CMH Working Paper Series

Paper No. WG5:9

Title

The Evidence Base for Interventions to Reduce Under Five Mortality in Low and Middle-income Countries

Authors H. Gelband, S. Stansfield

WHO Focal Points: L. Nemer, P. Jha

Date: July 2001

Abstract

The global decline in child mortality since 1950—from 150/1000 to 40/1000 in the 1990s—is a success story for vaccines, improved living conditions, and access to basic health services. Disturbingly, during the 1990s the decline has slowed, stopped, and even reversed itself in some countries, mainly in sub-Saharan Africa. Of the 10.5 million children under 5 who died in 1999, nearly all—more than 10 million—lived in developing countries. Rates are highest in Africa (150/1,000) followed by South-East Asia (88/1,000). Within countries, children at the bottom of the socioeconomic ladder consistently fare worst.

Diarrhoea, acute respiratory tract infections, measles, malaria, and malnutrition account for at least 70% of all childhood deaths. Children die because they lack access to basic, inexpensive interventions that can prevent nearly all such deaths. Childhood illness and death can be reduced through environmental and general health measures (clean water and food, reduced exposure to indoor cooking smoke, insecticide-treated bednets), vaccination, improved feeding (appropriate complementary feeding of infants and young children, supplementation with iron, vitamin A, zinc) and prompt treatment for bouts of illness. General social measures, particularly better education of women, also promise long-term benefits in child survival. Integrated case management of childhood illness has been identified as among the most cost-effective of all health interventions, at less than \$100 per DALY saved.

Introduction

The death of a child has come to be a very rare event in developed countries, but it remains, if not common, not entirely unexpected in the poorest countries. "Childhood" has come to be

defined in routine statistics as the period up to age 5, and as such, takes in periods of substantially different risk, from the highest risk in the days, weeks and months right after birth, decreasing through to age 5. The earlier deaths—practically speaking, the neonatal deaths (in the first month of life)—are invariably related to events in utero and the birth process itself, so both the causes and the interventions to prevent them are related more to pregnancy and childbirth than childhood itself.

One month after birth is not a biological cutoff point, and deaths occurring later, though limited largely to the infant period (up to 1 year) may also be the consequences of gestation and birth (deaths related to some congenital anomalies may occur years later, however). But for the most part, babies who survive the first month of life are thereafter vulnerable more to the external world than to conditions of gestation and the birth process. Infection and poor nutrition, which are strongly influenced by socioeconomic and environmental factors, are the greatest hazards.

This paper focuses on the epidemiology and management of diseases of childhood, which are largely preventable and treatable. Other papers in this series are complementary to this one, covering specific conditions and types of interventions that affect children. The topics listed under the titles are, therefore, covered only briefly or not at all in this paper.

- A. Reducing the Toll of Pregnancy and Childbirth for Mothers and Neonates
 - Neonatal period (birth through one month)
- B. The Evidence Base for Interventions to Reduce Malnutrition in Children Under Five and School-age Children in Low and Middle-Income Countries

- Malnutrition, infant feeding, micronutrient supplementation (iron, vitamin A, zinc), multi-faceted nutrition interventions
- C. The Evidence Base for Interventions to Reduce Mortality from Vaccine-Preventable Diseases in Low and Middle-Income Countries
 - Vaccine-preventable diseases, new vaccines
- D. The Evidence Base for Interventions to Reduce Malaria Mortality in Low and Middle-Income Countries
 - o Issues in malaria management
- E. Indoor Air Pollution
 - Respiratory effects and interventions

This paper is organized in the following sections:

- A. Epidemiology
- B. Causes of morbidity and mortality in children under five
- C. Interventions to reduce morbidity and mortality in children under five
- D. Specific Measures in Case Management for ARI, Diarrhoea, and Malaria
- E. Strategies for delivering health care to poor children
- F. Cost-effectiveness of interventions to reduce childhood morbidity and mortality
- G. Conclusions

Section A: Epidemiology

1. Scope of the Problem

More than 10 million of the 10.5 million children under age five who died in 1999 lived in developing countries. By far the highest rate, at 150 per 1,000, is in the African region, followed by 88 per 1,000 in the South-East Asian region, each of which accounts for about one-sixth of the deaths worldwide.

(Table 1 about here)

The overall distribution of deaths by area and by country are indicators of where interventions might be most usefully targeted. But just as the risk of death in childhood varies among regions and countries—the poorest ones usually having highest risks—the situation is similar *within* countries. The poorest children in a poor country are worse off than those better off. Figure 1 (2) shows the range of under-5 mortality among several countries, which demonstrates that per capita income alone does not predict child mortality rates. It also clearly demonstrates that within each country, children in the poorest one-fifth of the population have higher mortality rates (top bar of each line) than either the country average (box) or the richest one-fifth (bottom bar of each line). The patterns are interesting for their differences as well as their similarities. While every country has an under-5 mortality gap between rich and poor, the magnitude of the gap varies considerably.

2. Trends in Child Mortality

Child mortality rates in low and middle income countries have been declining since 1950, from a global median of about 150 per 1000 live births, to 40 per 1000 in the 1990s (1). But the decline has been quite heterogeneous among countries, but has generally been downward, in both developed and developing countries. During the 1990s, the decline slowed, stopped, and even reversed itself in some countries, mainly in sub-Saharan Africa (3).

The African region had the smallest decline (about 42%) in child mortality, from about 264 deaths per 1000 live births in the late 1950s to about 152 in the late 1990s. In other regions, the decline ranged from 60 to 72%. The rates of decline vary substantially by country, with only half the countries achieving at least a 20% decline: in the late 1990s, the low rate was 21 per 1000 in Mauritius to a high of 334 per 1000 in Niger. Africa also has greatest number of countries (5) in which child mortality increased between 1980 and 1999 (1).

In the South-East Asia region, child mortality declined from about 222 per 1000 live births in the late 1950s to about 90 per 1000 in the late 1990s, with some narrowing of the differentials among countries. Only in North Korea did the rate increase, and in Myanmar it changed little.

The Western Pacific region fared very well, with a 70% overall reduction (from about 154 per 1000 in the late 1950s to about 48 in the late 1990s), and two countries (Mongolia, where rates were stagnant; and Papua New Guinea, where they increased) failing to achieve major gains. The Eastern Mediterranean region had a similar overall large decrease, but with a wide range

among countries throughout the period. In the late 1990s, the lowest rate was 9 per 1000 in Cyprus and the highest, 271 in Afghanistan.

All the countries of the Americas achieved a greater than 20% decline in child mortality between the late 1950s and 1990s, and an overall reduction of 70%. The European region began the period with the lowest rate—63 per 1000—which dropped to 19 per 1000 by the late 1990s. Intercountry differentials also decreased, but several countries in eastern Europe had relatively smaller gains. In the Americas, the infant mortality differential between the United States and Canada on one hand and most of the Latin American countries has been growing (4).

The worldwide declines in child mortality have been greatest beyond the neonatal period. In 1995, an estimated 44% of deaths among children in developing countries occurred in the perinatal and neonatal periods (Table 2). The biggest contributor to the decline in child mortality is the remarkable decline in deaths from diarrhoea. While still claiming 1.5 million lives each year, according to the best estimate for 1999 (6), this is down from an estimated 4.6 million in 1980, and 3.3 million in 1990.

In this paper, the focus is on deaths beyond the neonatal period that are not covered in other disease-specific papers for this report. Those topics that are covered elsewhere are: vaccine-preventable diseases (measles being the most important to this age group, but including all EPI vaccines), malaria, HIV/AIDS, and tuberculosis.

Section B: Causes of morbidity and mortality in children under five

The direct causes of most childhood deaths are infectious diseases, with deaths occurring because they were neither prevented nor successfully treated, though nearly all could be. These deaths can be seen within the context that Mosley and Chen (7) described as "proximal" determinants of child survival: maternal factors, malnutrition, environmental contamination, injury, and personal illness control. Overarching the proximal factors are the "distal" socioeconomic factors, such as education and income, that affect all aspects of life important to health.

Children die in substantial numbers from just a few causes, once they have survived the first month of life. Not uncommonly, very sick children—those at highest risk of death—have more than one of these acute conditions, often have evidence of acute or chronic malnutrition (Table 3) (as well as having missed key preventive measures, particularly immunizations). The specific infectious diseases that take the greatest toll are diarrhoea, ARI, measles and malaria. Malnutrition claims lives directly, and also contributes to deaths from infectious diseases. Malnutrition includes both undernutrition, denoted by poor growth (measured as stunting) as well as micronutrient deficiencies, the most important being iron, vitamin A, and zinc.

1. Direct Causes

(i) Acute Respiratory Tract Infections (ARIs)

Infections of the respiratory tract—overwhelmingly pneumonia—are directly responsible for 19% of deaths of children under 5, but are also associated with a proportion of the death toll from measles, pertussis, and HIV. For 1990, the estimate was 2.7 million deaths directly from

acute lower respiratory tract infections (ALRI; nearly all from pneumonia), and an additional 1.1 million from these other causes (Table 4) (9).

Most cases of severe pneumonia among children in developing countries are caused by bacteria, about 65-75% due to *S. pneumoniae or H. influenzae* and another 10% due to *S. aureus* (10,11) (in contrast to developed countries, where most pneumonias among children are viral). Not uncommonly, more than one pathogen may be involved, however. The younger the child, the greater the risk of dying from pneumonia, with risk decreasing up to age 5. This contrasts with the risk of death from diarrhoea, which is more constant throughout the period (Table 5).

Many factors—most modifiable—are related to the risk of children contracting and dying from pneumonia and other ARIs (9). Low birth weight remains an important risk factor, as does poor nutrition; indoor environmental conditions, e.g., crowding, smoke from cooking and environmental tobacco smoke, also raise the risks of severe pneumonia. Once a child is ill, death can come very rapidly, so lack of recognition by the mother of the severity of the situation, and delays or difficulties in getting care can mean the difference between survival and death, which often occurs from 2-3 days after the onset of symptoms.

(ii) Diarrhoea

Despite the impressive gains over the last two decades, diarrhoea remains one of the most common illnesses of children and a major cause of infant and childhood mortality in developing countries. Contaminated food and water are the source of most infectious agents that cause diarrhoea in children. Infants are often infected through complementary foods, after a period of exclusive breastfeeding, a time when they appear to be particularly susceptible. In general, infants and children are more susceptible than adults to these pathogens, which may cause acute, watery and bloody diarrhoea (as well as other specific diseases).

The major categories of diarrhoea have different implications for management. Diarrhoea is defined generally as passage of loose or watery stools, usually increased in frequency (usually at least three times per day):

- Acute watery diarrhoea (including cholera) is the most common form in children, lasting hours or several days, and risking dehydration and weight loss.
- Acute bloody diarrhoea (dysentery), often caused by *Shigella* risks intestinal damage, sepsis and malnutrition, as well as dehydration.
- Persistent diarrhoea, usually defined as lasting at least 14 days, risks malnutrition and serious non-intestinal infection, as well as dehydration.
- Diarrhoea with severe malnutrition (marasmus or kwashiorkor) risks severe systemic infection, dehydration, heart failure and vitamin and mineral deficiency.

A wide variety of bacterial, viral, and protozoal pathogens can cause severe diarrhoea. Rotavirus is responsible for about one-third of all diarrhoea-related deaths. Enteropathogenic subtypes of *E. coli* are common causes of episodes, and other common pathogens are the bacteria *Shigella spp., Salmonella spp., Vibrio Cholerae* and *Campylobacter jejuni*. Sources of infection range from nightsoil, polluted water, flies, pests, domestic animals, unclean utensils and pots, and dirty hands.

A much larger number of children are adversely affected by the morbidity and chronic effects of diarrhoea than those who die from it. Studies from around the world (e.g., in the Gambia, 12,13,14), beginning in the 1970s and 1980s, have provided evidence of growth faltering, weight loss, stunting and impaired physical growth associated with repeated bouts of diarrhoea (in contrast to ARIs, which do not have such pronounced effects).

Low socioeconomic status and its concomitants are risk factors for diarrhoeal morbidity and mortality in children. Many studies have found that risk increases with low family income, crowded and unclean living conditions, low levels of maternal education, low occupational status of the household head, etc. Nutrition also plays an independent role in diarrhoeal disease. Breastfeeding—specifically, exclusive breastfeeding—has a strong protective effect against diarrhoeal incidence, severity and mortality. Malnourished children may have more frequent episodes of diarrhoea. Low birthweight may also play a role, but the evidence is less clear (reviewed in [15]).

(iii) Malaria

Worldwide, malaria accounts for 1.1 to 2.7 million deaths (16) of which 1 million are children under age five in sub-Saharan Africa. Most occur in very young children before they acquire immunity. These deaths, mostly from cerebral malaria and anemia (which leads to congestive heart failure), make up about 25% of child mortality in sub-Saharan Africa. Case fatality rates of 10-30% are reported in children referred to hospital with severe malaria, but these rates are likely to be higher in rural and remote areas where patients have restricted access to adequate treatment. At least in some places, even children who are treated within the health care system may not receive a full course of treatment (because of cost or lack of communication to the mother of the importance of completing the course), and may not receive curative treatment with a second-line drug if the first-line one is not effective (17).

Malaria has always been high on the agenda of WHO and other organizations interested in global health. Over the past few years, WHO and a range of partners have dramatically stepped up efforts to develop tools and approaches to controlling malaria all over the world, but with a focus on sub-Saharan Africa, where the problem is of greatest magnitude. These projects (including "Roll Back Malaria" and the Multilateral Initiative on Malaria) are described in detail in Meek and colleagues CMH paper on malaria.

(iv) Measles

Measles could be eliminated entirely by immunization of the world's children. Despite substantial progress toward that goal, however, more than 40 million children still contract measles each year, and about 750,000 die from it. Most deaths follow complications that occur in severe measles. The three major problems associated with higher mortality rates in developing countries, and which account for nearly all measles hospitalizations, are pneumonia, diarrhoea, and laryngotracheobronchitis (croup). Survivors may suffer permanent damage from measles-related blindness, chronic lung disease, and malnutrition (18).

Poor children are particularly susceptible to developing severe measles because they are more likely to be subject to the factors that increase risk, which include:

- overcrowding, which intensifies exposure
- malnutrition
- congenital or acquired immunodeficiency syndromes (including HIV infection)
- vitamin A deficiency
- lack of adequate health care in early stages

2. Indirect Causes

(i) Malnutrition

Childhood malnutrition results from a complex of interrelated conditions and causes, beginning in utero. The types and amounts of food available are obvious contributors, but so are bouts of infectious disease, helminth infections, and environmental conditions (particularly lack of clean water). Levels of malnutrition are correlated with national socioeconomic factors, such as gross national product and female literacy, but the relationship with national health expenditures varies among regions (19,20).

In the early 1990s, Pelletier and colleagues (21) provided the best quantitative estimate of an association long observed: they determined that malnutrition contributes to about half of all deaths among children, most of which are due to infectious diseases. The risk of death is increased even with mild and moderate malnutrition, and not just the most severe cases. The general association between malnutrition and deaths from infectious diseases is well accepted, particularly in the case of childhood diarrhea and acute respiratory illnesses. It should also be noted that strong evidence links poor growth to delayed mental development (22,23) as well as poor school performance and intellectual achievement (24,25).

To better understand the general relationship, work has begun to elucidate the importance of malnutrition to specific, major causes of childhood death: diarrhea, acute respiratory illness, malaria and measles. An exhaustive analysis of the literature focusing on these four conditions provides a more detailed picture, but also points out large gaps in the evidence base (26). As expected, studies varied in quality and design. The measures used to describe nutritional status were largely anthropometric, which do not provide much insight into the nature of the malnutrition: whether acute or chronic, due to general lack of calories, or more specifically, of protein or micronutrients, or associated with past infectious disease. Nonetheless, this study provides a baseline of the available information for these four conditions.

The peak age for growth faltering to become manifest is before age two. This is also the period of highest diarrhoea incidence and deficiencies of certain micronutrients. If a child experiences stunting before age two, it is very difficult to reverse later on (27). Inadequate complementary feeding (the addition of foods starting usually at around 6 months, in addition to breastfeeding) is often the most important factor leading to stunting. Foods provided may be qualitatively poor (i.e., low energy and nutrient density), not supplied in sufficient quantity, and/or lacking in essential micronutrients, particularly, iron, vitamin A, and zinc (28).

Globally, nutrition appears to be improving. The prevalence of stunting among children (defined as at least 2 standard deviations below the mean in height-for-age) has fallen from an estimated 47% in 1980 to an estimated 33% in 2000 (29), but gains are not being made everywhere (Table 6), and in any event, one-third of world's children in developing countries—an estimated 181 million—still suffer the effects of malnutrition. In fact, the prevalence of stunting has increased in Eastern Africa over this period, from 46.5% to 48.1%, and has changed little in Western Africa (34.9% in 2000). The prevalence of stunting is highest in Asia (which also has the largest population, so the largest number of such children, with the largest number in India), where steady progress is being made. Current Asia-wide rates are about the same as for Africa (34.4% vs. 35.2%, respectively), but fell from over 50% in 1980. Not unexpectedly, the countries in each region do not all follow the regional pattern (e.g., prevalence increased in Venezuela while the all-South America rate decreased), but most do.

Section C. Interventions to reduce morbidity and mortality in children under five

Serious childhood health problems are, in the broadest sense, almost entirely "environmental" the physical as well as the economic and social environment. The magnitude of child morbidity and mortality is strongly correlated with poverty, both among countries and among the socioeconomic strata within countries. In high income countries, the dramatic decline in childhood mortality is attributable both to a decline in the incidence of *severe* diarrhoea and to better treatment of cases. In contrast, the substantial (though smaller) declines in low and middle income countries are largely attributable to improved case management, particularly the widespread use of oral rehydration therapy for diarrhoea. In the case of ARI, better treatment in high-income countries most likely does account for the fact that so few such children die compared with ARI mortality in poor countries. The additional problems of malaria and widespread malnutrition also must be addressed where they are prevalent in low and middle income countries. Further progress can be made both in preventing serious illness and increasing the reach of effective case management, employing interventions within and outside the health sector.

1. Interventions Largely Outside the Health Sector (Non-Clinical)

Three broad categories of interventions outside the health sector can reduce the incidence of and mortality from childhood infectious diseases: environmental improvements, improved nutrition, and maternal education. Environmental improvements can reduce transmission of the bacteria, viruses, and parasites that cause most childhood illnesses.

(i) Environmental Measures

(a) Water and Sanitation

Child mortality and morbidity, and diarrhoea in particular, have been strongly associated with household water and sanitation in countries in all parts of the world. An early major review of 67 studies in 28 countries (30) and an additional 17 studies reviewed by the same authors a few years later (31) found a median reduction in diarrhoeal morbidity of 20-26% with improved water and sanitation. More recent studies have reported similar results (32).

Esrey (33) carried out a more detailed analysis to determine, to the extent possible, the independent effects of water and sanitation services, and to distinguish among levels of improvement in both. Outcome measures were diarrhoeal morbidity and growth (height-for-age, weight-for-age, and weight-for-height) in children. Sufficiently detailed data were available for eight countries from the Demographic and Health Surveys of the late 1980s: Burundi, Ghana, Togo, and Uganda in Sub-Saharan Africa; and Bolivia and Guatemala in the Americas. Water

was categorized as unimproved, improved public water (intermediate), and on the premises (optimal). Sanitation was categorized as unimproved, latrines (intermediate), and flush toilets or water-seal latrines (optimal). Data for urban and rural areas were analyzed separately.

Health benefits were more pronounced for sanitation than for water, and more so in urban than in rural areas. Improvements in sanitation resulted in decreased diarrhoeal morbidity and improved anthropometry regardless of the type of water supply (i.e., even unimproved water). Improvements in water alone (i.e., no improvement in sanitation) did not appear to improve health outcomes significantly. Improvements in water and sanitation together were synergistic, with impacts greater than either alone, particularly in rural areas. Measurable effects from water were generally confined to optimal water.

From this study, it was not possible to determine whether the effects of optimal water were mainly due to quality or quantity of water, but other studies have suggested a greater effect of quantity of water over quality (31). The implication is that personal and domestic hygiene is enhanced by having plentiful water for cleaning. A beneficial effect of water quality on food hygiene cannot be discounted, but direct evidence from these studies is lacking.

Many of the same studies included in the earlier reviews by Esrey and colleagues looked at impacts on water-associated diseases other than diarrhoea (31). In reviewing these other outcomes measures, Esrey and colleagues concluded that elements of improved water and sanitation also reduced rates of morbidity and severity of ascariasis, dracunculiasis, schistosomiasis, and trachoma (but not hookworm). The median reduction in overall childhood mortality (including from diarrhoea) of the studies categorized as "rigorous" by the authors was 55% (although this may be an overestimate due to economic and social co-factors). Access to clean water and sanitation alone do not guarantee a health benefit. Other factors such as overcrowding, which enhances the spread of pathogens and infections, may also reduce the positive effects of clean water and sanitation on child mortality. And the importance of household practices that involve water and sanitation must be appreciated by mothers, in particular (discussed below).

(b) Improved Family/Household Practices

The health improvements seen with better water supply—in particular, increased quantities of water—have been ascribed to better hygiene made easier by water availability. Since the mid-1980s, a number of intervention studies have been carried out to encourage the types of behaviors that might lead to better health, with largely positive results. Ten studies of improved hygiene practices were identified in a review by Huttly and colleagues (32), and all resulted in reduced diarrhoeal morbidity in children (Table 7). Five studies (in the United States, Burma, Bangladesh, India, and Indonesia) encouraged handwashing, and resulted in a median 35% reduction in diarrhoeal morbidity. Three projects integrated water supply, sanitation, and hygiene education programs and the other included a range of behaviors, including handwashing. These latter five studies resulted in reductions in diarrhoeal morbidity of 11 to 40%.

The studies, while small in number, do demonstrate that changes in behavior can be encouraged and that they result in expected reductions in childhood diarrhoea. This evidence forms part of the basis for incorporation of household hygiene behaviors in IMCI (see below). Household use of insecticide Treated Mosquito Nets (ITNs) have emerged over the last 2 decades as a very promising intervention for reducing the risk of malaria infection and death. Intervention trials have been conducted in a number of countries representing a range of transmission intensities. A systematic review (34) of 18 trials (11 of which were in Africa) concluded that, under trial conditions, ITNs reduce overall mortality by about a fifth in Africa (range from 14% to 29%) and that for every 1,000 children under age 5 protected, about 6 lives can be saved per year in the. ITNs also reduce substantially clinical episodes of mild malaria from both *Plasmodium falciparum* and *P. vivax* infections, with a 50% reduction in episodes under most conditions. Actual protection from malaria deaths and episodes outside of field trials has been has, not surprisingly, fallen short of the trial results, but this is an active area of operational research, with potential for improvement.

(c) Reduced Exposure to Burning Biomass

Exposure to burning biomass can be reduced through the use of cleaner fuels, improved stoves, improved ventilation, and behavior change (i.e., keeping children away from cooking areas). The extent to which these are practicable are largely unknown, however. Past efforts have been made to develop cleaner-burning stoves, but these do not appear to have had a worldwide impact.

(ii) Maternal Education

Measures of women's education and of child health are correlated, particularly in developing countries, but the precise nature of the relationship is not obvious. In nearly all cases, education is a proxy for socioeconomic status, so the other factors that go along with greater prosperity also may contribute to better child health. But education may have an independent effect. According to the 1993 World Development Report (35) education increases a woman's ability create healthy households, to benefit from health information, and to make good use of health services. Other child health advantages of better educated women are delay in marriage, better spacing of pregnancies, greater use of antenatal care in pregnancy, and skilled attendance at deliveries, better domestic hygiene, better nutrition, and higher immunization rates for children (see Box *Impact of Maternal Education on Child Mortality*).

Box: Impact of Maternal Education on Child Mortality

Many researchers acknowledge the strong correlation between levels of education among females and child health. The extent to which the relationship is causal is an area of some disagreement, however, because of the strong correlation of female education with other socioeconomic variables. The 1993 World Development Report stated that education increases a woman's ability to create healthy households, to benefit from health information, and make good use of health services. It may also increase personal income, enabling them to live healthier lives (35). Increased levels of maternal education may lead to delays in marriage and childbearing, diminishing risks to child health, and greater use of antenatal care and assisted deliveries, better domestic hygiene, better child nutrition, and higher child immunization rates.

Caldwell (36) found that higher levels of education bring about 1) a reduced sense of fatalism for children's survival; 2) increased sense of control over distribution of household resources; and 3) increased ability to take positions different from those advocated by mothers-in-law or other authority figures. A study in Nigeria showed that a higher proportions of women with secondary or higher education used effective health services (87% immunization during pregnancy vs. 63% for women with no education; 82% of pregnancies were delivered by trained health personnel vs. 47% for women with no education) (37).

Examining data from 22 countries, Desai and colleagues (38) found the relationship between maternal education and child health weaker than reported elsewhere. Statistically significant effects of mothers' primary education on child health were found in 11 countries and, of mothers' secondary education, in 15 countries. The effect on infant mortality and child heightfor-age was attenuated when husbands' education and access to piped water and toilets were taken into account.

In Uttar Pradesh, India, neonatal mortality was significantly higher among children of illiterate women compared with educated women. Adjusting for socioeconomic factors reduced the effect of maternal education but it still remained significant. Post-neonatal mortality for children of illiterate mothers was nearly twice that of children born to mothers who had at least middle school education (39).

Van Ginneken and colleagues (40) found relatively little effect of maternal education on prevention of post-neonatal pneumonia in 11 countries (based on DHS surveys, 1986-88), but they did find that maternal education was associated with more appropriate responses when pneumonia occurred. In a 17-country study, Bicego and colleagues (41) found levels of maternal education were associated with the risk of death for children under age two, and that the effect was greatest in the post-neonatal period. Adjusting for household economic factors strongly attenuated, but did not completely neutralize the effect of maternal education.

It has been suggested that the economic advantages resulting from female education account for roughly half of the strength of the education-mortality relationship, and the studies reviewed here seem consistent with that. Overall, however, they also suggest substantial benefits to children beyond the purely economic advantages that better education may bring.

2. Health Sector Interventions

There are powerful interventions to prevent and treat serious childhood illnesses and reduce mortality that can be delivered largely through a primary health care system. On the prevention side are immunization, improved feeding (not entirely a "health sector" intervention, but covered here), and micronutrient supplementation. Treatment of ARIs, diarrhoea, measles, and malaria through basic case management has the potential to save the lives of nearly all children who have adequate access to services.

(i) Immunization

WHO estimates that an additional 1.6 million deaths in low and middle-income countries from the 'childhood cluster' of diseases are preventable with existing vaccines (measles, tetanus, pertussis, diphtheria, polio) (Please refer to vaccines paper for a more in-depth discussion). Most of these deaths occur among children under age 5, with measles causing about half of all deaths. Newer vaccines can increase the number of preventable deaths considerably. Most childhood pneumonia is caused by *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) (42). Use of the Hib vaccine is being promoted and is spreading, and vaccines for infants combining protection against up to 9 forms of pneumococcus are currently undergoing clinical trials.

Rotavirus causes severe diarrhoea and an estimated 600,000 deaths per year (out of about 1.8 million) and shigella, another significant fraction (15). A rotavirus vaccine has been licensed but was withdrawn after potentially serious adverse effects were detected. Other rotavirus vaccines

are in the pipeline and may be ready for clinical evaluation by the end of 2001 and in efficacy trials by 2003. Two shigella vaccines are in development and a phase III trial of one in a developing country is anticipated by 2003.

The Global Alliance for Vaccines and Immunization (43) estimates that a concerted effort to introduce Hib and pneumococcal conjugate vaccines could reduce associated mortality by 10% by 2005, saving 300,000 lives a year. By year 2010, 800,000 lives per year could be saved using these vaccines. Introducing new vaccines against diarrhoea, (rotavirus and shigella) would reduce mortality in children by 250,000 per year by 2005. Six hundred thousand lives per year could be saved by 2010.

(ii) Breastfeeding

There has been little debate about the benefits of early and exclusive breastfeeding for at least the first 4-6 months of life, with the major exception of the potential risks of HIV transmission through breast milk (discussed below). Breast milk is beneficial to infants for reasons of nutrition as well as protection from infectious diseases, both through transmission of antibodies, and avoidance of contaminated water that might be used to mix infant formula.

A recent meta-analysis of relevant studies from the 1980s and 1990s examined the risk of death from infectious disease over the first two years of life for babies who were not breastfed, subdivided into several age groups (44). Original data from six major studies, involving about 18,000 children and about 1200 deaths before age 2 were available for reanalysis. Protection against dying from any infectious disease was greatest at younger ages (excluding deaths during the first week of life, which are largely due to events related to birth and congenital anomalies), declining over time, but remaining significant through the second year of life (Table 8).

Considering the two main categories of infectious disease death, the risk of death without breastfeeding was greater for diarrhoeal disease during the first 6 months of life (pooled OR 6.1; 95%CI 4.1-9.0) than for ARI (OR 2.4; 95%CI 1.6-3.5), but was similar from 6 months to one year (diarrhoea, OR 1.9; ARI, OR 2.5, with overlapping 95% CIs). When the data were stratified by mother's education (into terciles), the risk of death with no breastfeeding was substantially higher for lower education levels.

Even though this overview took in all relevant data, it is based on relatively few studies, and the results in some analyses had substantial heterogeneity. The main results, however, appear to be robust. A key piece of information that this study adds is the finding of a greater protective effect of breastfeeding for poorly educated mothers, suggesting that it is more difficult for these mothers—for a variety of economic and other reasons—to provide safe breastmilk substitutes for their children. This should weigh into the policy recommendations about breastfeeding at varying levels of HIV prevalence.

Net benefits of breastfeeding in areas of high HIV are an area of controversy. Since HIV can be transmitted through breast milk, the need arises to understand the benefits of breastfeeding more precisely. Models to develop policy recommendations about breastfeeding in areas of high HIV prevalence are still evolving, but have generally assumed constant protection from infectious

diseases with breastfeeding in the first year of life (see paper on HIV prevention for fuller discussion and recommendations).

(iii) Complementary Feeding

The introduction of foods to infants in addition to breastfeeding, usually at around 6 months of age through about two years, is referred to as complementary feeding. The types of amounts of food are critical to growth and development. Good nutrition during this period is critical to prevent stunting, which may be irreversible. This idea is reinforced by findings from intervention trials showing that food supplementation has its greatest effect in children under age two (45,46).

There is no single "correct" approach to complementary feeding. In a comprehensive review of approaches to complementary feeding, Dewey (28) reviewed current guidelines from national and international organizations, which are broadly similar in promoting the gradual introduction of soft, pureed foods, in a progression eventually leading to eating "family foods." The specifics of when various foods should be introduced, how often they should be given, their energy and vitamin content, micronutrient supplementation, and other aspects do vary considerably, however. One important point is a lack of clear guidance on continuation of breastfeeding during the period of food introduction.

There are three general approaches to improve the quality of complementary feeding each of which can be accomplished in a number of ways, and may be combined (28):

• improving the energy and/or nutrient density of home-prepared foods,

- micronutrient supplementation, and
- use of processed (commercial) foods.

It is clearly possible to develop foods appropriate to a range of economic and social conditions, but their use depends on mothers (or other caregivers) understanding how the foods can best be used. Information on the frequency and quantity of complementary feeding (which changes as the child grows) is vital so that the child gets enough calories and nutrients, but so that undue displacement of breastfeeding does not occur. Recommendations and programmes have varied in the content of these messages, and some appear to encourage too much feeding so that breastfeeding is, indeed, reduced too soon or too much (28). However, given the appropriate messages, studies in a number of developing countries provide convincing evidence that mothers can learn better feeding regimens for their infants and small children.

A number of well-designed trials of complementary feeding and micronutrient supplements have been carried out, most since the 1990s, with generally positive, but mixed, results. They show clearly that knowledge and practices can be improved, and some have shown increased growth and improved micronutrient status. One methodologic concern with most of the studies was failure to determine whether breastfeeding was displaced by complementary feeding. In this relatively new field of research and programmatic activity, it is likely that effectiveness will improve to the extent that a comprehensive approach reinforcing continued breastfeeding and refining recommendations on frequency and amount of complementary feeding will result in better growth and other nutritional outcomes (28).

(iii) Micronutrient Supplementation and Treatment of Helminths

Correction of dietary micronutrient deficiencies—particularly iron, vitamin A, and zinc—are known to reduce child morbidity (and at least for vitamin A, mortality). Mental development are also affected by inadequate iron and iodine. Anemia, while most often caused by an irondeficient diet, is exacerbated by helminth infestation (particularly hookworms) and malaria. Where these conditions are prevalent, treatment with antihelminthics and antimalarials also play a role in effectively reducing anemia. (See the CMH paper on interventions for malnutrition and treatment for parasitic infections for detailed discussion.)

(iv) Case Management

Appropriate treatment of episodes of serious illness in children is very effective at saving lives, and for the main causes, relatively inexpensive, where accessible. Case management— specifically, integrated management of serious childhood illness—was identified in the 1993 World Development Report (35) as the intervention likely to have the greatest impact on the global burden of disease, potentially averting 14% of that burden in low income countries. 'Integrated' denotes an approach that recognizes the fact that poor, sick children often have more than one specific diagnosis as well as underlying factors (particularly poor nutritional status) that contribute to a bout of illness. This concept is the underlying premise of the WHO/UNICEF programme on Integrated Management of Childhood Illness (IMCI; described below), in which sick children are classified according to a concise set of symptoms and managed (at the appropriate level in the health care system) with both specific treatments and health promoting activities.

The following section describes elements of case management for ARI, diarrhoea, and malaria. This will be followed by a brief discussion of modes of delivery care for case management.

Section D. Specific Measures in Case Management for ARI, Diarrhoea, and Malaria

1. ARI

WHO began developing a systematic approach to case management of ARI in the 1980s, which resulted in the ongoing Programme for the Control of Acute Respiratory Infections, and more recently, inclusion of detection and treatment algorithms for ARI in the IMCI programme (see Box: *Studies of ARI Case Management*). The key to success has been early treatment with appropriate antibiotics, with diagnosis based on easily detectable clinical signs. A guiding principle behind the recommendations is that they be highly sensitive so that most children in the initial stages of pneumonia receive effective antibiotics (11).

The WHO protocol comprises three steps:

- Identify children who should be examined for possible pneumonia ('case finding' based on entry criteria)
- 2. Identify cases of pneumonia based on clinical signs
- 3. Institute appropriate treatment in appropriate setting (institutional for severe and very severe cases, home management for less severe pneumonia)

Even in developed countries, where perhaps 5-15% of pneumonia in children is caused by bacteria, empirical treatment with antibiotics is the norm, because of the difficulty of isolating and identifying causative agents. In developing countries, where the majority of cases are

bacterial, the justification for empiric treatment is strong. WHO recommends, and has validated the use of, simple clinical signs to classify the nature and severity of ARI, which dictates place and type of treatment (Figure 2). Fast breathing and chest indrawing in children with cough or difficult breathing are the cardinal signs.

The selection of an antibiotic is influenced by the age of the child (roughly, younger or older than 2 months), severity of disease, and place of treatment. Infants less than 2 months old may be infected with a wide range of gram-negative or gram-positive bacteria, so a broad spectrum antibiotic is indicated (benzyl penicillin, gentamicin). For children older than 2 months, an antibiotic with good activity against the most common pathogens, *S. pneumoniae* and *H. influenzae*, is essential. The drug of choice for very severe pneumonia treated in the hospital is chloramphenicol and for severe pneumonia treated in the hospital, benzyl penicillin. For home care, four common antibiotics are widely effective : cotrimoxazole (trimethoprim-sulfamethoxazole), amoxycillin, ampicillin, and procaine penicillin. Other aspects of treatment include oxygen for very severe, hospitalized children, treatment of fever, and other supportive measures.

No case management protocol can be effective if children are not seen promptly after when symptoms appear: it is not uncommon for pneumonia to lead to death within 3 days. Prompt medical attention requires that mothers, in particular, be informed about the danger signs that mean care should be sought. It has been demonstrated that families can be taught to recognize the fast breathing that often predicts pneumonia. This depends on an accurate understanding of local beliefs and practices regarding pneumonia and provision of information to the mother that is culturally acceptable and understandable in the local context.

Box 2 : Studies of ARI case management

Recognizing the need for prompt treatment close to home, WHO sponsored seven pneumonia case management studies in the 1980s, in India, Indonesia, Nepal, Pakistan, Philippines, and Tanzania, and similar two studies were carried out in other sites in India and Bangladesh. The studies tested a standardized case management strategy within the primary health care system, involving community health workers.

Study areas had generally high infant mortality, and some had high low birthweight rates and prevalence of malnutrition. In most of the studies, treatment relied almost entirely on community health workers and home treatment by mothers, because referral facilities were inaccessible. In all 9 studies, compared with non-intervention areas, pneumonia-specific mortality was reduced, with reductions ranging from 25% to 67%, and overall child mortality reduced from 13-41%.

These results are the more impressive acknowledging that a substantial (though difficult to estimate) fraction of cases went undetected and untreated. In the Tanzania study, the treatment status of children who died of pneumonia in both intervention and non-intervention areas were investigated, and it was found that 68% of death in the control are and 46% in the intervention area had gotten no antibiotic treatment.

Sazawal and Black (47) meta-analyzed the results of these 9 studies and found an overall reduction in total infant mortality of about 16 deaths per 1000 live births as a result of the intervention. Infant mortality due to ALRI was reduced by about 11 deaths per 1000 live births, and mortality among children under 5 years, by 36 deaths per 1000 live births. Infant mortality was reduced by 20% and under-5 mortality, by 25% in these areas where infant mortality is high (at least 90/1000 live births).

2. Diarrhoea

Case management of acute, watery diarrhoea in children centers on prevention and correction of

dehydration, and on appropriate feeding of children during and after the diarrhoeal episode.

Antibiotics have a more limited, but still essential, role in the management of bloody diarrhoea

and cholera. An important aspect has been the worldwide push for home treatment of most

episodes with easily available oral rehydration solutions given by mothers. WHO has developed

a programme for the control of diarrhoeal diseases that takes in these aspects (CDD), and is also the basis of diarrhoea treatment in the IMCI programme.

Case management also includes appropriate hospital care (mainly intravenous rehydration) for children with severe dehydration from diarrhoea.

(i) Oral Rehydration Therapy (ORT)

Until about 20 years ago, intravenous fluids were the mainstay of treating dehydration due to diarrhoea. This severely limited access to treatment and posed its own risks of hospital-acquired infection. The development of ORT, based on scientific studies in the 1960s, has changed this picture completely. Dehydration can now be prevented or managed in up to 95% of all cases of acute watery diarrhoea. ORT is effective in rehydrating children with persistent diarrhoea and with bloody (dysenteric) diarrhoea, but it is not sufficient treatment for them. One consequence of the success of ORT for acute watery diarrhoea has been an increase in the proportion of diarrhoea deaths due to persistent diarrhoea (48).

Several acceptable oral rehydration solutions have been developed, all containing electrolytes and a source of sugar (glucose, sucrose, or rice powder). WHO currently recommends a solution of 3.5 grams of sodium chloride (table salt; and accepts as efficacious a range of 2.5-3.5 grams), 2.9 grams of trisodium citrate dihydrate, 1.5 grams of potassium chloride and 20 grams of glucose per liter of water. (WHO continues to refine this formula and will soon make public a new version.) Fluids that can be prepared at home (gruels, soups, yoghurt based drinks) have also been—and continue to be—investigated, and found effective, as long as sodium and glucose concentrations are within acceptable ranges.

There is also a need to assure that appropriate information is provided to mothers regarding the correct administration of ORT (e.g., that an appropriate solution is used and appropriate amounts given) and the warning signs of under- and overhydration.

(a) Impact of ORT

At the time ORT was first promoted widely, around 1980, diarrhoea was the leading cause of child mortality, when it was responsible for an estimated 4.6 million deaths per year. Although the details of recommended ORT have changed over the years, the basic message is that liberal oral fluids (with electrolytes) can replace the fluids lost through diarrhoea and save children's lives. The data are not entirely reliable, but it appears that most episodes of diarrhoea in children the world over are now treated with some form of ORT. This has been accomplished through national diarrhoeal disease control programmes around the world (in 80 countries by 1990), which involve treatment in health facilities, but more importantly, by mothers at home (6).

It is impossible to assess the impact of ORT alone since its introduction because of data limitations, and the many other changes that have taken place over the last two decades. However, case studies in four countries—Brazil, the Philippines, Egypt, and Mexico—suggest that ORT has been a major (in some cases, the main) contributor to improved survival after diarrhoeal infections, but also demonstrate the difficulty of determining the magnitude of the effect. ORT was introduced in Northeast Brazil in the early 1980s with a strong mass media campaign, training programmes, and distribution of measuring spoons for home preparation of ORT solution. By 1991, an estimated 35% of all cases, and 62% of serious cases of diarrhoea (as determined by mothers) were treated with ORT. Over that period, infant deaths due to diarrhoea declined by an estimated 57%. Despite worsening socioeconomic conditions, however, there were also improvements in water supply, vaccine coverage, duration of breastfeeding, and improved nutritional status, all of which would have contributed to improved infant health. The best estimate from a simulation model suggests that the factors other than ORT could account for about one-third of the reduction in infant mortality. This and other indirect analyses suggest a large effect of ORT (48).

In Egypt, most of the reduction in mortality from diarrhoea during the 1980s appears to be attributable to ORT, based on a comprehensive national evaluation (49). (Unlike the home preparation promoted in Brazil, the use of Oral Rehydration Salts solution was promoted in Egypt.) In Mexico, ORT played a key role, but not necessarily stronger than that played by improved water and sanitation (50). In the Philippines, ORT implementation during the 1980s and early 1990s was accompanied by a marked decline in diarrhoea mortality, but the data available on ORT and other changes makes for difficult interpretation (6).

(ii) Antibiotics and Other Drugs in Diarrhoea Management

The routine treatment of acute, watery diarrhoea requires no antibiotics or other drugs. But for bloody diarrhoea (dysentery), much of which is caused by *Shigella*, and for cholera, antibiotics

have a legitimate role and should be used in children. They can shorten the duration of the episode and diminish its severity, and for Shigella, decrease the period of pathogen excretion (15). Where cholera is suspected (based on symptoms and presence of cases in the community) or bloody diarrhoea is noted, no more specific diagnosis is necessary before initiating antibiotic treatment.

Other than anti-infectives, no other medications are recommended for diarrhoea, but a large number are on the market and sold for relatively high prices all over the world. They not only divert money from appropriate treatment, they can have adverse effects, actually worsening the disease.

(iii) Appropriate Feeding During and After Diarrhoeal Episodes

Nutritional losses occur during diarrhoea due to reduced food intake, malabsorption, and increased catabolism. In children, these losses can be compounded by increasing susceptibility to further diarrhoeal episodes, leading to ever-increasing malnutrition. WHO has developed guidelines for appropriate feeding during and after diarrhoeal episodes that focus on the need for continued feeding (including breastfeeding) and compensation for loss of nutrients once the episode is over. It is clear that even with continued diarrhoea, nutrients are absorbed and recovery hastened by adequate food intake.

(iv) Education of Mothers in Diarrhoea Case Management

ORT is, for the most part, administered at home by caregivers, mainly mothers. A wide range of interventions and programmes have been carried out to teach the mixing and giving of

appropriate fluids and foods. These include a major mass-media intervention in Egypt, with emphasis on short television dramas; a series of radio spots and training of village focal points in Gambia; training of kaders in Indonesia; and the programme in Brazil described earlier. Those programmes that have been evaluated suggest that awareness, knowledge, and practice can be significantly modified in the short term, but that if the mass media and training efforts are not sustained, the knowledge and practice levels decrease dramatically.

3. Malaria

Malaria case management involves prompt diagnosis and treatment of severe malaria in children. Major diagnostic approaches used are presumptive (syndromic) diagnosis, microscopic diagnosis (i.e., identification of the parasite), and antigen testing for rapid diagnoses. In poor setting, often there are no laboratory facilities for testing, and diagnosis and treatment is largely syndromic.

Successful case management for malaria is challenging for a number of reasons. First is that it requires prompt recognition that a child may have malaria and receive treatment before complications ensue. Diagnosis and choice of treatment is complicated by the fact that the presenting symptom, fever, is common to a number of childhood diseases. In particular, during periods of high malaria transmission, a majority of children with fever may also meet the clinical case definition for pneumonia (although the overlap is less when laboratory diagnosis is used to define cases, both malaria and pneumonia have been found in several studies in about 15% of such children) (51). This overlap, in particular, makes choice of drug treatment of children more difficult than for treating malaria in adults. The use of both antibiotics and antimalarials when
not strictly needed may not be a problem for an individual child, but if done on a routine basis, may contribute to increased drug resistance.

Delays in treatment or treatment failures may occur for a number of reasons. In many places, mother will try a traditional remedy in addition to, or instead of, a pharmaceutical antimalarial, and may delay seeking professional care. When antimalarial drugs are purchased from a shopkeeper, the family may only have enough money for a partial course and, particularly if the child improves, may not complete it. The quality of antimalarials also varies considerably, and products may not contain as much active ingredient as they should. These and other factors are well known, but exceedingly difficult to counter on a large scale. Research in recent years has increasingly focused on such questions, however (see [52]).

The key issue of which drugs to use as first- and second-line treatment must be decided locally, and is considered a function of the health care system. The status of antimalarial treatment is discussed in detail in Meek and colleagues CMH paper on malaria.

4. Measles

The single most important intervention for all children with measles is treatment with high-dose vitamin A. Randomized trials of vitamin A therapy have provided definitive evidence of a greater than 50% reduction in case fatality for children hospitalized with severe measles (53), as well as significantly reduced morbidity. Significantly reduced morbidity and mortality has been confirmed outside of trials in routine hospital practice after the institution of vitamin A treatment for measles in South Africa (54).

Children with specific complications of measles do require active treatment for those conditions, in addition to vitamin A. Appropriate treatments are the same as those given as for primary cases of the complications.

Section E. Strategies for delivering health care to poor children

Interventions to prevent and manage most serious childhood illnesses are known, do not require high-technology inputs at delivery, and are not unduly costly (though still out of reach economically of many of the world's poor). The specific interventions described earlier—ORT, antibiotics, antimalarials, etc.—have saved many children's lives through use in vertical programmes and health services provided in a variety of ways. Where primary health care functions well and children have access to services, these, as well as preventive services, can be delivered adequately. However, as described earlier, the decline in child mortality has slowed and even reversed in some of the poorest areas, where there is clear lack of access to essential health care. This is dramatized by the fact that up to 80% of childhood deaths in Africa (the region with the highest child death rates) occur at home, without a child seeing a health care provider (55).

In previous decades, WHO and other organizations developed a number of disease-specific and sector-specific programmes (e.g., ORT, EPI, ARI) that have witnessed considerable success. These have involved a range of elements, including facility-based services and home treatment. There has, at times, also been an emphasis on general primary health care programmes (56). But

there is a need for better ways of managing childhood illness and into approaches that can work in places where many children die.

Most recently, in the 1990s, WHO and UNICEF have developed an approach (with continual new development) that relies on syndromic case management as the centerpiece of a strategy to establish basic child health services in very poor areas. The strategy, Integrated Management of Childhood Illness (IMCI), is distinguished by the fact that it is not simply a stacking of individual interventions. IMCI developers have produced treatment algorithms based largely on signs and symptoms, appropriate to situations where laboratory and clinical resources are limited. IMCI providers are also trained to use encounters as opportunities to evaluate a child's overall health, rather than simply as a treatment episode. IMCI may not be appropriate in all situations, and difficulties have been encountered in its establishment in various places, but it has taken root in many places and continues to expand into new areas. It is the most prominent integrated strategy specifically for children, so is given considerable attention in this paper as the extant model.

(i) Improved primary health care

There are still many rural areas, particularly in Africa and Asia, that are isolated geographically (or economically) from formal health care facilities, where children die from lack of medical attention for serious acute illnesses. Efforts to bridge this gap in services with low-cost community based health programmes were begun in a number of poor countries in the 1980s, following the 1978 Alma Ata declaration (under the banner of 'Health for All by the Year 2000'). Some of these were more specific ('vertical' e.g., vaccines, pneumonia treatment) and

some more general. The effects of these programmes overall are not entirely clear; the evidence for an effect on child mortality has generally been considered weak (57). The multiplicity of programmes and the level of implementation makes generalization difficult, however. Evaluation of the impact of primary health care in The Gambia sheds a somewhat different light on the issue.

In 1978, The Gambia adopted, and has continued to support, community-based primary health care as the basis of a national health policy. Unlike many other countries, where only specific aspects of primary health care were implemented (58), in rural areas of The Gambia, attempts were made over the course of time to incorporate not only direct health services and simple medical technologies, but also health education, improved water supply and sanitation services, and other disease control measures. A pattern was established, placing full-time Community Health Nurses in larger villages who could provide local treatment, refer to higher-level facilities, and link with village health workers and trained birth attendants in about five smaller villages. By 1997, there were 402 'PHC' villages in the country, reaching 50-60% of the population with primary health care services (although virtually the entire population is covered by vaccination and other specific programmes). Process measures improved (e.g., maternity care visits and attended deliveries), but it effects on child mortality have only recently been studied.

Briefly, infant and child mortality in15 PHC villages (total 1996 population about 11,000) was compared with 25 smaller, but otherwise similar, non-PHC villages (total 1996 population about 16,000) over the period 1982 to 1996. Indicators such as level of immunization (which was already high before 1982), breastfeeding rates, water supply, and general economic conditions remained similar in the two groups of villages over the period of the study. So it is not unreasonable to examine what happened to infant and child mortality to determine the impact of the primary health care services, and this is what Hill and colleagues (64) have done.

Breaking the 15 years into 5 time periods, they found was a steep decline in infant mortality in both PHC and non-PHC villages, mainly during the 1980s, but the rates were consistently somewhat lower in the PHC villages during each period except the last one. Child mortality rates changed less, but were also generally somewhat lower in PHC villages. In this poor, rural and largely uneducated population, considerable gains were made in reducing infant, and to a lesser extent, child mortality. Hill and colleagues conclude that the analysis supports the hypothesis that primary health care contributed to the improvement. It is probably not possible to pin this effect down any more clearly. If anything, the results may understate the effect, because services in PHC villages were also used by non-PHC village residents. But there were also major political and economics ups and down during the period of observation, and many other influences.

This study does provide a benchmark for evaluation of primary health care in other areas, but to date none have been reported as completely as this from The Gambia. It will be important, however, to understand the impact of such low-cost systems in decisions to establish new services in other poor, rural areas with inadequate existing health services.

(ii) Integrated Management of Childhood Illness (IMCI)

(a) **Description of IMCI**

IMCI is an evidence-based strategy developed by WHO and UNICEF to improve the management of childhood illness in places with high childhood mortality. It brings together interventions that have been proven effective in one package (Table 9). This delivery strategy identifies the major childhood infections by means of its classification system, thus providing the opportunity for treatment. Services are provided through the existing primary health care system, using health workers in first-level health facilities, but also including substantial community and family involvement. A major focus is case management of the five conditions that contribute, in many developing countries, to more than 70% of all deaths of children under five: pneumonia, diarrhoea, malaria, measles and malnutrition. The strategy is aimed at countries with infant mortality rates of >40/1,000 live births and where malaria is endemic, but the interventions are more broadly applicable. The basic IMCI elements are: assessment of the child, classification of illnesses, treatment, and counseling of the mother. Other key elements include prevention through immunization and improved nutrition, and care and feeding of children within the family. Health workers are trained to use tools developed through IMCI.

IMCI, built upon previous decades work on the treatment of the conditions included, was launched fully in 1996, after years of field research and early implementation in a few countries. The guidelines are based on evidence from research as well as expert opinion, and, to the extent possible, incorporated existing successful guidelines, or parts of guidelines. A research agenda to answer specific questions about specific treatments and management is also part of IMCI, so continuous improvement is envisioned. A hallmark of the programme has been field testing and refinement of all measures, with continued evaluation of the programme in different countries. The training course, which is adapted for use in each country, has also been field tested, evaluated and improved over time.

Case detection techniques rely on assessment by health workers of clinical signs only (i.e., no laboratory testing). The algorithms originally developed were refined through field testing in a number of African countries and early on in Bangladesh. Health workers are trained to use these algorithms, which are presented clearly in wall charts and booklets. They lead to identification of the common causes of childhood illness (pneumonia, diarrhoea, malaria, measles, otitis media, malnutrition).

Depending on classification of the illness (or more often illnesses), the result is either an urgent referral to a higher level health provider (possibly with some essential treatment immediately), specific medical treatment and advice, or simple advice on home management. The process of introducing IMCI into a new country involves adapting generic WHO treatment guidelines for epidemiologic and cultural relevance, and creating language- and culture-appropriate "mothers counselling cards."

Treatment includes basic drugs (antibiotics, antimalarials) at the appropriate level of care, and informing the mother about how to continue treatment and supportive care at home. Mothers are also informed of danger signs that require the child to be brought back for care. If the child is malnourished, general advice on feeding is also given.

The community component of IMCI requires a strategy to cover elements as diverse as health education, drug and other commodity supply and availability at community level, adapted messages, resource persons, capacity, building on current interventions, partnerships, and sustainability. Some of the challenges include:

- Prioritising behaviours and interventions to be promoted,
- Influencing behaviours or sets of behaviours: care-seeking, feeding practices, adherence to treatment
- Building capacity at all levels
- Going to scale with participatory (time-consuming and personnel-intensive) approaches
- Ensuring local ownership

(b) Impact of IMCI

As of December 2000, IMCI had been implemented at some level in 74 countries (Figure 3). Of these, 19 countries were in the expansion phase, 40 in the early implementation phase, and 33 in the introductory phase. Part of the implementation strategy has been the development of evaluation tools and early application of them in pilot settings in different countries (termed the Multi-Country Evaluation of IMCI Effectiveness, Cost and Impact; MCE) by evaluators independent of the IMCI strategy itself (60). Still, the strategy is fairly new (launched in 1995), so few results are available. The evaluation includes the following components: 1) availability, accessibility and quality of IMCI Health Facilities, 2) utilization of IMCI health facilities by the target population, 3) coverage of target population by IMCI, 4) impact and improvements in knowledge, behavior, nutrition and health, and 5) the possibility of ruling out external causes as being responsible for the observed improvements in knowledge, behaviors, nutrition and health.

As of April 2001, the following overall findings had been reported:

- In two districts in Tanzania, IMCI is addressing the most common serious health problems of children, and a 35-45% of sick children were brought to a formal health care provider for first-line treatment. Children in the two IMCI districts received a more thorough health assessment and better quality care than in comparison, non-IMCI district.
- In Bangladesh, the baseline survey (before IMCI establishment) indicates the major challenges will be in improving careseeking behavior for sick children and improving the quality of care in facilities.

Evaluations are in earlier stages in several other countries.

IMCI could have a substantial impact on overall child health as it becomes better established and widespread. The strategy is a means to improve the efficiency of services and personnel already dedicated to primary health care, rather than establishing new services. The initial emphasis in the development and introduction of IMCI has been on services at the health facility level and less so on community outreach for prevention and family-level treatment. Initial training and establishment requires a substantial commitment of resources and provider time (e.g., training last 11 days). Trainees also require follow-up and supervision. Currently, the community component is being refined and key elements, pilot tested for further expansion of this critical component.

(c) Challenges to Implementing IMCI

IMCI brings together many partners and sectors. Its implementation requires clear vision and policy direction and sustained support from other programme areas to create the enabling environment needed to sustain it in the health sector and the community.

Constraints associated with IMCI implementation in countries commonly relate to competing interests, inconsistent or non-supportive policies and strategies across different programme areas, and the lack of an overall master plan for how to strengthen the health system.

The introduction of IMCI in a country first requires the political will to give priority and devote the necessary resources to child health. Support and commitment are needed from the top levels of government down to the peripheral health sector and the community itself, and must be seen as a long-term commitment of at least 5-10 years initially. A mix of inputs that include training, supervision, and secure drug supply must be guaranteed early on.

Certain elements of IMCI are unique and can be influenced directly by IMCI managers (e.g., development of adapted guidelines, training). Other elements must be integrated in other initiatives or programme areas; therefore, IMCI must have partner support (e.g. drugs, referral pathways, supervision), and this has proven an obstacle in a number of countries.

Where priorities for development of the health care system have not been laid out, it can be difficult for IMCI to become established. In addition to the uncertainties of future development, competition within the health sector may preclude sufficient resources being made available for IMCI implementation. A lack of management tools can exacerbate this problem. In many countries, ministries of health are organized according to the vertical programmes favoured in the 1980s. Integrated approaches, therefore, can have a difficult time fitting in. IMCI supporters have worked around this problem by promoting the establishment informal collaborative arrangements or working groups, but experience seems to indicate that eventually, structural changes in ministries will be needed to facilitate the collaboration of departments and units. All IMCI components do not necessarily move at the same pace; however, there are elements of complementarity and mutual support that make it essential to advance certain activities simultaneously, so coordination is vital.

(iii) Linking to existing programmes

The Expanded Programme on Immunisation (EPI) has become established as one of the most successful programmes in the world for delivering vaccines to infants, even in poor areas where routine health services are scarce. Because it reaches such a large proportion of poor infants, it may be that the vaccine contacts could be used to good advantage for other simple, safe, and effective intermittent interventions. For instance, supplementation with vitamin A during EPI visits has been recommended (61); discussed in more details in the CMH nutrition paper).

In a randomised trial recently reported from an area of Tanzania highly endemic for falciparum malaria (and concomitantly, severe anaemia), infants were given intermittent curative doses of the currently-recommended antimalarial (sulphadoxine-pyrimethamine; S/P) or placebo during their EPI visits at 2, 3 and 9 months (62). Mothers of infants in both S/P and placebo groups were given iron drops to give their children through 6 months of age. The result was a reduction in the number of infants in the S/P group getting clinical malaria to less than half the rate in the placebo group, and a reduction of almost half for severe malaria. Severe anaemia was also

reduced by about half in the S/P group (and the rate of iron drop dosing was about the same in both groups). (All primary analyses used a rigorous 'intention-to-treat' approache, which included the 701 children recruited into the study.)

The economic implications this approach, linking intermittent antimalarial dosing to EPI, are not known directly, but an economic analysis using efficacy results of an earlier trial (the antecedent of this one) of antimalarial treatment and iron supplementation in the same population (but with weekly dosing), was carried out, assuming delivery of the interventions as in this trial, through regular EPI visits (63). The strategy was not only relatively cost-effective, but remarkably, cost-saving over the costs of case management of malaria and anaemia, and over either single intervention.

(iv) Outreach programs for specific conditions

(a) Pneumonia

Because pneumonia is such an important cause of serious childhood illness, it has been the focus of efforts to bring treatment to isolated communities. Two studies of such efforts are described here. Both used the co-trimoxazole, and both measured treatment impact on childhood mortality. The studies took place in India (64) and Nepal (65).

The study in central India was carried out in an area with poor medical services (one primary health center for about 20,000 people). In 58 villages (with about 6,000 children aged 0-4), which were those served by two primary health centers, an intervention programme was established to improve the treatment of childhood pneumonia. Mass health education about pneumonia and treatment with co-trimoxazole through village health workers and traditional birth attendants were the tools used. The co-trimoxazole was given as a syrup preparation.

Forty-four villages (with about 4,000 children aged 0-4) neighboring the intervention villages (and similar to them) served as a control.

In the first year of the intervention, the mortality rate for pneumonia among children 0-4 was 8.09/1000 children in the intervention villages, and 17.5/1000 in the control areas. The corresponding all-cause death rates were 28.5/1000 and 40.7/1000. These differences are substantial and were reported as statistically significant. The village health workers and traditional birth attendants provided some services in addition to treating pneumonia, so the change cannot be attributed entirely to co-trimoxazole.

The study in Nepal was focused only on providing treatment for pneumonia, with no other services provided by the volunteer health workers who dispensed co-trimoxazole. The intervention programme was established in a roadless, mountainous region, one of the poorest and most poorly medically served in Nepal. The programme was phased in over the course of a year, eventually reaching 115 villages (including about 6700 children under age 5). The study reports results over the first three years, comparing mortality before and after programme implementation.

Co-trimoxazole was given as a 5-day b.i.d. course, using a liquid formulation. Initially, the programme relied on active case detection, with the volunteer workers visiting all children regularly. When a presumptive case of pneumonia was found, the worker gave the parents co-trimoxazole with instructions about dosing, and watched as the parents administered the first dose. By the third year, presumably because parents had become better informed about pneumonia, case finding became less important, as most cases were treated based on the

mothers' bringing the child for treatment. During the three years of the study, more than 15,000 courses of co-trimoxazole were given.

As the programme progressed, the risk of death from all causes under age 6 declined steadily. The relative risk in years one, two, and three were: 0.87, 0.76, and 0.72 (based on a total of 2101 deaths). The declines in years two and three were reported as statistically significant. This study was the first step in a programme that has now been expanded to additional areas in Nepal (66)

It is clear that, under some circumstances, low-cost local programmes can be established that effectively reduce childhood mortality, largely through case management, but without highly trained medical personnel. What is not clear is how widely applicable these measure are, what the vital elements are for success, or how sustainable the approach is over the longer term.

(b) Malaria

There is growing interest in outreach approaches to malaria treatment . A recent randomised trial in Tigray, Ethiopia evaluated home treatment of children in holoendemic malaria areas (67). In this trial, clusters of villages, with a population of approximately 70,000, were assigned to an intervention group or a control group. By means of local training of mother coordinators, mothers learned how to administer chloroquine to their children. The intervention group received instruction on the recognition of possible malaria and the administration of chloroquine, whereas the control group had only the existing facility-based malaria care. The trial found that 190 of 6,383 children in the intervention group died compared with 366 out of 7,294 in the control group, with a relative risk reduction 40% (95% CI, 29.2-50.5%). This translates into treating about 1000 children to prevent 20 deaths.

The Special Programme for Research and Training in Tropical Diseases (TDR; World Bank/UNDP/WHO) has established a task force on malaria home management to find ways to improve the ability of families to provide effective treatment for children with malaria. The task force has projects under way and has issued calls for proposals in a number of subject areas (57).

Section F: Cost-effectiveness of interventions to reduce childhood morbidity and mortality Estimates have been made of the cost-effectiveness of various interventions for controlling ARI and diarrhoea, and other serious childhood conditions. These are summarized here and updated, where possible.

The cost-effectiveness of broad groups of interventions for ARI are presented in Table 10, based on an original analysis by Stansfield and Shepard (42), and for diarrhoea in Table 11, by Martines, Phillips and Feachem (15). Most of the interventions for ARI and diarrhoea were also included in a broad-ranging analysis of the cost-effectiveness of 40 health interventions in the Republic of Guinea by Jha, Bangoura and Ranson (79). The 17 of these interventions (16 individual interventions and one 'package') most directly affecting children are listed in table 12, ranked by estimated cost-effectiveness.

The estimates in the tables use somewhat different metrics to describe cost-effectiveness, so they cannot be compared directly. Some general patterns emerge, however. Case management for ARI and diarrhoea (all estimates) and the 'package' of pneumonia, malaria, and diarrhoea treatment at a health centre in Guinea are among the most cost-effective interventions. In fact, all the most effective interventions are also highly cost-effective (in the Guinea study, <US\$100 per life year saved).

Meaningful estimates of the cost-effectiveness of piped water and sewage disposal are difficult to develop, because the array of benefits is broad, including some that are quantifiable but not directly in terms of health (e.g., reduced time spent seeking water) and others that are more qualitative (e.g., improved home atmosphere with fewer odors). Estimates based on direct effects on health outcomes suggest a high cost-effectiveness ratio compared with the best preventive and clinical interventions. Jha and colleagues (79) estimated a cost of US\$343 per year of life saved for providing safe water and constructing pit latrines in Guinea in the 1990s, which is consistent with earlier World Bank estimates. Martines and colleagues (15) estimated the cost of promoting personal and domestic hygiene at US\$5-500 (median US\$10) per averted episode of diarrhoea in children under 5. The very wide range of plausible costs mirrors a range of 14-48% in the effectiveness of the interventions.

The estimates all presuppose availability of services, so the costs do not include major infrastructure investments that would be needed in places where primary health care is unavailable. Initial investments to allow access for unserved populations would have to be factored into any estimates for expanded coverage. In isolated areas, where establishment of facilities and fully-trained professional health workers may not be practicable, these estimates also may not apply. No estimates of cost-effectiveness for programmes using village health workers were found.

Section G: Conclusions

Effective, and cost-effective measures to prevent serious childhood illnesses and deaths are known and are technologically feasible to apply all over the world. Specific health-sector interventions, as well as general environmental and economic improvements in many countries

have, in fact, brought down child mortality in all but a few countries over the past 50 years. But rates have stagnated or worsened in some places, and everywhere, the poorest in society also have the sickest children and the highest rates of childhood mortality.

The evidence presented in this paper supports the continued expansion of existing preventive services (immunization, feeding, micronutrient supplementation, environmental measures), but places a high value on expanding case management of severe episodes of illness at the local level and improving child feeding. IMCI is the most prominent example of a health-facility based strategy combined with community and household outreach. Countries should be encouraged and helped to adopt IMCI or similar approaches to child health. Priority should also be given to further development of village-based approaches to case management that reach into ever less accessible, poor areas, using village health workers and increased education of mothers and families. The longer term goal is to bring these areas more professional primary health care and accessibility to a full range of essential health services. Finally, progress already achieved must be sustained and protected, particularly in populations with high rates of child mortality where improvement has slowed or stopped.

REFERENCES

1. **Ahmad OB, Lopez AD, Inoue M**. The decline in child mortality: a reappraisal. *Bulletin of the World Health Organization*, 2000,**78**(10):1175-1191.

2. **Claeson M, Griffin C, Johnston T, McLachlan M, Soucat A, Wagstaff A, Yazbeck** A. Health, nutrition, and population, draft for comments, April 2001. In: World Bank, *Poverty Reduction Strategy Sourcebook. http://www.worldbank.org/poverty/strategies/sourctoc.htm*

3. **Rutstein SO**. Factors associated with trends in infant and child mortality in developing countries during the 1990s. *Bulletin of the World Health Organization*, 2000,**78**(10):1256-1270.

4. **Casas JA, Dachs JN**. Socioeconomic and health inequalities in the Americas. Submitted for publication.

5. **Wegman ME.** Foreign aid, international organizations, and the world's children. *Pediatrics* 1999,**103**(3):646-654.

6. **Victora CG, Bryce J, Fontaine O, Monasch R**. Reducing deaths from diarrhoea through oral rehydration therapy. *Bulletin of the World Health Organization*, 2000,**78**(10):1246-1255.

7. **Mosley HW, Chen LC**, eds. *Child Survival: Strategies for Research* New York Population Council, 1984 (Population and Development Review, supplement vol. 10).

8. **WHO**. EIP/CAH. [data on distribution of deaths]

9. **Kirkwood BR, Gove S, Rogers S, Lob-Levyt J, et al**. Potential interventions for the prevention of childhood pneumonia in developing countries: a systematic review. *Bulletin of the World Health Organization*, 1995,**73**(6):793-798.

10. **Shann F**. Etiology of severe pneumonia in children in developing countries. *Pediatric Infectious Diseases*, 1986,**5**:247-252

11. **WHO**. *Technical bases for the WHO recommendations on the management of pneumonia in children at first-level health facilities*. Programme for the Control of Acute Respiratory Infections. Geneva: WHO, 1995a.

12. **Rowland MGM, et al**. Impact of infection on the growth of children from 0 to 2 years in an urban West African community. *American Journal of Clinical Nutrition*, 1988,**47:**134-38.

13. **Mata LJ.** Nutrition and Infection. *Protein Advisory Group Bulletin*, 1971,**11**:18-21.

14. **Condon-Paoloni D, Cravioto J, Johnston FE, De Licardie ER, Scholl TO**. Morbidity and growth of infants and young children in a rural Mexican village. *American Journal of Public Health*, 1977, **67**(7):651-656.

15. **Martines J, Phillips M, Feachem RGA**. Diarrheal diseases. In: Jamison DT et al., eds. *Disease Control Priorities in Developing Countries*. New York, Oxford University Press, 1993:91-116.

16. **WHO**. WHO Expert Committee on Malaria: Twentieth Report. Technical Report Series No. 892 2000.

17. **Baume C, Helitzer D, Kachur SP**. Patterns of care for childhood malaria in Zambia. *Social Science and Medicine*, 2000,**51**:1491-1503.

18. **WHO**. *Technical basis for the case management of measles*. Geneva: WHO, 1995b.

19. **Frongillo EA, de Onis M, Hanson KMP**. Socioeconomic and demographic factors are associated with worldwide patterns of stunting and wasting of children. *Journal of Nutrition*, 1997,**127**:2303-2309.

20. **Smith LC, Haddad L**. Explaining child malnutrition in developing countries: a crosscountry analysis. Food Consumption and Nutrition Division, Discussion Paper No. 60. Washington, DC: International Food Policy Institute, 1999.

21. **Pelletier DL, Frongillo EA Jr, Schroeder DG, Habicht JP**. A methodology for estimating the contribution of malnutrition to child mortality in developing countries. *Journal of Nutrition* 1994,**124**(10Suppl):2106S-2122S.

22. **Pollitt E, et al**. Early supplementary feeding and cognition. Monographs of the Society for Research in Child Development 1993;58:1-99.

23. **Mendez MA, Adair LS**. Severity and timing of stunting in the first two years of life affect performance on cognitive tests in late childhood. *Journal of Nutrition*, 1999,**129**:1555-1562.

24. **Martorell R, et al**. Long-term consequences of growth retardation during early childhood. In: Hernandez M, Argente J, eds. *Human Growth: Basic and Clinical Aspects*. Amsterdam: Elsevier, 1992:143-149.

25. **Pan American Health Organization**. Nutrition, health and child development. PAHO Scientific Publication No. 566. Washington, DC: PAHO, 1998.

26. **Rice AL, Sacco L, Hyder A, Black RE**. Malnutrition as an underlying cause of childhood deaths associated with infectious diseases in developing countries. *Bulletin of the World Health Organization*, 2000,**78**(10):1207-1221.

27. **Martorell R, Kettel Khan L, Schroeder DG**. Reversibility of stunting: epidemiological findings in children from developing countries. *European Journal of Clinical Nutrition*, 1994,**48**(Suppl 1):S45-S57.

28. **Dewey KG**. *Approaches for Improving Complementary Feeding of Infants and Young Children*. Background paper prepared for the WHO/UNICEF Technical Consultation on Infant and Young Child Feeding (WHO, Geneva, 13-17 March 2000).

29. **de Onis M, Frongillo EA. Blossner M**. Is malnutrition declining? An analysis of changes in levels of child malnutrition since 1980. *Bulletin of the World Health Organization*, 2000,**78**(10):1222-1233.

30. **Esrey SA, Feacham RG, Hughes JM**. Interventions for the control of diarrhoeal diseases among young children: improving water supplies and excreta disposal facilities. *Bulletin of the World Health Organization*, 1985,**63**:757-772.

31. **Esrey SA, Potash JB, Roberts L, Shiff C**. Effects of improved water supply and sanitation on ascariasis, diarrhoea, dracunculiasis, hookworm infection, schistosomiasis, and trachoma. *Bulletin of the World Health Organization*, 1991,**69**(5):609-21.

32. **Huttly SRA, Morris SS, Pisani V**. Prevention of diarrhoea in young children in developing countries. Bulletin of the World Health Organization 1997;75(2):163-174.

33. **Esrey SA**. Water, waste, and well-being: a multicountry study. *American Journal of Epidemiology*, 1996,**43**(6):608-623.

34. **Lengeler C**. Insecticide treated bednets and curtains for malaria control (Cochrane Review). In: *The Cochrane Library*, Issue 3, 1998. Oxford: Update Software.

35. **World Bank**. World Development Report, 1993: Investing in Health. Oxford: World Bank, 1993.

36. **Caldwell JC**. Education as a factor in mortality decline: an examination of Nigerian data. *Population Studies*, 1979,**33**:395-413.

37. Adetunji JA. Infant mortality and mother's education in Ondo State, Nigeria. *Soc Sci Med* 1995, **40**(2):253-263.

38. **Desai S, Alva S**. Maternal education and child health: is there a strong causal relationship? *Demography*, 1998,**35**(1):71-81.

39. **Ranja PN, Mishra AK, Krishnamoorthy S**. Impact of maternal education and health services on child mortality in Uttar Pradesh, India. *Asia-Pacific Population Journal*, 1979,**13**(2):27-38, 1998.

40. **Van Gineken J, Lob-Levyt, Gove S.** Potential interventions for preventing pneumonia among young children in developing countries: promoting maternal education. *Tropical Medicine and International Health*, 1996,1(3):283-95.

41. **Bicego, GT and Boerma, JT.** Maternal Education and Child Survival: A Comparative Study of Survey Data from 17 Countries. *Soc. Sci. Med*, 1993, 36(9):1207-1127.

42. **Stansfield SK, Shepard DS**. Acute respiratory infection. In: Jamison DT et al., eds. *Disease Control Priorities in Developing Countries*. New York, Oxford University Press, 1993:67-88.

43. **England S, Melgaard B, Milstein J, Kou U, Jha P**. The Evidence Base for Interventions to Reduce Mortality from Vaccine-Preventable Diseases in Low and Middle-Income Countries. Commission on Macroeconomics and Health, Working Paper 10, 2001.

44. WHO Collaborative Study Team on the Role of Breastfeeding in the Prevention of Infant Mortality. Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: a pooled analysis. *Lancet*, 2000,355:451-455.

45. **Lutter CK**. Processed and complementary foods: summary of nutritional characteristics, methods of production and distribution, and costs. *Food and Nutrition Bulletin*, 2000,**21**(1): page number?

46. **Schroeder DG, Martorell R, Rivera JA, et al**. Age differences in the impact of nutritional supplementation on growth. *Journal of Nutrition* 1995,**125**1051S-1059S.

47. **Sazawal S, Black RE**. Meta-analysis of intervention trials on case-management of pneumonia in community settings. *Lancet*, 1992,**340**:528-533.

48. **Victora CG, Olinto MT, Barros FC, Nobre LC**. Falling diarrhoea mortality in Northeastern Brazil: did ORT play a role? *Health Policy and Planning*, 1996,**11**(2):132-41.

49. **Miller P, Hirschhorn N**. The effect of a National Control of Diarrheal Diseases Program on mortality: the case of Egypt. *Social Science and Medicine*, 1995,**40**:S1-S30.

50. **Gutierrez G, et al**. Impact of oral rehydration and selected public health interventions on reduction of mortality from childhood diarrhoeal diseases in Mexico. Bulletin of the World Health Organization 1996; 74:189-197.

51. **WHO**. *The overlap in the clinical presentation and treatment of malaria and pneumonia in children: report of a meeting*. Geneva: WHO, 1992.

52. **TDR** (Special Programme for Research and Training in Tropical Diseases). Task force on malaria home management. TDR Web site. 2001. *http://www.who.int/tdr/grants/workplans/home.htm*

53. **Glasziou PP, Mackerras DEM**. Vitamin A supplementation in infectious diseases: a meta-analysis. *British Medical Journal*, 1993,**306**:366-370.

54. **Hussey G, Klein M**. Routine high dose vitamin A therapy for children hospitalized with measles. *Journal of Tropical Paediatrics*, 1993,**39**:342-345.

55. Oluwole D, Mason E, Costello A. Management of childhood illness in Africa. *BMJ*, 2000,320:594-595.

56. **Claeson M, Waldman RJ**. The evolution of child health programmes in developing countries: from targeting disease to targeting people. *Bulletin of the World Health Organization*, 2000,**78**(10):1234-1245.

57. **Ewbank DC, Gribble JN**, eds. *Effects of Health Programs on Child Mortality in Sub-Saharan Africa*. National Academy Press, Washington, D.C. 1993.

58. **Bobadilla JL, Cowley P, Saxenian H, Musgrove P**. *The Essential Package of Health Services in Developing Countries*. Background Paper no. 1, *World Development Report* World Bank, Washington, D.C., 1993.

59. **Hill AG, MacLeod WB, Joof D, et al**. Decline of mortality in children in rural Gambia: the influence of village-level Primary Health Care. *Tropical Medicine and International Health*, 2000,**5**(2):107-118.

60. **WHO**. *The Multi-Country Evaluation of IMCI Effectiveness, Cost and Impact, Draft Progress Report.* Geneva, WHO, 2001.

61. **Humphrey JH, Rice AL**. Vitamin A supplementation of young infants. *Lancet*, 2000,**356**:422-424.

62. Schellenberg D, Menendez C, Kahigwa E, et al. Intermittent treatment for malaria and anaemia control at time of routine vaccinations in Tanzanian infants: a randomised, placebo-controlled trials. *Lancet*, **357**:1471-1477.

63. Alonso P, Gonzalez M. Menendez C, Font F, et al. Cost-effectiveness of iron supplementation and malaria chemoprophylaxis in the prevention of anaemia and malaria among Tanzanian infants. *Bulletin of the World Health Organization*, 2000,**78**(1):97-105.

64. **Bang AT, Bang RA, Tale O et al**. Reduction in pneumonia mortality and total childhood mortality by means of community-based intervention trial in Gadchiroli, India. *Lancet*, 1990,**336**:201-6.

65. **Pandey MR, Daulaire NMP, Starbuck ES, et al**. Reduction in total under-five mortality in western Nepal through community-based antimicrobial treatment of pneumonia. *Lancet*, 1991,**338**:993-7.

66. **Dawson P**. Community based intervention for control of pneumonia—Nepal. Background document prepared by Penny Dawson, MD, child survival resource person, John Snow International/Nepal for presentation at 3rd Canadian Conference on International Health, November 10-313, 1996, Ottawa, Canada.

67. **Kidane G, Morrow RH**. Teaching mothers to provide home treatment of malaria in Tigray, Ethiopia: a randomised trial. *Lancet*, 2000,**356**(9229):550-555.

68. Alam N, Wojtyniak B, Henry FJ, Rahaman MM. Mothers' personal and domestic hygiene and diarrhoea incidence in young children in rural Bangladesh. *International Journal of Epidemiology*, 1989,**18**:242-247.

69. **Haggerty PA**. *Community-based hygiene education to reduce diarrhoeal disease in rural Zaire: a prospective, longitudinal study*. PhD Thesis, University of London, 1991.

70. **Torun B.** Environmental and educational interventions against diarrhea in Guatemala. In: Chen LC, Scrimshaw NS, eds. *Diarrhea and Malnutrition: Interactions, Mechanisms, and Interventions*. New York, Plenum Press, 1982:235-266.

71. **Pinfold JV**. *A hygiene intervention designed to reduce the incidence of diarrhoeal disease in rural northeast Thailand*. Final report. Department of Civil Engineering, University of Leeds, England.

72. Ahmed NU, Zeitlin MF, Beiser AS, Super CM, Gershoff SN. A longitudinal study of the impact of behavioural change intervention on cleanliness, diarrhoeal morbidity and growth of children in rural Bangladesh. *Social Science and Medicine*, 1993,**37**:159-171.

73. Black RE, Dykes AC, Anderson KE, Wells JG, Sinclair SP, Gary GW Jr, Hatch MH, Gangarosa EJ. Handwashing to prevent diarrhea in day-care centers. *American Journal of Epidemiology*, 1981,**113**:445-451.

74. **Han AM, Hlaing T**. Prevention of diarrhoea and dysentery by hand washing. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1989,**83**:128-131.

75. **Khan MU**. Interruption of shigellosis by hand washing. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1982,**76**:164-168.

76. Sircar BK, Sengupta PG, Mondal SK, Gupta DN, Saha NC, Ghosh S, Deb BC, Pal SC. Effect of handwashing on the incidence of diarrhoea in a Calcutta slum. *Journal of Diarrhoeal Diseases Research*,1987,**5**:112-114.

77. Wilson JM, Chandler GN, Muslihatun, Jamiluddin. Hand-washing reduces diarrhoea episodes: a study in Lombok, Indonesia. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1991,85:819-821.

78. **Gove S**. Integrated management of childhood illness by outpatient health workers: technical basis and overview. *Bulletin of the World Health Organization*, 1997,**75**(Supplement 1):7-24.

79. **Jha P, Bangoura O, Ranson K**. The cost-effectiveness of forty health interventions in Guinea. *Health Policy and Planning*, 1998,**13**(3):249-262.

Region	Number of deaths	% worldwide deaths	Mortality rate Per thousand
Africa	3,806,000	36.2	150
Americas	453,000	4.3	34
Eastern Mediterranean	1,511,000	14.4	67
Europe	226,000	2.2	18
South-East Asia	3,502,000	33.3	88
Western Pacific	1,029,000	9.8	46
ALL	10,527,000	100.00	67

Table 1. Estimated Mortality Under Age 5, 1999

Table 2. Underlying Causes of Death Among Children Under Age 5, Developing Countries,1995

	%		
CAUSE	(deaths in		
	millions		
Prematurity	10 (1.5)		
Asphyxia	8 (0.9)		
Congenital anomalies	4 (0.5)		
Birth trauma	4 (0.4)	Neonatal and	
Neonatal sepsis & meningitis	4 (0.4)	perinatal	
Other neonatal and perinatal causes	10 (1.1)	causes:	
Neonatal tetanus	4 (0.5)	44%	
Measles	10 (1.1)		Vaccine-
Pertussis	3 (0.4)		preventable:
Tuberculosis	1 (0.1)		18%
Diarrhea (excluding neonatal)	19 (2.1)		
Acute lower respiratory tract	13 (1.5)		
infection (excluding neonatal			
pneumonia)			
Other causes (including medical and	10 (1.1)		
nonmedical causes)			
	100		
TOTAL	(11.2)		

Source: 5

NOTE: ¹Preventable with widely available vaccines. Newer vaccines (e.g., for *Haemophilus*

influenzae type b) should increase this percentage.

Table 3.	Distribution of	Causes of 10.8	3 Million Death	s at Age 0-4 in	All Developing
Countrie	es, 1998				

CONDITION	Percentage of Deaths
ARI	17
Diarrhoea	17
Measles	8
Malaria	7
Injuries	6
Congenital conditions	4
HIV/AIDS	3
Perinatal	20
All other	18
Malnutrition	Contributes to about 50% of
	all deaths under age 5

Table 4. Distribution of 3,774,000 deaths from ARI or Associated Conditions in <5 Year</th>Olds, Developing Countries, 1990

Condition	Number of deaths
ALRI (mostly pneumonia)	2,654,000
AURI (mainly otitis	58,000
media)	
ARI-measles	578,000
ARI-perinatal	240,000
ARI-pertussis	230,000
ARI-HIV	14,000

Table 5.	Percentage Distribution of Pneumonia and Diarrhoea Deaths by Age Group
Children	n in Developing Countries

Age	Pneumonia	Diarrhoea
(in full months)	(%)	(%)
0	22	9
1-5	36	37
6-11	17	14
12-17	9	15
18-59	16	35

	19	980	20	2000		
UN Regions	% Prevalence	Number (10 ⁶)	% Prevalence	Number (10 ⁶)		
and Subregions	(95% CI)	(95% CI)	(95% CI)	(95% CI)		
Africa	40.5	34.8	35.2	47.3		
	(36.2-44.8)	(31.1-38.5)	(31.1-39.3)	(41.8-52.8)		
Eastern Africa	46.5	12.9	48.1	22.0		
	(39.0-53.9)	(10.8-15.0)	(40.7-55.4)	(18.7-25.4)		
Northern Africa	32.7	6.0	20.2	4.4		
	(25.1-40.3)	(4.6-7.4)	(12.8-27.6)	(2.8-6.1)		
Western Africa	36.2	9.0	34.9	14.7		
	(29.9-42.4)	(7.5-10.6)	(29.2-40.6)	(12.3-17.1)		
Asia	52.2	173.4	34.4	127.8		
	(47.6-56.8)	(158.2-188.6)	(29.8-39.0)	(110.8-144.8)		
South-central	60.8	89.4	43.7	78.5		
Asia	(54.0-67.6)	(79.3-99.4)	(36.7-50.6)	(66.1-91.0)		
South-eastern	52.4	27.7	32.8	18.9		
Asia	(42.6-62.2)	(22.5-32.9)	(23.1-42.6)	(13.3-24.5)		
Latin America	25.6	13.2	12.6	6.8		
and the	(21.4-29.7)	(11.1-15.3)	(7.9-17.3)	(4.3-9.3)		
Caribbean						
Caribbean	27.1	0.9	16.3	0.6		
	(15.8-38.3)	(0.5-1.3)	(5.0-27.7)	(0.2-1.0)		
Central America	26.1	3.9	24.0	3.9		
	(15.9-36.2)	(2.4-5.4)	(9.9-38.0)	(1.6-6.2)		
South America	25.1	8.4	9.3 3.2			
	(20.3-29.9)	(6.8-10.0)	(4.1-14.4)	(1.4-4.9)		
ALL	47.1	221.3	32.5	181.9		
DEVELOPING	(42.7-51.6)	(200.3-242.4)	(28.0-37.0)	(156.9-207.0)		
COUNTRIES						

Table 6. Prevalence of stunting in preschool children, by UN regions and subregions1980 and 2000

SOURCE: 29

Handwashing		Several Behaviours		
Location	% reduction in	Location	% reduction in	
	morbidity		morbidity	
USA (73)	48	Bangladesh (68)	ca. 40	
Burma (74)	30	Zaire (69)	11	
Bangladesh (75)	35	Thailand (70)	34	
India (76)	32	Bangladesh (71)	26	
Indonesia (77)	89	Guatemala (72)	14	
Median	35	Median	26	

 Table 7. Impact of hygiene behaviour interventions on diarrhoea morbidity

SOURCE: 32

Age	Pooled OR (95% CI)
<2 months (excluding week 1)	5.8 (3.4-9.8)
2-3 months	4.1 (2.7-6.4)
4-5 months	2.6 (1.6-3.9)
6-8 months	1.8 (1.2-2.8)
9-11 months	1.4 (0.8-2.6)
12 months-2 years	1.6-2.1

Table 8. Risk of Dying Before Age 2 If Not Breastfed

Table 9: AIMS AND COUNTRY INTRODUCTION OF IMCI

Aims:

- To improve case management skills of health workers through training with locally adapted guidelines
- To improve the health system, including provision of essential drugs
- To optimise family and community practices in relation to child health, particularly care seeking behaviour

Introduction into a country involves:

- Orientation of national decision makers and the establishment of an IMCI working group
- Early implementation in a few districts, including adaptation of the guidelines, training of health workers, and health system support
- Scaling up, including community level activities

SOURCE: 78

TADIE IU: CALCULATED CUST-EFFECTIVENESS OF INTERVENTIONS FUR ARI CUNTRUM	Table 10:	CALCULATED	COST-EFFECTIVENESS	OF INTERVENTIONS FOR	ARI CONTROL
--	-----------	------------	---------------------------	-----------------------------	--------------------

Intervention	Expected	Proportio	Expected	Deaths	Cost per	Total cost	Cost per	Cost per
	disease-	n of ARI	ARI-	averted in	person in	(per million	death	DALY
	specific	mortality	specific	children	target	population)	averted	saved
	mortality	addressed	mortality	under 5	population	(US\$)	(US\$)	(US\$)
	reduction ^a	(%)	reduction	(per million	(US\$)			
	(%)		(%)	population)				
Case	60-90	38-52	23-47	351-676	3.61	220,000-	379-1610	37
Management	(80)	(49)	(39)	(585)		940,000	(926)	
						(541,777)		
Breastfeeding	50-80	4	2-3.2	15-96	5.00	40.00	417-2667	38
promotion	(72)		(2.8)	(42)			(952)	
EPI vaccines	44-80	20-25	8.8-20	66-600	9.08	122,580-	409-1857	40
	(65)	(22.5)	(14.6)	(219)		245,160	(995)	
						(217,920)		
Reduction of	50-95	70-90	35-85	263-2550	15.00	810,000-	697-3080	63
malnutrition	(80)	(80)	(64)	(960)	(malnourish	1,777,500	(1563)	
					ed)	(1,500,000)		
					11.85			
					(all			
					children)			
Pneumococcal	0-30	30-50	0-15	0-450	7.28	98,280-	437-?	67
vaccine	(15)	(40)	(7)	(105)		196,560	(1664)	
						(174,720)		

SOURCE: Based on [42])

Note: Most likely values in parentheses.

^a Disease is pneumonia except for EPI vaccines, where diseases are pertussis and measles; for pneumococcal vaccine, disease is pneumococcal pneumonia
Strategy	Intervention	Effectiveness (%) ^a :	Cost-effectiveness ^b
		Reductions in	Range (median), 1982 US\$
Child health	Promoting	Diarrhoea morbidity:	10-75 (45)
	breastfeeding	0-6 months: 8-20	
		0-59 months: 1-4	
		Diarrhoea mortality:	
		0-6 months: 24-27	400-10,750 (1000)
		0-59 months: 8-9	
	Improved	Diarrhoea mortality	50-2000 (1070)
	weaning	6-59 months: 2-12	
	practices		
Immunization	Rotavirus ^c	Diarrhoea incidence: 4	3-30 (5)
		Diarrhoea mortality: 13	140-1400 (220)
	Cholera ^d	Diarrhoea incidence: 0.2 ^e	90-1450 (174)
		Diarrhoea mortality: 2.8 ^e	1075-16,710 (2000)
	Measles ^f	Diarrhoea incidence: 3	3-60 (7)
		Diarrhoea mortality: 22	66-1156 (143)
Interrupting	Improving water	Diarrhoea incidence: 27	No meaningful estimates
transmission	supply and	Diarrhoea mortality: 30	
	sanitation		
	Promoting	Diarrhoea incidence: 14-48	
	personal and		5-500 (10)
	domestic hygiene		
Case	ORT	Diarrhoea mortality: ?	1,000-10,000
management			
[from text]			

 Table 11: Effectiveness And Cost-Effectiveness Of Interventions For Diarrhoea Control
 Among Young Children

SOURCE: 15

^a For children from birth to age 59 months, unless otherwise specified

^b Only considers diarrhoea deaths or episodes averted in children under age 5

^c Assumes 100% coverage with 80% vaccine efficacy ^d Assumes 100% coverage with 70% vaccine efficacy

^e In Bangladesh

^f Assumes 100% coverage with 85% vaccine efficacy

Intervention	Level of Delivery	US\$ per life year saved	Estimated % Guinea's years of life lost addressed by interventions		
<\$50 PER LIFE YEAR SA	VED	-			
Treat pneumonia	Centre	3	8.1		
Rehydration for mild diarrhoea	Centre	7	8.6		
Treat pneumonia, malaria and diarrhoea	Centre	8	13.9		
Treat malaria	Centre	13	7.4		
Vaccinate children	Centre	25	9.4		
Treat severe pneumonia	Hospital	31	0.6		
Treat severe malnutrition	Hospital	42	0.1		
Distribute impregnated bednets	Outreach	43	10.6		
Treat complicated measles	Hospital	48	0.1		
\$50-\$100 PER LIFE YEAR SAVED					
Deworming, vitamin A, iodine supplements	Outreach	67	2.4		
Treat rheumatic fever	Hospital	69	0.3		
Treat severe diarrhoea	Hospital	74	0.6		
Treat severe malaria	Hospital	87	0.5		
\$100-\$300 PER LIFE YEA	AR SAVED	-			
Educate mothers on	Hospital	108	8.1		
childhood pneumonia					
>\$300 PER LIFE YEAR S	AVED				
Construct pit latrines, provide safe water	Outreach	343	0.1		
Monitor growth, counsel mother on nutrition, pneumonia	Centre	600	8.5		
Treat mild malnutrition	Centre	779	0.4		

Table 12: Health Interventions in Guinea, Ranked by Cost-Effectiveness

SOURCE: 79



Figure 1: Under-5 Mortality: Gaps Between and Within Countries

SOURCE: 2

Figure 2: Pneumonia Management at the Small Hospital

For the child age 2 months up to 5 years with cough or difficult breathing (who does not have stridor, severe undernutrition, or signs suggesting meningitis)

CLINICAL SIGNS	CLASSIFY AS:	SUMMARY OF TREATMENT
		INSTRUCTIONS
Central cyanosis	VERY SEVERE	ADMIT
or	PNEUMONIA	Give oxygen.
• Not able to		Give an antibiotic: chloramphenicol.
drink.		Treat fever, if present.
		Give supportive care.
		Reassess twice daily.
• Chest indrawing	SEVERE	ADMIT
and	PNEUMONIA	Give an antibiotic: benzylpenicillin.
• No central	If child is wheezing,	Treat wheezing, if present.
cyanosis	assess further before	Give supportive care.
and	classifying.	Reassess daily.
• Able to drink.		
No chest	PNEUMONIA	ADVISE MOTHER TO GIVE HOME
indrawing		CARE.
and		Give an antibiotic: cotrimoxazole,
• Fast breathing.		amoxycillin, ampicillin or procaine
		penicillin.
		Treat fever, if present.
		Treat wheezing, if present.
		Advise the mother to return in 2 days for
		reassessment, or earlier if the child is
		getting worse.
No chest	NO PNEUMONIA:	If coughing more than 30 days, assess for
indrawing	COUGH OR COLD	causes or chronic cough.
and		Assess and treat ear problem or sore throat,
 No fast 		if present.
breathing.		Assess and treat other problems.
		ADVISE MOTHER TO GIVE HOME
		CARE.
		Treat tever, if present.
		Treat wheezing, if present.

[Notes omitted]

SOURCE: 11

Figure 3

Implementation of IMCI (December 2000)*

Discussions started in at



*Based on information available in December 2000

Source:

Under five mortality