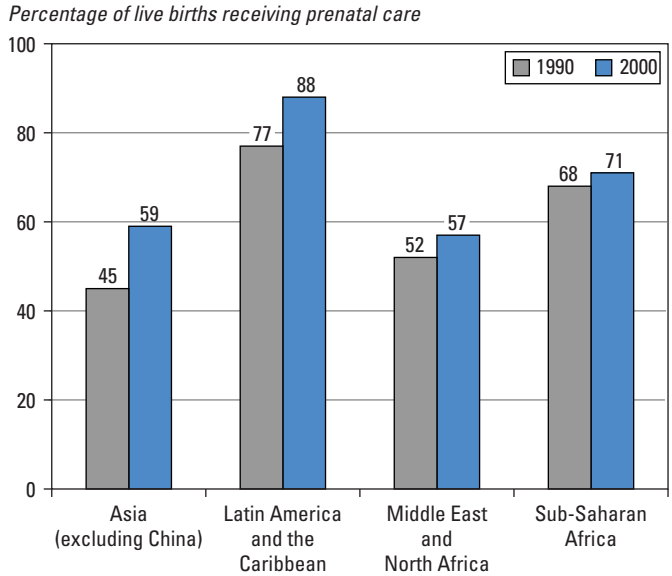
Just five conditions account for three-quarters of maternal deaths: hemorrhage, sepsis, hypertensive disorder, obstructed labor, and unsafe abortion. Many of these conditions can be effectively mitigated through prenatal screening and skilled attendants, and differences in access to such care explain a large part of the regional disparities. For example, fewer than 30 percent of women in the poorest countries have access to skilled birth attendants, compared with more than 98 percent of women in the world's richest countries. Yet progress on this front is frustratingly slow: the regional average for birth attendants in Sub-Saharan Africa has increased by only 0.2 percent per year in the past decade (figure 4.2).

Given the nature of pregnancy and childbirth, no single intervention or approach can fully address their associated disease burden. The only relevant analysis is to compare alternative packages that differ by content and means of distribution. For example, a comprehensive safe motherhood strategy might include the following range of interventions:

"... the regional average for birth attendants in Sub-Saharan Africa has increased by only 0.2 percent per year in the past decade"

- adolescent reproductive health education and services
- community education on safe motherhood and newborn care
- prenatal care and counseling, including nutritional supplements, blood pressure screening, STI screening, treatment for syphilis, breastfeeding advice, tetanus toxoid immunization, and treatment of urinary tract infections
- skilled assistance at delivery

Figure 4.2 Levels of Antenatal Care Coverage, 1990 and 2000



Source: Adapted from WHO 2003.

- care for obstetric complications and emergencies
- postpartum care.

Other than avoiding unwanted pregnancies, averting problems in maternity involves ensuring general good health, especially adequate nutrition. Complications should be prevented or treated if they occur. Interventions can be population-based or personal; can occur during pregnancy, labor and delivery, or postpartum; and may vary by level of care, whether in the home, at a primary health care facility, or in a hospital.

Population-based interventions address two major risk factors: lack of contraception and maternal undernutrition. Undernutrition is manifested in two ways: being underweight and/or stunted and being deficient in micronutrients, principally iron and vitamin A. Because undernutrition is often chronic, long term, and intergenerational, when and how interventions will be most effective is not clear. Efforts can concentrate on women when they are young, during pregnancy, or while they are of reproductive age. Personal interventions cover a wide range of services that share one important characteristic: they need to be integrated in a continuum. That continuum ranges over time, that is, from conception

"... four prenatal visits with a health care provider can be cost-effective. Training for such providers should include how to recognize danger signs and arrange for rapid transfer to an appropriate facility in the event of an emergency ..."

to the postpartum period; over space, encompassing the home, primary health services, and referral for sophisticated care when necessary; and across caregivers, potentially including outreach workers, public health workers, midwives, nurse-attendants, doctors, and surgeons.

Studies have shown that four prenatal visits with a health care provider can be cost-effective. Training for such providers should include how to recognize danger signs and arrange for rapid transfer to an appropriate facility in the event of an emergency, and should also emphasize the use of skilled attendants during childbirth. Other essential elements of prenatal care include prevention and treatment of malaria and anemia, screening and treatment for syphilis, and immunization against tetanus. Nutritional supplementation is often included, but its effectiveness and cost-effectiveness are not conclusively established.

Women and infants run the greatest risks of disability and death during and just after delivery. In this period, skilled attendants with the possibility of referral to a more sophisticated level of care can be critical. The exact definition of skilled attendants is itself a subject of debate, but the MDGs propose the proportion of deliveries attended by a health professional (doctor, nurse, or trained midwife) as a proxy indicator. The rate of skilled attendants at birth varies substantially across developing regions and across socioeconomic groups within countries, ranging from 48 percent in Sub-Saharan Africa to 59 percent in South Asia and 82 percent in Latin America and the Caribbean.

DCP2 evaluates several different proposed packages of care that would improve the coverage and/or the quality of routine maternal care. The three most cost-effective packages, all of which include nutritional supplementation, range in cost from US$77 to US$104 per DALY averted in Sub-Saharan Africa to US$150 per DALY averted in South Asia. Direct costs are higher in Sub-Saharan Africa but are offset by greater effectiveness because of the higher prevalence of maternal problems (box 4.4).

"About 1 million infants die during their first day of life, another 2 million die during the subsequent week, and a further 1 million die before reaching one month of age."

Neonatal Conditions

The risk of death is greatest during the first 28 days of life (neonatal mortality).[13] About 1 million infants die during their first day of life, another 2 million die during the subsequent week, and a further 1 million die before reaching one month of age. These figures are showing little improvement. In 1980, the infant mortality rate (deaths occurring

[13] This section is based on *DCP2,* chapter 27.

Box 4.4 Implementation Case Study: Indonesia

An intense effort by the government of Indonesia to increase the number of births attended by skilled health providers began in 1993 with the introduction of three-year nursing training followed by a year of training in midwifery. From 1996, this was supplemented by a further package of training interventions, including an in-service course; a supervisory system with peer review and continuing education; a maternal and perinatal audit system; and an information, education, and communication strategy aimed at the community.

Data were collected in three districts of South Kalimantan from 1996, before and after the additional package of training, which permitted measurement of its added value. Before the additional training, 90 percent of births took place at home and only 37 percent were attended by a skilled attendant. By 1998–99, 510 midwives were posted in the districts and skilled attendants at delivery had increased to 59 percent. The training package allowed the midwives to gain confidence and skills in the management of obstetric complications, but despite this, the proportion of women admitted to a hospital for a cesarean section declined from 1.7 percent to 1.4 percent. The proportion admitted to hospital with a complication requiring a life-saving intervention also declined from 1.1 percent to 0.7 percent (Ronsmans and others 2001). Significantly more of the midwives who had participated in the training programs were competent in five key skills than those who had not participated.

Walker and others (2002) undertook an economic analysis of the training programs, distinguishing between those programs run for facilities-based midwives and those run for village-based midwives, which included residential internship at district hospitals. They assessed the incremental cost-effectiveness of these programs from the standpoint of the health care provider. Walker and others estimated that the first scheme could be expanded to increase the number of competent midwives based in facilities and villages in South Kalimantan by 1 percent at incremental costs of US$765 and US$1,176, respectively. Replication in other regions would cost between 50 and 60 percent extra.

Source: Authors.

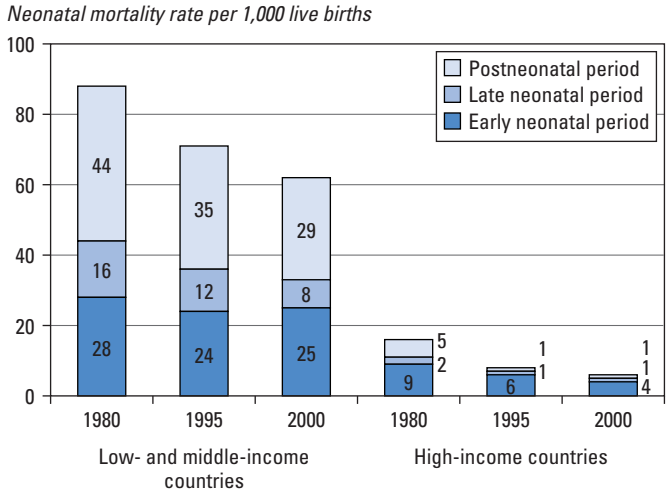
"The MDG of reducing mortality among children under five by two-thirds by 2015 cannot be achieved without addressing mortality in the first 28 days of life."

from birth to one year, including the postneonatal period) in low- and middle-income countries was approximately 88 per 1,000 live births (figure 4.3). Of these, 28 deaths occurred in the early neonatal period, the first week of life. By 2000, the infant mortality rate had fallen to 62 per 1,000 live births; however, almost all the progress was in the late neonatal or postneonatal periods. The rate of early neonatal deaths hardly diminished, declining only to 25 per 1,000 live births in 2000. The MDG of reducing mortality among children under five by two-thirds by 2015 cannot be achieved without addressing mortality in the first 28 days of life.

Appropriate interventions are not highly complex. Up to 40 percent of neonatal deaths could be averted with home- and community-based solutions. Sometimes they require no more than keeping an infant

"Up to 40 percent of neonatal deaths could be averted with home- and community-based solutions."

Figure 4.3 Time Trends in Infant Mortality



Source: Authors' calculations, based on UNICEF, WHO, various years. (*DCP2*, chapter 27, figure 27.2).

warm, breastfeeding regularly, and protecting against infection by means of proper hygiene and/or timely treatment with antibiotics (box 4.5). In many cases appropriate care is available, but gaps occur in the quality or continuity of care. The difference between obtaining care and obtaining adequate care can mean the difference between life and death (boxes 4.6 and 4.7). Delays in access to care are also an important factor contributing to maternal and neonatal deaths. Such delays occur for many different reasons, for example, failure to recognize the need for clinical attention, cultural norms that inhibit the use of medical services, limited physical or financial access to health care facilities, and delays in receiving care once at a facility.

Strategies to improve neonatal survival that focus only on the supply of health care within facilities will therefore fail unless they are integrated

Box 4.5 Successful Strategies for Neonatal Survival

In South Asia and Sub-Saharan Africa, the decline in late neonatal deaths was influenced by the halving of neonatal tetanus deaths that occurred during the 1990s as a result of increased tetanus toxoid protection and clean delivery practices. By 2000, two-thirds of low- and middle-income countries had eliminated neonatal tetanus and an additional 22 countries were nearing this goal.

Source: Adapted from *DCP2*, chapter 27.

Box 4.6 Institutionalizing a Neonatal Resuscitation Program in a Chinese Province

A hospital-based study from China reports baseline surveillance of 1,722 newborns followed by a two-year prospective assessment of 4,751 newborns, while instituting standardized resuscitation guidelines. Previous traditional resuscitation involved infusing central stimulants plus vitamin C and 50 percent glucose; wiping the baby with alcohol; and pressing the philtrum. Health professionals recognized that asphyxia was the leading cause of neonatal death and the second leading cause of infant death nationally. They also recognized that child survival goals could not be met unless asphyxia was addressed. They developed and implemented an evidence-based neonatal resuscitation program, training staff in using the new guidelines. The early neonatal mortality rate fell significantly—by 66 percent, to 3.4 per 1,000.

Source: Adapted from *DCP2,* chapter 27.

Box 4.7 Reducing Newborn Deaths Is Possible in Low-Income Countries

Sri Lanka achieved neonatal mortality of 11 per 1,000 live births in 2000 despite a low GNP per capita of US$800 and less than US$1.50 per capita per year of health spending on maternal and neonatal health. In 1959, maternal and neonatal mortality were high, with a neonatal mortality rate (NMR) of 50 per 1,000 live births, and GNP per capita was US$290. Maternal and infant mortality were halved by 1980 because skilled childbirth care was scaled up and because prenatal, childbirth, and postnatal and newborn care services were provided close to communities and without user charges. The period 1980–2000 saw a further 50 percent reduction in the neonatal mortality rate without the use of intensive care, apart from one unit in the capital.

Malaysia also followed a policy of rapid scale-up of the coverage of skilled care at birth. It trained large numbers of midwives and encouraged collaboration with traditional birth attendants to promote a gradual transition to skilled care over several decades. The NMR is now 6 per 1,000 live births, and 95 percent of women deliver with a skilled attendant.

Source: Adapted from *DCP2,* chapter 27.

with efforts to improve families' practices and to encourage people to make use of health care services. In many cases, this requires appropriate attention to addressing cultural barriers to care, such as training female birth attendants when having male attendants assist at a birth is culturally improper or allowing new mothers and their babies to leave the home in the first weeks of life if an emergency arises, and financial barriers, including service fees and transportation costs.

DCP2 reviews several packages of services that address care of the newborn in the first 28 days of life. Some of these interventions are

"... several packages of services that address care of the newborn in the first 28 days of life. . . . are universally applicable and are feasible even without skilled health care professionals."

"... the best way to improve newborn care is to fill the gap in what should be a continuum of care that includes prenatal services, skilled birth attendance, and follow-up support through the first month of life."

universally applicable and are feasible even without skilled health care professionals. Others require skilled attention, are more complex, or rely on critical medical supplies. Packages of interventions that have a high impact and are feasible in most contexts can be divided into five groups: family care of the newborn, essential newborn care, resuscitation of the newborn, care for low birthweight babies, and emergency care. The first two emphasize maintaining warmth, breastfeeding, and employing hygiene (including proper care of the umbilical cord and hand washing). The latter three require some training, although resuscitation can often be accomplished with simple equipment costing less than US$5.

Creating a separate program for newborn care does not make sense. Rather, the best way to improve newborn care is to fill the gap in what should be a continuum of care that includes prenatal services, skilled birth attendance, and follow-up support through the first month of life. Adding newborn interventions to existing services (*DCP2*, chapter 63) or introducing them along with basic services where these are lacking would be more cost-effective than trying to introduce neonatal interventions in isolation.

Interventions to improve neonatal health and mortality rates are often simple, but require a functioning network of health services capable of providing continuity during the prenatal, birthing, and postpartum periods. Extending these services into marginalized urban and rural areas is the biggest challenge. As a first step, simple approaches can be implemented in even the poorest settings to improve family practices, particularly with regard to cleanliness, warmth, and breastfeeding. Where basic health care services are available, introducing training and equipment for well-tested interventions such as neonatal resuscitation and case management of infections is feasible, but fully addressing the problem of neonatal survival requires plugging the gaps in the continuity of care and strengthening the network of health care services and outreach. This means assuring that professional midwives can attend births and provide follow-up attention, that families learn when to seek health care, and that health care is readily accessible.

"... basic maternal and child health services that would reduce neonatal mortality by 6 percent to as much as 41 percent ..., would cost between US$2 and US$10 per capita."

DCP2 finds that modest expenditures can have a significant effect on neonatal survival. For example, in Sub-Saharan Africa, providing basic maternal and child health services that would reduce neonatal mortality by 6 percent to as much as 41 percent, depending on the preexisting coverage of primary services and the baseline neonatal mortality rate, would cost between US$2 and US$10 per capita. An additional US$0.21 to US$0.95 in spending per capita could reduce neonatal deaths by

as much as 71 percent. Estimates put the specific costs of adding neonatal resuscitation training, equipment, refresher courses, and supervision at less than US$0.02 per capita for an anticipated reduction in neonatal mortality of around 5 percent in Africa and South Asia.

While some resource-poor countries have demonstrated success, the process of building a functional system, especially for clinical care, takes time. Even though the costs appear small relative to spending in middle- and high-income countries, they are large relative to current spending on health care in low-income countries. Spending in India would have to be doubled and in Africa would have to be tripled to provide the basic maternal and child health care package along with the special interventions related to neonatal survival. International funding is therefore necessary to reduce the disease burden in low-income countries associated with neonatal conditions.

"Spending in India would have to be doubled and in Africa would have to be tripled to provide the basic maternal and child health care package along with the special interventions related to neonatal survival."