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The Evidence Base for Interventions to Reduce Malnutrition in Children Under Five and School-age Children in Low and Middle-Income Countries

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Introduction

Nutritional deficiencies adversely affect the health and development of children and contribute to high levels of morbidity and mortality in the developing world. The aim of this paper is to examine the effectiveness of selected interventions impacting children under five and school-age children. This paper considers the scientific evidence for effective interventions to reduce malnutrition in childhood and asks some key questions: Which interventions have been shown to effectively treat malnutrition ? Which interventions need more documented evidence? What are challenges in implementing these interventions ? What is the way forward?

Although there are several different types malnutrition, this paper will focus on two types - micronutrient malnutrition and macronutrient malnutrition. Unlike many infectious diseases, nutritional deficiencies cannot be eradicated - they must be treated for elimination and the effects of the intervention must be sustained. This sustainability issue is the challenge that nutrition interventions face.

Several approaches to correct micronutrient deficiencies exist: vitamin supplementation, food-based approaches, multi-faceted approaches (growth monitoring and promotion, infant feeding), and general public health measures. The role of female education overall improvements in socioeconomic status are also key but do not fall into the scope of this paper.

Six types of interventions will be discussed. First, we examine the evidence around micronutrient supplementation (iodine, iron, and vitamin A) since we know the symptoms of these deficiencies, how to correct them, their public health significance, and the role they play in increasing child morbidity and mortality in developing countries. Zinc deficiency will not be discussed in-depth since there is not enough information yet on the public health significance of this deficiency. Second, interventions to deal with macronutrient deficiencies (PEM) such as food supplementation will be discussed. Third, public health measures such as treatment of intestinal helminths, improving sanitation and changing hygiene behaviors, and vector control for helminthic infections are addressed. Immunization, treatment of malaria, and interventions for the most common childhood illnesses are fully addressed in separate background CMH papers (see paper number 6 and 9). Fourth, we look at multi-faceted interventions such as growth monitoring and promotion (including nutrition education) and infant feeding (promotion of breastfeeding and improvement of complementary feeding practices). When well planned and implemented, such multi-faceted interventions have the potential to reach large populations and eliminate many deficiencies. Fifth, we briefly discuss food based approaches to combating nutritional deficiencies highlighting food fortification successes. Sixth, we look at interventions that involve food distribution in the school setting.

The paper is organised into six sections. Section A reviews the epidemiology of malnutrition, the main causes of malnutrition, including a description of the deficiencies. Section B reviews the evidence-base for the 6 types of interventions previously mentioned. Section C looks at delivery mechanisms. Section D looks at intervention-specific constraints and gaps in implementation. Lastly, based on our examination, conclusions are drawn and areas of further research identified in Section E.

SECTION A. Epidemiology of Malnutrition

Malnutrition and infection increase child mortality rates due to their synergy. Poor food intake linked with loss of nutrients from vomiting, diarrhea, malabsorption, and fever, such as with persistent diarrhea, all lead to nutritional deficiencies. These have serious consequences for the growth and immune system of the infants and children. On the other hand, infections can cause malnutrition by decreasing food intake, nutrient absorption, increasing metabolic requirements, and by direct nutrient loss. Thus, a child whose immune system is already suppressed becomes vulnerable to infection and is caught in a vicious cycle of malnutrition and infection.

1. Scope of the Problem

As a cause of death and disability, malnutrition is an important as a cause of death, both from its direct synergistic effect and its direct non-synergistic effect. In malnutrition, the vast majority of deaths are due to the direct synergistic effect of malnutrition whereas about 3% are due to the direct non-synergistic effect. Furthermore, an unmeasured amount of these deaths are due to an indirect effect that increases the incidence of the direct effect such as can be found in famine situations or in refugee camps.

(i) Malnutrition's direct synergistic effect

Malnutrition's potentiating effects on infectious disease mortality are well known, particularly in the case of childhood diarrhea and acute respiratory illnesses. In the early 1990s, Pelletier and colleagues (1994) provided the best quantitative estimate of this observed association: they estimated that in developing countries, malnutrition contributes to about half of all deaths among children, most of which are due to infectious diseases (1). The risk of death is increased even with mild and moderate malnutrition, and not just the most severe cases.

The cornerstone of Pelletier's methodology is knowledge of the strength of the association between malnutrition and mortality in developing countries as measured in eight prospective studies. These studies revealed remarkable consistency in relative risk across different grades of malnutrition. The mean and standard error of relative risk was 8.4 ± 2.1 for severe malnutrition, 4.6 ± 0.9 for moderate malnutrition, and 2.5 ± 0.3 for mild malnutrition (1). When this methodology was applied to survey data from Ethiopia, Malawi, Guatemala and India, it indicated that 42-57% of child deaths in the sample were attributable to malnutrition's effects on infectious diseases, of which 76-89% were attributable to mild-to-moderate malnutrition.

Murray and Lopez estimate that worldwide, malnutrition is a risk factor responsible for approximately 16% of disability adjusted life years (DALYs) and 15% of the burden of disease and injury in developing countries (1996) (2). The burden of disease attributable to malnutrition and its effects in children is 33% in Sub-Saharan Africa, 18% in India, and about

10% in the Middle Eastern Crescent and Other Asia and Island regions, whereas in Latin America and the Caribbean and China, the impact of malnutrition on the burden of disease is much lower (3). These calculations are based on work done by Mason and colleagues, who "estimated the burden of disease attributable to malnutrition with data from 55 studies on relative risk of mortality as a function of the standard deviation of nutritional status"(2). The proportion of the population aged 0-4 years with a weight-for-age lighter than 2 standard deviations below the National Center for Health Statistics reference population mean was used to estimate the attributable fraction of child mortality in each region. This methodology has not yet been peer reviewed. Nevertheless, the estimates indicate the magnitude of health gains possible if nutritional status of children could be improved so that no child had a weight-for-age more than 2 SDs below the population reference mean. These estimates also do not take into account low calorie or protein intake nor infectious disease episodes (3).

(TABLE 1 ABOUT HERE)

More recently, Rice and colleagues have examined the importance of malnutrition for specific causes of childhood death: diarrhea, acute respiratory illness, malaria and measles. A comprehensive analysis of the literature focusing on these four conditions provides a more detailed picture, but also points out large gaps in the evidence base (4). As expected, studies varied in quality and design. The measures used to describe nutritional status were largely anthropometric and did not provide much insight into the nature of the malnutrition, acute or chronic, or association with past infectious disease. Nonetheless, this study provides a baseline of the available information for these four conditions.

Diarrhea. The known relationship of malnutrition with diarrhea emerged clearly from the literature review. Diarrhea tends to be more severe and last longer in poorly nourished children, for whom the mortality risk is also higher. The mortality risk is increased for malnourished children with all types of diarrhea, but they appear to be highest for dysentery and persistent diarrhea (compared with acute watery or non-watery diarrhea, diarrhea occurring after measles).

Acute Respiratory Infections. Poor nutritional status conferred a twofold to threefold increased risk of death from lower respiratory infections and pneumonia in poorly nourished children, regardless of the organism causing the infection.

Malaria. Relatively few studies have reported on nutritional status of children with malaria, but the ones that have been published suggest a higher risk of death for malnourished children.

Measles. The evidence for an effect of malnutrition on death from measles is equivocal. Hospital based studies have reported a relationship, but this was not seen in any of the community-based studies. This is consistent with previous work that has pointed to other factors—overcrowding, intensity of exposure, and patterns of disease transmission—as more important risk factors for measles mortality (5;6).

HIV/AIDS. An emerging area of research is the contribution of malnutrition to HIV/AIDS mortality as nutritional status appears to affect HIV-related disease progression and mortality. Current understanding of the potential impact of nutritional interventions is very incomplete though. A review by Piwoz and Preble (2000) examined preliminary evidence that improving nutrition status may improve some HIV-related outcomes.

Early, longitudinal observational studies found that low blood levels of several nutrients, and low hemoglobin, were associated with faster HIV disease progression and reduced survival, after controlling for various conditions such as antiretrovirals use, dietary intake, and CD4 cell count, an indicator of HIV disease progression (7). Several reviews have been published recently on the role of micronutrients in HIV disease progression and mortality (8-12). These reviews concluded that “micronutrient deficiencies associated with HIV vary across populations according to disease stage:; are associated with an accelerated progression of HIV infection to AIDS and are predictive of AIDS-related mortality”. Piwoz and Preble found that results from micronutrient supplementation trials are mixed. The role of specific micronutrients in HIV progression and mortality are summarized in table 2:

(TABLE 2 ABOUT HERE)

The review by Piwoz and Preble suggested that as HIV affects nutritional status, nutritional status also appears to affect HIV-related disease progression and mortality. Improving nutrition status (particularly of the key nutrients reported here) may improve some HIV-related outcomes. They conclude that the benefits of nutrition interventions are likely to be greatest early on – to reverse underlying deficiencies and to prevent nutritional depletion. Once metabolic abnormalities are playing a leading role, the impact of nutritional intervention is likely to be limited (7).

(ii) Malnutrition’s direct non-synergistic effect

In low and middle income countries, deaths directly attributable to nutritional deficiencies are estimated to be about 300,000 of total under five deaths (approximately 3% of total deaths in children under five). Morbidity from nutritional deficiencies is also high in children under five and those 5-15 years old- 4.5% and 5% of total DALYs. Variation across WHO regions are listed in Annex 1, Table 1.

(TABLE 3 ABOUT HERE)

2. Causes of Malnutrition

Malnutrition is mainly caused by inadequate intake of calories, protein, and micronutrients. It is also caused by nutrient losses resulting from infections, and is further aggravated by metabolic increases. Contributing factors to malnutrition are inadequate food quantity and quality, insufficient income, knowledge, improper infant feeding, and inadequate child care. Insufficient knowledge, poor water and sanitation, unhealthy hygiene behaviors, inadequate supplies of drugs and vaccines, dehydration, and inadequate medical care also contribute to malnutrition.

Below we review definitions of deficiencies resulting from malnutrition.

(i) Iodine deficiency

Iodine deficiency is now recognized as a global problem in populations who live in an environment where the soil has been deprived of iodine. The main consequences of iodine deficiency is brain damage that can range from low IQ to severe mental retardation. Other consequences are impaired reproduction, increased neonatal and perinatal mortality, and impaired mental and physical development and hypothyroidism. Gioter, while one of the most visible consequences of iodine deficiency, is not a public health problem.

Those most vulnerable to this deficiency are pregnant women, the fetus, and newborns- making targeting women of reproductive age a priority for both their protection and that of the under five age group (13).

(ii) Anemia

Anemia is the most common form of malnutrition worldwide, with its most severe effects on pregnant women and young children. It is a condition in which the level of hemoglobin in the blood is below the normal range and there is a decrease in the production of red blood cells, often causing pallor and fatigue. Perhaps half of all children in developing countries have some level of iron deficiency anemia. While diets low in iron and with poor iron bioavailability are significant contributors to anemia, it is not the only cause. Where it is endemic, malaria is a major contributor, as are helminth infections, which are widespread throughout the developing world. Infants (except low birthweight infants) are usually born with good iron stores provided that the iron status of the mother is adequate, but after about 6 months, the iron content of breast milk is insufficient to meet their needs, and complementary foods are not usually high in iron. The risk of anemia is increased after 6 months as the child might no longer get enough iron from breastmilk. Additionally, complementary foods are usually based on cereals, low in iron.

(iii) Vitamin A deficiency

Vitamin A deficiency is the first cause of blindness in childhood. It increases the risk of morbidity and mortality in young children as well as that of mother. This deficiency is caused by dietary inadequacy, increased unmet physiological requirements, and by cultural factors which determine individual availability and consumption. The age groups at highest risk for vitamin A deficiency are children from the age of 6 months to six years during the complementary feeding period when the child often moves from a diet based on breastmilk to one based on cereals and, possibly, not varied. This transition increases the child's risk of vitamin A deficiency. Prevalence of the deficiency peaks from the period of 6 months to 2 years and is also greatest in low income groups and during seasons when food sources of the vitamin are scarce. Vitamin A deficiency can lead to interference with ocular function, impaired growth and reproduction, and increased morbidity and mortality. Measles can also be a precipitating factor in blindness due to vitamin A deficiency. Both mild and severe forms of vitamin A deficiency are associated with increased morbidity and mortality, especially from respiratory and diarrheal disease. Respiratory infection and other diseases increase the requirement for the vitamin and interfere with its intake through decreased appetite (13).

Vitamin A deficiency is widespread, particularly in Africa and South-East Asia, where some 3 million children under five years show signs of xeropthalmia. In 1998, WHO estimated that vitamin A deficiency was a problem in 118 countries. An estimated 250,000 to 500,000 children with the severest deficiencies become blind each year, and even larger numbers die preventable deaths from infectious diseases, mainly diarrhea and measles.

(iv) Protein-energy malnutrition (PEM)

PEM develops in children and adults whose consumption of protein and energy is insufficient to satisfy the body's nutritional needs. It is caused by either infectious diseases, insufficient intake of energy and protein, or a combination of the two. PEM inhibits child growth, increases morbidity, affects cognitive development, and reduces school performance and future labor productivity. Severe PEM affects brain growth, attention span, and short-term memory as well as activity level. In pre-school children it results in impaired learning and poor school attendance. While pure protein deficiency can occur when a person's diet provides enough energy but lacks the protein minimum, in most cases the deficiency will be dual. PEM may also occur in persons who are unable to absorb vital nutrients or convert them to energy essential for healthy tissue formation and organ function.

PEM is measured by low weight-for age and mid-upper arm circumference. WHO 2000 estimates of PEM prevalence in children under five by region are 42% in South East Asia Region (SEARO), 31% in Africa Region (AFRO), 20% in Eastern Europe Mediterranean Region (EMRO), 16% in Western Pacific Region (WPRO) and 6% in the Americas (AMRO) (14).

(v) Stunting or growth failure

Stunted children have low height-for-age when compared to the normal height for the age group. An estimated one-third of all preschool children—182 million—in developing countries were stunted, as indicated by low height-for-age, in the year 2000, a reduction of about one-third since 1980, when nearly half of preschool children were stunted. While the overall trend has been downward, and will probably continue in most places, the numbers are still staggering, and in some parts of the world little progress is being made or ground actually lost (Table 4.)

In terms of numbers, 70% of the world's stunted children live in Asia (mainly South-central Asia), 26% in Africa, and about 4% in Latin America and the Caribbean (15). Eastern Africa has the highest current prevalence of stunting (48.1%), a rate up slightly higher than it was 20 years ago (46.5%). The decrease all sub-regions of Asia has been steady and appears to be continuing. In Latin America, there has been little change in prevalence in Central America, but steep improvements in South America, as well as the Caribbean.

(TABLE 4 ABOUT HERE)

(vi) Zinc deficiency

Zinc is an essential trace element required for normal intestinal mucosal integrity, skeletal growth, sodium and water transport, and immune function. Deficiency in zinc has been associated with diarrhea and impaired immunity. Malnourished children are often zinc deficient and stores may be further depleted through fecal zinc losses during diarrhea episodes. As children in developing countries often suffer from 3-4 episodes of acute diarrhea per year, those in the cycle of infection-fecal nutrient loss may have low zinc stores putting them at risk of growth faltering and increased morbidity. Since zinc is associated with cell-mediated and humoral immunity, supplementation may enhance immune functions. More research is needed to confirm that supplementing malnourished children in diarrhea episodes may reduce growth faltering and morbidity.

(vii) Helminth Infections

Various helminth infections affect nutritional status in the under five and 5-15 year old age groups since they are most at risk for infection. An estimated 320 million school-age children are infected with roundworm, 233 million with whipworm, and 239 million with hookworm (16). Roundworm and whipworm infections usually occur in the pre-school years, with a peak prevalence among 4-5 year olds, and then remain at a high prevalence in all subsequent age groups; the intensity of infection peaks in children 5-10 years (13).

Three consequences of helminth infections are 1) direct disability, 2) protein-energy malnutrition and growth retardation, and 3) anemia. Anemia is one of the main consequences of infection with hookworm and whipworm. Other helminths contribute to varying degrees of PEM, growth faltering and anorexia. The blood loss to hookworm infection is proportional to the number of worms in the intestine (which feed on the intestinal mucosa), so untreated, the loss will generally increase as the child ages. The greatest effect is to increase the prevalence of moderate and severe anemia. Schistosomal infection, affecting an estimated 200 million people, also is a cause of severe anemia. Growth retardation (e.g., (17)) and reduced ability to learn (e.g., (18)) are major effects of these infections and their associated anemia.

SECTION B: Interventions for malnutrition

There are various interventions to address the causes of malnutrition infections. The table below briefly summarizes these interventions.

(TABLE 5 ABOUT HERE)

Certain nutritional deficiencies have a greater impact on children under five and school children. Table 6 shows the deficiencies or conditions, age group most affected, and the corresponding interventions that will be addressed in this review.

(TABLE 6 ABOUT HERE)

Interventions aimed at reducing malnutrition should focus on 1) increasing intake of protein and calories and 2) increasing intake and absorption of micronutrients, and 3) reducing infection.

This section examines the six types of interventions that impact nutrition

1. Micronutrient supplementation

This section examines micronutrient supplementation interventions found to be effective in treating micronutrient deficiencies. The discussion covers iodine, iron, vitamin A and zinc supplementation.

(i) Iodine supplementation

Iodine supplementation has its most pronounced effect when given during the prenatal or neonatal period because of its effect on prevention of early infant and child deaths. For mass supplementation, a 1 ml iodized oil injection (in poppyseed oil) containing 480 mg iodine is suitable. This dosage should be repeated in 3 years in iodine deficient areas. For iodized oil given by mouth, a single oral dose of iodized oil may be effective for 1-2 years (19).

A 1999 Cochrane review of two trials assessed the effects of iodized oil supplementation before or during pregnancy in geographic areas of iodine deficiency. Iodine supplementation was found to reduce risk of endemic cretinism at age four by 73% (95% C.I. 40-78%) and resulted in better psychomotor development scores in children between 4 to 25 months old. Iodine supplementation was associated with a 29% (95% C.I. 10-44%) reduction in risk of death during infancy and early childhood (20).

A trial by Cobra et al that examined the effect of iodine supplementation on newborns in Indonesia showed that it plays a role in the reduction of infant mortality. This study administered either 100 mg of oral iodized oil in poppyseed oil or a placebo and involved a total of 617 infants 6-10 weeks old. The findings were significant at the first 1 and 2 month follow-up with a mortality decrease of 81% (95% C.I. 15-96%) and 72% (95% C.I. 18-91%) respectively. The findings were non-significant at 4^{th} month of follow-up, with a mortality decrease of 52% (0.21-1.28) (21).

An overall 72% relative risk reduction of death was found within two months of treatment with the supplement (CI 95% 18-91%). Deaths in the iodine supplemented group occurred at a mean of 48 days after the treatment, while deaths in the placebo group occurred at a mean of 17.5 days after. The unadjusted risk ratio of death in the iodine supplemented group compared to the placebo groups was 0.19 and 0.28 respectively, during the 1st, 2nd and 4^{th} months of follow-up (21).

(ii) Iron supplementation

There are several ways to improve iron status in children. A long-term goal is overall nutritional improvement, through selection of iron-rich foods. Fortification of staples (e.g., flour, milk-based foods) or other widely used foods (e.g., fish sauce, curry powder, salt) with iron also allows increased iron intake with the usual diet. This section addresses iron supplementation, either through direct administration of liquid or tablet supplements, or, for children, the addition of a micronutrient preparation directly to foods by mothers. The key to iron supplementation is that it must be administered frequently in relatively small doses to be safe and effective. (This contrasts with vitamin A, which can be given in relatively large doses infrequently, as it is stored in the liver and used over time.) As discussed elsewhere in this paper, malaria prevention and helminth control are necessary components of anaemia prevention where these conditions are prevalent. Approaches to iron supplementation and malaria and helminth control may, in some cases, be combined.

The groups most likely to benefit from iron supplementation are young children, from about 6 months to 2 years, and pregnant women who should also receive folic acid for prevention of neural tube defects. These groups have the highest physiological demands for iron and are at greatest risk of iron deficiency anaemia, so are often the first target groups for supplementation. Particularly where malaria and helminth infection are also major causes of anaemia, other segments of the population may also benefit from supplementation. School children and adolescents are often targeted. Adolescent girls may benefit considerably from supplementation that improves their iron stores for future pregnancies (WHO/UNICEF/INACG).

WHO/UNICEF/International Nutritional Anemia Consultative Group (INACG) recommend daily supplementation (12.5 mg iron + 50 ug folic acid) starting at 6 months (2 months for low birthweight infants) for all children where anaemia is prevalent. Where the prevalence in children is <40%, the recommendation is to continue until 1 year of age, and where it is higher, until 2 years of age. Above 2 years, supplementation is still valuable where there is a continued significant prevalence of anaemia.

It is clear from decades of research and intervention studies that anaemia is a widespread and serious problem in a large number of poor countries, and that when iron supplements are used, they are effective in reducing the prevalence of anaemia. A meta-analysis of 22 trials examined the effectiveness of daily or weekly iron supplementation for pregnant women, adolescents and school children, and pre-school children (22). Outcomes included hemoglobin levels, ferritin levels, and anaemia prevalence. Both daily and weekly supplementation were efficacious at significantly improving outcomes, although weekly programmes suffered if supervision in taking the supplements was lax. For pregnant women, daily programmes were clearly more advantageous (22).

Direct supplementation of infants in conjunction with intermittent malaria treatment

In a randomised trial recently reported from an area of Tanzania highly endemic for falciparum malaria and severe anaemia, mothers of all infants (both control and experimental groups) were provided with iron drops to give their children daily from 2 through 6 months of age. The randomised portion was either intermittent curative doses of the currently-recommended antimalarial (sulphadoxine-pyrimethamine; S/P) or placebo during their EPI visits at 2, 3 and 9 months (23). 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). It was also reduced in the placebo group, due to the iron supplements alone, but there was a clear synergistic effect of both treatments. Use of the iron supplements was very high in the entire study group. (All primary analyses used a rigorous ‘intention-to-treat’approach, which included all 701 children recruited into the study.) An important feature of this trial was that conditions surrounding provision of the interventions were kept as “usual” as possible—for example, if mothers did not bring their children for EPI visits, they were not contacted specially to do so. This suggests that this basic approach of providing mothers with iron drops and giving them sufficient information about dosing can be effective.

Iron supplementation in complementary feeding

In addition to direct supplementation of infants and young children, approaches to adding iron and other micronutrients to complementary foods have been developed. Micronutrient “sprinkles” have been developed that include two or more of the following: iron, zinc, vitamin C, vitamin A, and iodine. These can be packaged in single-use doses, to be mixed once a day with whatever complementary food is being used. Preliminary trial results from Ghana suggest that this is an effective approach to treating anaemic children, and should probably be effective as a general anaemia preventive (24).

Another product that has been developed is a fat-based spread (like peanut butter) that is fortified with iron and other micronutrients. One teaspoonful per day can be mixed with complementary foods to provide all the micronutrient needs of infants. The product has been used with preschool children, who find it very acceptable, and acceptability trials are under way for infants in Bangladesh and Ghana (24)

(iii) Vitamin A supplementation

Three meta-analyses of vitamin A supplementation found decreases in overall mortality risk of 23-30% among children under five from supplementation (25-27). Vitamin A capsules providing 200,000 international units (IU) have been found to have at least 90% prophylactic efficacy for 4-6 months against developing mild xeropthalmia and corneal disease (28). Vitamin A supplementation has also been found to impact the severity of infections. Furthermore, there is strong evidence that the administration of vitamin A after the onset of severe illness is effective in reducing mortality from diarrhea, respiratory diseases and measles. In the analysis by Beaton, 5 of the 16 trials provided cause-specific mortality data with diarrhea, respiratory diseases and measles defined in common across trials. Fawzi et al examined 12 vitamin A hospital and community-based controlled trials looking at the effect of vitamin A on mortality due to pneumonia and total mortality. Glasziou et al examined 20 controlled trials of the effect of vitamin A supplementation on total mortality, cause-specific mortality, and morbidity from infectious diseases.

Overall Mortality

When looking at the impact of supplementation on mortality, a meta-analysis of 8 trials by Beaton et al showed a 23% relative risk reduction (95% C.I. interval 16-29%) in child mortality from vitamin A supplementation (25). Another meta-analysis by Glasziou et al found a 30% reduction in all cause mortality in children due to supplementation. In a third meta-analysis of 8 community-based studies, Fawzi et al found that mortality risk was decreased by approximately 25% with supplementation (26;27).

Infection-specific mortality

When looking at the effect of vitamin A supplementation on severity of infection, Beaton et al found that vitamin A supplementation had a greater impact on diarrheal disease and measles mortality than respiratory tract or malaria mortality. On the other hand, Beaton found that supplementation found no *important* effect on *incidence* or *duration* of the illness episode (25). Fawzi's meta-analysis found risk of diarrhea-specific mortality reduced by

30% (95% C.I. 16-34%) with supplementation. Administering vitamin A to children who developed pneumonia before or during a hospital stay was effective in reducing mortality by about 70% (95% C.I 15-42%), suggesting that supplementation reduced the *severity* of pneumonia among these patients once they had acquired the illness (27). They also found a protective relationship between supplementation and measles-specific mortality. Glasziou's meta-analysis found a 39% (confidence interval 24-50%) reduction in deaths from diarrhea, a 70% reduction (confidence interval 15-90%) in deaths from respiratory diseases and a 34% reduction (confidence interval 15-48%) in deaths from other causes from supplementation. Combined analyses in Glasziou's suggest a reduction of 30% (confidence interval 21-38%) in all-cause mortality (26).

Morbidity

Of the three meta-analyses, only Glasziou's meta-analysis found morbidity reductions (non-significant) from supplementation (26). Beaton's meta-analysis looked at morbidity but found the effect of vitamin A supplementation to be insignificant (25). Fawzi's meta-analysis only looked at mortality reduction and found the protective effect of vitamin A supplementation on all-cause mortality to be highest within the first year of life as well as a significantly protective relationship in the 12-23 month age group. They also found a protective non-significant relationship among children age 2 and older (27).

(iv) Zinc supplementation

There is preliminary evidence that zinc deficiency is related to the incidence or outcome of serious childhood infectious diseases and that supplementation can have both therapeutic and preventive effects. Zinc supplementation has been associated with reductions in incidence and duration of both acute and persistent diarrhea.

Diarrhea incidence and duration

A meta-analysis of zinc supplementation trials by Black found that zinc supplementation led to an overall 8-45% reduction in incidence of diarrhea, with greater effects in low zinc groups, underweight, and stunted children. Of five other zinc supplementation trials occurring after Black's meta-analysis, only Lira found a 28% reduction in diarrhea prevalence (29). Zinc supplementation was also attributed to 9-23% shorter diarrhea illness duration than in control children (30). The five other trials examined had findings that agreed with Black's on the direction of the effect but not magnitude. These other studies found reductions in diarrhea duration ranging from 14% to 43% (31-33).

Preventive for diarrhea, ARI and malaria

A number of trials have suggested that shorter term zinc supplementation during and shortly after diarrheal illness may help a child recover from excess zinc losses. The above meta-analysis by Black found reductions in diarrhea incidence ranging from 8-35%. The trials in the meta-analysis that examined zinc's preventive effect on ARI showed reductions from non-significant to 45%. For malaria prevention, the trials in the meta-analysis found zinc supplementation resulting in a reduction of 32-40% in clinic visits for malaria-related fever (30).

Zinc supplementation has been shown to play a role in decreasing incidence, duration and severity of diarrhoea in a limited number of studies. Some evidence exists that zinc supplementation is effective in preventing both ALRI and malaria but this needs to be investigated further. Despite preliminary findings, there is no evidence zinc supplementation leads to a reduction in child mortality chiefly because of few and insufficient numbers of large-scale trials to date. At the moment, no official national programs exist for control of zinc deficiency; only research projects in selected countries (34).

2. Food Supplementation for treatment of PEM

Although the evidence of the impact of food supplementation in reducing under five mortality is scarce but points to the fact that targeting malnourished children for a limited time period may be more effective than overall food supplementation programs. Rivera compared three month recovery rates for moderate wasting in four Guatemalan villages. Children were randomly assigned either a high-energy drink, a*tole,* or a low supplemental energy drink, *fresco*. Recovery rate from malnutrition was 12% higher in the *atole* group than in the *fresco* groups with the range of recovery of the children in the high-energy supplement group was between 29-52% attributable to supplementation (35). The results of a this study indicate that targeted supplementary feeding programs that increase dietary intake of already malnourished children by at least 10% may have a substantial effect on recovery from moderate wasting, even in populations with high prevalence of diarrhea. Food supplementation is most effective when targeted at most malnourished. Ideally, programs should provide high protein/high energy supplement for short time period. Past experience has shown that untargeted food supplementation is not effective and can become a financial burden.

Box 1: Targeted Supplementary Feeding: Tamil Nadu and Child Nutrition

India's Tamil Nadu Integrated Nutrition Project (TINP I), covering a rural population of more than 13 million, is one of the world's largest projects for nutrition education and targeted supplementary feeding. Though it did not achieve all its goals, it is one of the most successful efforts to date to reduce severe malnutrition.

The project was launched by the Indian Government in 1980 in response to previously unsuccessful untargeted public feeding programs that did not reach the most vulnerable. TINP I sought better targeted and more cost-effective ways to improve maternal and child nutrition and health. It covered the rural areas of those districts with the worst nutritional status -- about half the state, and a rural population of about 9 million. Its total cost of $81 million (originally estimated at $66 million) was supported by an IDA credit of $32 million. The credit became effective in 1980 and closed in 1989, two years later than planned.

TINP I sought to improve the nutritional and health status of pre-school children, primarily those 6-36 months old, and pregnant and nursing women. A central tenet of the project was that most malnutrition is the result of inappropriate child care practices, and not of income, famine, or unpreventable health problems, though these factors can be important. Growth monitoring -- monthly weighing of all children 6-36 months old -- was a critical element of this strategy. It was the way in which interventions were targeted only to problem cases, thereby controlling program costs. It was also an important educational tool, to explain to mothers why one child was receiving food and another not, and to provide them with objective feedback about how they were caring for their children. Indeed, this project was the first large-scale use of growth monitoring for this purpose.

The project's supplementary feeding component was also innovative. It focused on feeding very young children -- who are the most vulnerable to poor nutrition -- for relatively brief periods to help them recover their growth, in contrast to the more common approach of prolonged feeding of older children. It relied heavily on local nutrition workers, locally trained, working in conjunction with local women's groups (36).

3. Public health interventions

The following section looks at public health interventions that have an impact on nutritional status. We examine treatment with anthelminthics, improving sanitation and changing hygiene behaviors, and vector control for helminth infections.

(i) Anthelmintic drugs

An effective strategy for treatment of helminth infections is to administer anthelmintic drugs to individuals with the highest degree of exposure and the heaviest worm burdens. While parasitic infections in children under five and school-age children are not responsible for high rates of mortality (about 2% of total deaths), the burden of parasitic infections is sufficient to have an impact on child growth and development (37) (see table 2 and annex). Where ascariasis is the major helminth infection, the choice of anthelmintic is inconsequential since they all reduce egg rates effectively. Where hookworm and trichuriasis is prevalent, albendazole (single dose of 400 mg) has achieved the most effective reduction in worm burdens. The most commonly used dosage for albendazole is a single dose of 400 mg (2 tablets). Where trichuriasis is a problem, higher doses have also been tried. The treatment should be given thrice yearly (38).

De Silva reviewed a number of trials for the effect of anthelmintics on height and weight gain and found that treatment with anthelmintics resulted in an average weight gain up to 1.3 kg more and height gain 0.6 cm more than untreated children (37). Evidence of improvement in child weight and height after anthelmintic treatment was reviewed in a number of studies in developing countries. In Myanmar different age groups of children were treated with levamisole on a 6-month basis and showed morbidity declines despite small reductions in prevalence of ascaris (12-30%). Another trial in Kenya found high impact on growth from treatment with albendazole in an area with high prevalence of hookworm, trichuriasis, and ascariasis. Six months after treatment with albendazole, the treatment group had gained significantly more weight than the placebo group. A trial study in Myanmar that treated children age 2-12 in areas of high A. lumbricoides prevalence, found significant increments in height from six months onwards and significant weight gain at 24 months.

Further evidence of effectiveness is provided by a 2 year (1994-96) pilot randomized control trial by Awashthi et al (unpublished) in a heavily populated region of North Central India. This study involved approximately 4,000 children aged 1-4 and administered 6-monthly albendazole and vitamin A as the treatment whereas controls received vitamin A only. Outcomes examined were increases in height and weight (impact of vitamin A not examined in study). The researchers found that the treatment group had a 35% better weight gain ($p<0.0001$) (an absolute weight gain of 1kg), than the control group (39). There was a non-significant 6% improvement in height than the control group. The results confirmed the need for a larger mortality study with a 4 year duration beginning in 1997-98 in which much larger areas would be randomized. In this study, the treatment group will consist of at least 250,000 children whereas the control group will be at least 750,000 children aged 1-4 (39).

The impact of anthelmintic treatment on growth and cognitive performance was recently reviewed by Dickson et al (2000) (40). The review looked at 30 trials of children aged 1-16 years in which anthelmintic drug treatment for intestinal nematodes with any anthelmintic drug or placebo was administered. Immediate outcomes such as drug effect on worm infection were not examined. The review found little evidence to support the use of routine anthelmintic treatment to improve growth and cognitive performance in children in developing countries. When assessing effect of treatment on growth, for single dose trials, the pooled estimated of increase in weight were 0.24 kg and 0.38 kg. For multiple dose trials, the figures were 0.10 kg and 0.15 kg for up to one year of follow-up and 0.12 and 0.43 for more than one year of follow-up (40). This trial looked at cognitive performance in 5 of 30 studies and found inconclusive results. The review reported overall poor quality of trials and inconclusive evidence of the impact of mass treatment with anthelmintics on growth and cognitive performance to implementation of mass chemotherapy.

The Dickson et al review generated discussion by experts in the field that disagreed with the review's conclusions. Bundy and Peto claim that the review does not evaluate infrequent but regular treatment with anthelmintics from an early age, pointing to few trials and small numbers of subjects (41). Michael points to the positive average effect of mass treatment on both growth and cognitive performance and the fact that parasitic infections contribute to anemia, leading to poor learning, is further evidence of the need to mass treatment with anthelmintics (42). Other points of debate focus on short duration of treatment in the studies Dickson et al review as well as high rates of reinfection (43). Finally, Savioli and colleagues draw attention to the impact of population-based chemotherapy on variation in infections from mixed patterns of nematode infections transmitted in soils, prevalence of iron deficiency anemia and hookworm infection, stunting, intensity of transmission, nutritional intake, and retreatment schedules, all which impact effectiveness. In sum, the experts believed that all relevant evidence needed to be looked at before concluding that treatment with anthelmintics was ineffective and not worth investing in (44). It is important to note that Dickson et al did not look at the impact of a large, randomized trial such as the one currently taking place in India (trial does not look at cognitive performance outcomes).

(ii) Improving sanitation and changing hygiene behaviors

The impact of improved sanitation and changes in hygiene behaviors cannot be ignored in the overall discussion of improving nutritional status by means of public health measures. For a more in-depth review of water and sanitation interventions, please refer to the CMH "Water and Sanitation" note.

Esrey conducted several reviews that examined the evidence of the impact of sanitation on health outcomes. Of 30 studies reviewed that looked at sanitation, 21 documented some reduction in diarrhoeal disease, with a median reduction of 22% *(45;46)*. The type of improved excreta disposal method was important, with the greatest reductions reported for flush toilets, although pit latrines were also associated with morbidity reductions. Additional studies, such as one in Lesotho, document similar reduction levels *(47)*. Another review looking at the effect of improved infrastructure on diarrhoea rate reduction found that improving sanitation but not water resulted in a 37.5 % reduction in diarrhoea rates. The review also found that improving water but not sanitation resulted in a 20.8 % reduction, and improving both resulted in a 37.5 % reduction *(48)*. Improving access to sanitation can lead to greater improvements in health outcomes than improving access to water.

- Hygiene

Work by Feachem noted reductions in diarrhoeal diseases of 32-43% through handwashing with soap in different settings *(49)*. Three studies reviewed by Boot and Cairncross showed that handwashing education and soap availability resulted in reductions of 30-48% in disease prevalence *(50)*. Huttly et al reviewed the impact of hygiene on diarrhoeal prevalence, and calculated that a 35 % reduction in diarrhoeal prevalence was possible *(51)*. Another review by Curtis reports morbidity reductions between 27 and 89% as a result of handwashing *(52).* There have not been many studies looking at the sustainability of such interventions. One small study, in Indonesia, found that 79% of the women participating in the program (n = 65) still used soap for handwashing two years after the intervention *(53).*

(iii) Vector control for helminth infections

Three main strategies have been used for vectors control of parasites: chemicals (molluscicides), environmental (removal of snail habitats), and biological (use of natural predators or competitors). Of these, molluscicides have been used most extensively in control programs. Recently, availability of safe drugs, environmental concerns and cost of commercially available molluscicides have curbed their use in control programs. Other significant trematode infections have been controlled by improvements in sanitation. Lymphatic filarial infections have depended on vector control, insecticides and larvicides, and the environmental reduction of breeding sites. Onchocerciasis control has traditionally been done by vector control strategies but evidence points that morbidity control is best through the use of the ivermectin (38). Dracunculiasis has also been locally eradicated by vector control, filtering of drinking water through a cloth, provision of clean water and health education have been shown to be effective (54). While vector control has been shown to be effective, it needs to be integrated in a program that administers anthelmintic drugs in areas with high helminth prevalence.

4. **Multi-faceted interventions**

This section looks at interventions that can reach large populations and cover many deficiencies. The focus will be on infant feeding (breastfeeding and complementary feeding) and on growth monitoring and promotion, which includes a large nutrition education component. The impact of these interventions can be significant when scaled-up in real world conditions.

(i) Infant feeding

Exclusive and continued breastfeeding

Breastfeeding plays a preventive role from mortality from infectious diseases. An approximate 1.5 million deaths of young children might be prevented by improved breastfeeding and complementary feeding practices. Furthermore, establishment of exclusive breastfeeding at the time of birth reduces the risk of neonatal deaths.

As many of the consequences of poor infant feeding are manifest before a child is measurably malnourished, specific contributions of early, exclusive and continued breastfeeding and adequate and safe complementary feeding must be addressed. Poor feeding of infants and young children underlies much mortality and morbidity from infections.

The evaluation of the importance of breastfeeding was started in 1984 with a detailed review of 35 studies from 14 countries by Feachem and Koblinsky. Eighty-three percent of the studies found that exclusive breastfeeding was protective compared to partial breastfeeding. Eighty-eight percent of the studies found that exclusive breastfeeding was protective compared to no breastfeeding and 76% of the studies reviewed found that partial breastfeeding was protective compared to no breastfeeding. Furthermore, the median relative risks for infants that did not receive breastmilk were found to be 3.0 for those 0-2 months old, 2.4 for 3-5 months olds, and 1.3-1.5 for those 6-11 months old (49).

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 infants who were not breastfed, subdivided into several age groups. Original data from six major studies, involving about 18,000 children and about 1200 deaths before age 2 were available for reanalysis. Breastfeeding provided protection against mortality from infectious diseases greatest at younger ages, then declining over time, but remaining significant through the second year of life (table 7).

(TABLE 7 ABOUT HERE)

Considering the two main categories of infectious disease death, the risk of death for a non-breastfeeding child was greater for diarrheal 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.

The scientific evidence of breastfeeding and morbidity in healthy infants has been based on observational studies as it is unfeasible and unethical to randomly assign infants to breastfeeding versus formula feeding. Such studies have been full of bias related to the measurement, selections, confounding, and reverse causality and created doubt about the magnitude and existence of a protective effect of breastfeeding against infection in developing countries. The Promotion of Breastfeeding Intervention Trial (PROBIT), the first randomized control trial of the Baby Friendly Hospital Initiative (BFHI) (1996) provided the opportunity to assess the direct relationship between a breastfeeding promotion intervention and infant health and the link between infant feeding and infant mortality in healthy mothers and their infants, due to the large number of mothers and infants involved. This trial succeeded in increasing the duration and exclusivity of breastfeeding in the first year of life. The intervention was modeled on the BFHI which emphasizes health care worker assistance with initiating and maintaining breastfeeding and lactation, and postnatal breastfeeding support whereas the control groups continued usual infant feeding practices and policies. The primary outcome looked at was the risk of one or more episodes of gastrointestinal tract infection. The secondary outcomes examined were the risk of two or more episodes of any respiratory tract infection; two or more upper respiratory tract infections; the prevalence of breastfeeding at 3, 6, 9 and 12 months of age; and prevalence of exclusive and predominant breastfeeding at 3 and 6 months.

Results from PROBIT showed that an average of 73% of mothers were still breastfeeding to some degree at 3 months in the intervention group (60% of mothers in the control group). The intervention group had significantly higher rates of continued breastfeeding at 3 months and throughout the first year. The proportion of women exclusively breastfeeding at 3 months was 7-fold higher in the intervention group (43.3% vs. 6.4%) and more than 12-fold higher at 6 months (7.9% vs. 0.6%). Twice as many women in the intervention group were mainly breastfeeding at 3 months (51.9% vs. 28.3%) and almost 7 times as many at 6 months (10.6% vs. 1.6%). The intervention group also experienced a 40% reduced risk of 1 or more gastrointestinal tract infections in the first year of life. For respiratory tract infections, the risk reductions in the intervention group were small and non-significant (55).

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 (56;57).

There are several approaches to complementary feeding. A WHO/UNICEF Technical consultation on Infant and Young Child Feeding (2000) looked at the efficacy and effectiveness of complementary feeding interventions. This review looked at interventions that involved provision of food or multiple micronutrient supplements, nutrition education trials, and large-scale programs with multiple components. In this comprehensive review, Dewey (2000) examined 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 complementary food introduction (24).

The review highlighted 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 (Dewey, 2000):

- improving the energy and/or nutrient density of home-prepared foods,
- micronutrient supplementation, and
- use of processed (commercial) foods (24).

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 (24). 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 methodological 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(24).

(ii) Growth monitoring and promotion (GMP*)*

Growth monitoring and promotion (GMP) is not an intervention in itself but a tool/strategy/process to generate action. It enables mothers to visualise their children's growth and to initiate appropriate changes in behaviour to ensure healthy growth. It also encourages community participation and serves as an integrating strategy for providing nutrition and health interventions. GMP uses growth monitoring as an educational and motivational tool to promote action by mothers and communities to improve their child's health. It also serves as an instrument for information generation for program managers and tool for nutritional surveillance(58). As this strategy makes children's growth visible to parents, it serves as a motivator to action(59).

GMP involves mothers in the routine weighing of children and teaches them what to do when growth faltering occurs. It is best suited to programs with a preventive approach since it catches an early sign of health and nutrition problems - growth faltering. While traditional growth monitoring classifies children into mild, moderate and severe malnutrition categories, GMP is meant to examine the child's growth pattern or weight gain over time to catch faltering. In this manner, the strategy provides a means of identifying children as they start to fall in the synergistic spiral of infections and malnutrition in time halt the process.

The strength GMP lies in the ability to identify families in need of assistance. GMP involves a problem-solving process, often neglected as many programs weigh and plot children without an action plan. GMP can be used in programs that involve multiple interventions such as nutrition, diarrheal disease, ARI control, and early child development.

Nutrition education is a critical component of any GMP program since improvements in child growth involve changes in feeding and caregiver behaviours in the home. The individual nutrition counselling that can take place after a child's growth has been checked cannot replace traditional group sessions where a mother must find which information given to her is applicable to her child's situation.

There has been criticism of the little impact growth promotion programs have had on the nutritional status and growth of children. Evidence from both successful and unsuccessful programs have shown that unless a program has been designed and implemented to use growth data for decision making and action, improvements in health and nutritional status of the child cannot be guaranteed(60).

The impact of GMP is dependant on the means by which it is operationalised under different social, cultural and environmental conditions. This strategy must be translated into action at the field level to be successful. As a result, it must be understood that GMP is supposed to trigger appropriate action rather than directly improve health and nutrition.

The full impact of this program can be achieved when this strategy is used to make decisions about three types of action:

1- recommendations for individual children's care (feeding practices and care during illness)

2- community activity plans that extend beyond a single household to facilitate the process for families to maintain positive child growth (such as improvement of poor water conditions, child care, and food shortages)

3- program activities that bring about community actions affecting households with special needs such as income-generation or income transfer schemes (60).

5. Food-based approaches

Food-based approaches are effective long-term strategies for improving the consumption and production of micronutrient-rich foods but should not replace therapeutic measures, effective in the short-term. The various approaches are: 1) increasing small-scale production of micronutrient-rich foods, by community fruit or vegetable gardening, school gardening or small animal, poultry or fish production; 2) increasing community production of micronutrient-rich foods, such as horticultural products, oil seeds, palm oil, beverages and natural nutrient supplements; 3) maintaining micronutrient levels in commonly eaten foods with food storage and preservation techniques, improving food safety, better food preparation; 4) plant breeding to increase micronutrient levels; 5) food fortification; and community strategies to increase consumption of micronutrient-rich foods (61).

The main benefit of food-based approaches are that they offer sustainable, cost-effective, community-based solutions to the problem of micronutrient deficiencies. Because they are broad-based and aim to improve the overall quality of the diet, they can address multiple nutrient deficiencies. Furthermore, because the amounts of nutrients are consumed within normal physiological levels, the risk of toxicity is minimized. Food-based strategies also support breastfeeding and infant feeding interventions. Lastly, they build partnerships among governments, consumer groups, the food industry and other organizations.

Gross and Tilden have suggested that dietary diversification is the most cost-effective measure to improve vitamin A status (1988) (62). In Thailand, a social marketing of vitamin A rich foods, promoting the production and consumption cost approximately US $0.42 per capita (63) . In Indonesia, the cost of increasing consumption of green, leafy vegetables was estimated at US $0.28 per mother (64). One of the largest initiatives to date has been the Nutritional Blindness Prevention program in Bangladesh that has aimed to increase the production of carotene-rich foods, with a cost of US $0.13 per year (65).

Gillespie and Mason (1994) reviewed the results of outcome evaluation of vitamin A programs (2 breastfeeding interventions, 13 dietary modification interventions, and 4 food fortification programs). They found breastfeeding to be associated with a reduced risk of xeropthalmia. Food fortification programs were found to be effective at raising serum retinol levels in children and adults within one year of initiation. Evaluation of a study in Bangladesh showed that children living in households with home gardens were less likely to suffer from xeropthalmia (61).

Food Fortification- A Public Health Success Story

Food fortification is a non-therapeutic intervention and delivery mechanism that, when properly implemented, reaches large numbers of people, serves as a good preventive measure, and has a broad impact. Important elements needed for successful food fortification are the selection of an accessible, low-cost and widely consumed food vehicle, active participation of the food industry, and standardization of the amount of fortificant that the food vehicle will carry.

Although food fortification cannot always reach 100% of populations with micronutrient deficiencies, it can make an enormous difference for the expanding populations that regularly purchase and consume commercially processed foods. Examples of successful food vehicles are cereals such as rice, corn and wheat flour, fats and oils, dairy products such as milk, and condiments such as sugars, spices, and starches.

A historical review of food fortification showed that since the early 20th century, food fortification has decreased and eliminated micronutrient deficiencies in many countries. In the early 20th century, Switzerland began salt fortification with iodine. In 1918 Denmark fortified margarine with vitamin A. During the 1930s and 40s, a number of industrialized countries fortified milk with vitamin A and flour with iron and B vitamins. As a result of such achievements, the elimination of vitamin A deficiency, iodine deficiency disorders and a reduction in iron deficiency anemia as well as the essential elimination of diseases such as xeropthalmia, pellagra, beri-beri, rickets, goiter, and ariboflavinosis has taken place in Europe and North America.

6. Interventions involving food distribution

School Feeding

School feeding and specifically, lunches have been viewed as a means for a child to receive a large meal in the middle of the day, helping the family since the child will not eat the mid-day meal at home. These programs are generally costly and their effect on improvement of nutritional status is small. Due to the fact that a large amount of resources are spent on school meals, policymakers need to know the benefits from investment in school feeding programs. For the most part, evaluations thus far have lacked scientific rigor and have had no pre-intervention measures or control group. Provision of food via school feeding programs is expensive. Aside from the cost of the food itself, logistics and management of these programs can create a financial burden for governments investing in this intervention (66).

One of the first randomized controlled trials of a school feeding program was conducted in rural Jamaica by Powel and colleagues. In this trial, about 800 children were randomly assigned to receive breakfast or to a control group. The treatment group received a daily breakfast of approximately 576-703 kcal and 27.1g protein and the control group received a quarter of an orange that supplied approximately 18 kcal and 0.4g protein (35). Children were divided into undernourished and well-nourished groups in both control and breakfast groups and only a small proportion of children in each class were given breakfast. Results showed that height, weight and educational performance in some subjects improved in the groups that were given the breakfast. Significant benefits of breakfast on arithmetic achievement were seen, especially in the 2^{nd} and 3^{rd} graders. No significant effects were seen in spelling or reading. Children who received breakfast gained more weight, increased in height, and BMIs more than those in the control groups. Furthermore, in the well-nourished group, the increase was significantly more than those in the undernourished group (67).

Children who received breakfast showed small but significant improvements in attendance compared with the control groups. Undernourished children in this study did not necessarily benefit more from provision of breakfast than the well-nourished group. The fact that both nutritional status and attendance improved indicates that school feeding, in the form of a school breakfast, could be an effective way of improving nutritional status where undernutrition is a problem. In light of the evidence, it might be appropriate to target undernourished children for school meals of this type where resources are too limited to feed all children (68).

A viable option for provision of food in a school setting is a breakfasts or snacks, provided early in the day, thus helping to improve attention, concentration, and achievement among children. A breakfast or snack may provide about one-third of the recommended daily allowance for energy and protein and be more effective than a lunch (68). Additionally, rations that fill in micronutrient gaps in children might have greater impact on learning.

The non-health benefits of school feeding programs such as increased enrollment and lower attrition rates are clear. Due to the high cost of these programs, more evidence is needed on the nutritional impact school feeding programs have on the recipients.

SECTION C: Delivery Mechanisms

1. Outreach-based Delivery Systems

Outreach-based delivery is an important mechanism for reaching children under five who cannot benefit from school-based programs. This mechanism is important since it offers the possibility of reaching children whose caretaker may not seek care at a health care facility. It is also critical for conditions such as vitamin A, iron, iodine supplementation, and for treatment with anthelmintics. Outreach mechanisms can enable a child to receive the supplement twice a year. Additionally, since children under five are not covered by school-based deworming or iron supplementation programs, they can also be reached by community outreach. The following section discusses a few of these outreach based interventions.

(i) Vitamin A supplementation during National Immunization Days (NIDs)

The use of National Immunization Days to deliver vitamin A is an example of another effective delivery mechanism where multiple child interventions can take place in a cost-effective manner. In 1997, more than 450 million children, almost two-third of those under age five, were immunized during polio NIDs (see vaccine paper for this issue). In 1998, a total of 22 African countries administered vitamin A during their NIDs. Vitamin A supplementation during NIDs has been shown to be a cost-effective delivery mechanism costing approximately $0.02 per dose (69). Furthermore, the availability of vitamin A has been shown to increase attendance during NIDs and the offer of vitamin A aside the polio vaccine acts as an incentive for caregivers to take children to immunization posts. As children with vitamin A deficiency should receive a supplement at least twice a year, a context for administration of the second vitamin A dose has been explored in such countries as the Philippines, Nepal, and Niger (69). They have organized “micronutrient days” or “vitamin A” days approximately 6 months after the NID has taken place. As polio is close to being eradicated, it will be necessary to sustain this delivery mechanism and find alternate means of administering vitamin A to children under five since the reduction in child mortality attributable to vitamin A supplementation is comparable to childhood vaccines.

(iii) School-based treatment of helminths and micronutrient supplementation

School-based helminth control serves as an effective delivery strategy for delivering anthelmintic drugs to children in areas where infection is prevalent. Since treatment is done without screening individuals for infection, it is an easy, cost-effective, and safe way of controlling helminth infections in children. Schools also offer existing infrastructure for low-cost delivery, clinical surveillance, and community mobilization for awareness building. Micronutrient supplementation can also be administered based on the premise that a large proportion of children in a particular area are deficient in iron, iodine or vitamin A. Delivery of micronutrients in the school setting is inexpensive if integrated with a helminth control program. If fortified foods are the micronutrient vehicle, then delivery of these can also be effectively done in the context of a school breakfast program.

(iv) *Community-based approaches*

In a rural area of Madhya Pradesh, India, a weekly "Nutrition and Health Day" has been designated on which pregnant women and children under age 2 receive a number of interventions from a health worker at the local "Anganwadi Centre" (a special centre for custodial care of young children). Included are iron-folic acid supplements, as well as nutritional supplements, appropriate immunizations, vitamin A, and nutrition education for mothers. In a before-and-after evaluation, a 2-5 fold increase in iron supplementation was reported (70).

Anganwadi Workers in India

Anganwadi Workers health workers go in to the community to look after the needs of mother and child immunization, antenatal and post-partum care for mothers, hygiene in the community, and to help build awareness of the facilities available to them. Anganwadis function under the Integrated Child Development Scheme of the Central Government and the Urban Social Nutrition Program of the norms (71). There is one Anganwadi for every 1,000 persons and the large part are women. An Anganwadi worker's main job is to provide pre-primary education and two meals, a day, to children below six years from the weaker sections of society.

For schoolchildren and adolescents, schools have been used in a number of places to distribute iron supplements. A recent placebo-controlled randomized trial compared daily (5 days per week) with weekly school supplementation for girls age 12-18, with both schedules being efficacious and practicable (72). The school structure provides the ability to monitor the taking of supplements in this age group.

2. Case management

Case management—specifically, integrated management of serious childhood illness—was identified in the 1993 World Development Report 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 (73). '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 strategy 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 IMCI strategy covers case management for ARI, diarrhoea, malaria, and malnutrition. This strategy also promotes actions within the community to support key family practices around nutrition such as supporting breastfeeding and complementary feeding of children with the aim of preventing malnutrition. For a more in-depth discussion of the IMCI strategy, please refer to the CMH under five mortality interventions paper.

Other types of case management for micronutrient deficiencies is focused on correcting micronutrient deficiencies upon diagnosis. With mild or moderate deficiencies, case management can be supervised by community health workers. For more severe deficiencies, hospitalization may be required. Case management looks at indicators and signs of deficiencies and improvement of these after treatment. For anemia, this means measuring hemoglobin levels, for iodine deficiency, goiter prevalence in a population or urinary iodine for individuals, and for vitamin A deficiency, looking for signs of night blindness, Bitot's spots, or corneal scars or ulceration as well as measuring serum and liver retinol levels (13).

Case management for malnutrition should also take into account malaria endemicity, measles and presence of other infections that can affect nutritional status.

SECTION D: Constraints

Constraints for nutrition interventions center around 1) linking supply and demand with logistics, 2) limited effectiveness of single interventions, 3) compliance with treatment 4) mobilization of communities, and 5) human resource issues.

1. Supply, demand and logistics

Adequate supply and demand of micronutrient supplements and anthelmintic drugs is important but not the only important factor needed for programs offering these interventions. Linked to supply and demand are logistics and the need to develop methods to deliver drugs on a regular basis. If people at the receiving end of an intervention that distributes drugs see that they cannot get what they need, they will lose trust in the program, and the intervention. Such a situation can make therapeutic, normally effective interventions are ineffective.

2. Limited effectiveness of single interventions

This constraint is present in supplementation with iron for anemia which is efficacious but insufficient in anemia control. Iron supplementation can only decrease the prevalence of iron deficiency anemia alone but is not effective as a single intervention when helminth infections or malaria are also present. Other nutrient deficiencies such as vitamin A also limit the response of anemia to iron supplementation.

3. Compliance with treatment

Many supplements cause minor side effects that affect compliance with recommended treatment. The classic case is with iron, many times having a disagreeable taste or causing stomach pains. A child may also experience vomiting or diarrhea after being given oral vitamin A. Such negative effects can affect compliance.

4. Mobilization of communities

Buy-in of community leaders, competing priorities, and passivity to responding to conditions such as helminths or diarrhea, that the community might not see as a contributor to morbidity all pose constraints to the effectiveness of nutrition interventions. Lack of awareness of the mortality risks associated with nutritional deficiencies and the high levels of morbidity from helminth infections are also constraints to the acceptance and sustainability of such programs.

5. Human resource issues

Human resource constraints such as inadequate number of health personnel, training for provision of care, lack of supervision, inadequate referral mechanisms for severe deficiencies. Inadequately trained or lack of staff to counsel the mother on breastfeeding, infant feeding, and care of the sick child pose constraints to interventions such as growth monitoring, food supplementation and nutrition education.

SECTION E: Conclusions

1. Micronutrient supplementation have been found to be effective in reducing child mortality and morbidity in randomized control trial settings. In the presence of helminth infections or malaria, iron supplementation alone cannot reduce anemia prevalence. There is preliminary evidence that zinc supplementation has an impact on reducing incidence and duration of both acute and persistent diarrhea. Despite preliminary findings, there is no evidence zinc supplementation leads to a reduction in child mortality. More trials are needed to evaluate the impact of zinc supplementation on under five mortality.

2. Food supplementation is an effective intervention for protein-energy malnutrition if it is carried out on a targeted and short-term basis.

3. Public health interventions have a large impact on nutritional status when combined with nutrition interventions. Vector control and interventions for improving sanitation and hygiene behaviors are effective but not sufficient to control helminth infections.

4. Multi-faceted interventions

A sufficient number of large and standardized studies (RCTs) have not been available to evaluate the nutritional impact of growth monitoring and promotion programs on their mortality reduction. Nonetheless, there is considerable literature evaluating the effectiveness of GMP programs. The same can be said for breastfeeding promotion in addition to the fact that it is unfeasible and unethical to randomly assign infants to breastfeeding versus formula feeding.

5. Food based approaches are long-term, sustainable interventions that need to be introduced in a staggered manner while maintaining short-term strategies such as micronutrient supplementation. These strategies are not effective in the short-term when timeliness of treatment is needed to prevent mortality.

6. School feeding programs - Although school feeding has been found to be effective in improving school attendance, it has been shown to have a small impact on nutritional outcomes. Due to their high cost and limited nutritional benefits, more evidence of the effectiveness of school lunch programs in improving nutritional status is needed. A school feeding option worth investing in could be a school breakfast program, targeted to the most undernourished.

The way forward

Overall there is substantial evidence investing in nutrition interventions to improve the health status of children improves health outcomes. Further research is needed to bolster evidence for multi-faceted interventions since the complex, multi-component nature of these interventions does not allow comparison to those interventions that be tested in randomized control trial settings. For such interventions, where there is not sufficient evidence of the type provided by experimental designs, more research is needed to create a pool of evidence that can serve as a policy instrument to promote these further in low and middle income countries.

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Table 1: Deaths caused by malnutrition's direct synergistic effect

Region	Deaths	% of total	DALYs	% of total
Established market economies	0	0.0	0	0.0
Former Socialist Economies	0	0.0	0	0.0
India	1,723	18.4	64,536	22.4
China	278	3.1	11,147	5.4
Other Asia and islands	679	12.3	25,758	14.5
Sub-Saharan Africa	2,619	31.9	96,434	32.7
Latin America and Caribbean	135	4.5	5,059	5.2
Middle Eastern crescent	447	9.8	16,641	11.0
World	5,881	11.7	219,575	15.9

Source: (3)

Table 2: Possible Effect of Specific Nutrients in HIV Progression and Mortality

Nutrient	**Effect**
Vitamin A	Reduced diarrhea morbidity and mortality, and improved several indicators of immune status in children (no impact in adults)
Vitamin B 12	Improved CD4 cell counts
Vitamins E and C	Reduced oxidative stress and HIV viral load
Selenium and beta-carotene	Increased anti-oxidant enzyme functions
Zinc	Infectious disease morbidity (though conflicting findings)
Multivitamins (A, B, C, E, folic acid)	Improved pregnancy-related outcomes and CD4/CD8 cell ratios in women (no impact on MTCT to date)
Reversing anemia	Increased survival time
N-3 fatty acids (fish oil):	Weight gain in some HIV-infected adults
High energy/protein liquid supplements	With counseling improved weight gain, maintenance in some HIV+ adults
Glutamine + vitamins C, E, Beta-carotene, selenium, and N-acetyl cysteine	Weight gain, and metabolically active tissue gain (BCM)

Source: (7)

Table 3: Deaths, DALYs, by Condition, 1998

	TOTALS			
	Deaths		**DALYs**	
	<5	**5-15**	**<5**	**5-15**
All Causes	**10 697 506**	**2 050 198**	**423 978 676**	**129 812 987**
Nutritional deficiencies	**292 952**	**46 048**	**19 093 527**	**6 545 913**
Protein-energy malnutrition	214 112	7 466	14 046 414	280 438
Iodine deficiency	11 906	2 874	866 126	120 341
Vitamin A deficiency	49 053	26 863	1 721 970	1 008 588
Anaemias	17 388	8 766	2 438 132	5 124 953
Other nutritional disorders	493	79	20 886	11 592

Table 4: Stunting in Preschool Children, by UN Regions and Sub-regions, 1980 and 2000

Prevalence (%) and Numbers (millions, in parentheses)		
Region	**1980**	**2000**
Africa	*40.5 (34.8)*	*35.2 (47.3)*
Eastern Africa	46.5 (12.9)	48.1 (22.0)
Northern Africa	32.7 (6.0)	20.2 (4.4)
Western Africa	36.2 (9.0)	34.9 (14.7)
Asia	*52.2 (173.4)*	*34.4 (127.8)*
South-central Asia	60.8 (89.4)	43.7 (78.5)
South-eastern Asia	52.4 (27.7)	32.8 (18.9)
Latin America/ Caribbean	*25.6 (13.2)*	*12.6 (6.8)*
Caribbean	27.1 (0.9)	16.3 (0.6)
Central America	26.1 (3.9)	24.0 (3.9)
South America	25.1 (8.4)	9.3 (3.2)
All developing countries	*47.1 (221.3)*	*32.5 (181.9)*

Source: **(15)**

Table 5: Causes of malnutrition and interventions

Causes of Malnutrition	Contributing Factors	Interventions
Inadequate intake of calories, protein, amino acids	Food (quantity & quality)	Resource transfer: supplementary foods✪
		Subsidies, transfer programs
		New foods
		Fortification✪
		Agricultural production
	Income	Income generation
	Knowledge	Nutrition education: information, behavior change ✪
	Infant feeding	Promotion of breastfeeding
	Time	Provision of child care
		Accessible cooking and water facilities ●
Nutrient losses	Knowledge	Hygiene ●
	Water	Improved quality Improved quantity ●
	Feces	Latrines ●
	Drugs	Drug administration
		Drug education
	Vaccines	Immunization
	Dehydration	Oral rehydration therapy or home remedies
	Medical care	Medical care

Source: (74)

✪ included in this review

● to be discussed in Water and Sanitation review

to be discussed in Immunization review

to be discussed in <5 mortality review

Table 6: Deficiencies, Consequences and Age Group Most Affected

Deficiency or Condition	Consequences of deficiency or condition	Age Group with Highest Burden	Interventions
Vitamin A deficiency	- Xeropthalmia - Impaired growth - Increased morbidity - Increased mortality	6 month old - 6 yr olds	- Supplementation - Food fortification - diet diversification - nutrition education
Iodine deficiency	- impaired reproduction - severe, mild mental retardation - growth inhibition - reduced productivity	- children < 12 months - pregnant women	- maternal supplementation - neonatal supplementation - food fortification
Anemia	- growth retardation - cognitive dysfunction - reduced productivity - increase morbidity	- children > 6 months age - school-age children - pregnant women	- supplementation - food fortification - diet diversification - nutrition education
Protein-energy Malnutrition	- wasting - stunting - kwashiorkor - marasmus - increased morbidity - increased mortality	Children <5	- food supplementation - growth monitoring - nutrition education
Zinc deficiency	- impaired immunity - increased morbidity - growth faltering	Children <5	- supplementation
Intestinal Nematode infections	- increased morbidity - anemia - other micronutrient deficiencies	- children <5 - school-age children	- anthelmintic treatment - vector control - hygiene education-behavior change

Source: (38;54)

Table 7: Risk of Dying Before Age 2 If Not Breastfed

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

Source: (75)

ANNEX Table 1: Deaths and DALYs due to Nutritional Deficiencies and Helminth Infections in Low and Middle Income Countries, 1998

	AFRO				AMRO				EMRO			
	Deaths		DALYs		Deaths		DALYs		Deaths		DALYs	
	<5	5-15	<5	5-15	<5	5-15	<5	5-15	<5	5-15	<5	5-15
All Causes	**4 028 710**	**722 769**	**150 511 836**	**40 239 825**	**485 324**	**105 160**	**20 902 397**	**8 386 985**	**1 324 874**	**241 877**	**52 400 659**	**13 339 358**
Tropical diseases	**1 374**	**14 538**	**184 199**	**1 761 306**	**241**	**283**	**10 922**	**36 269**	**471**	**1 623**	**30 320**	**176 807**
Schistosomiasis	24	413	42 887	506 972	5	15	1 145	19 249	9	136	4 331	56 828
Lymphatic filariasis	0	0	74 478	486 166	0	0	363	2 251	0	0	4 753	32 243
Onchocerciasis	0	0	14 088	170 838	0	0	52	584	0	0	868	10 977
Intestinal nematode infections	**0**	**880**	**3 139**	**207 270**	**3**	**1 450**	**5 646**	**387 886**	**0**	**382**	**2 329**	**79 156**
Nutritional deficiencies	**89 362**	**12 054**	**5 019 781**	**1 267 235**	**27 491**	**4 430**	**1 369 089**	**343 242**	**48 291**	**5 552**	**2 883 832**	**680 564**
Protein-energy malnutrition	69 576	1 655	3 948 577	62 137	21 789	1 728	977 479	64 902	36 232	334	2 144 129	12 529
Iodine deficiency	1 023	257	84 237	12 556	747	137	52 965	6 438	1 585	347	116 154	17 012
Vitamin A deficiency	16 167	8 862	567 809	332 746	2 436	1 013	85 669	38 054	8 406	4 217	294 975	158 335
Anaemias	2 596	1 280	419 158	859 795	2 316	1 533	245 278	232 585	2 068	654	328 574	492 687
Other nutritional disorders	0	0	0	0	202	18	7 698	1 263	0	0	0	0

	EURO				SEARO				WPRO			
	Deaths		DALYs		Deaths		DALYs		Deaths		DALYs	
	<5	5-15	<5	5-15	<5	5-15	<5	5-15	<5	5-15	<5	5-15
All Causes	**336 314**	**71 937**	**13 601 386**	**4 566 049**	**3 491 473**	**674 288**	**138 739 196**	**46 803 937**	**1 030 811**	**234 168**	**47 823 202**	**16 476 834**
Tropical diseases	**91**	**177**	**4 476**	**16 299**	**1 788**	**11 071**	**161 561**	**1 207 539**	**16**	**101**	**11 831**	**65 384**
Schistosomiasis	2	28	398	6 218	0	2	89	1 095	0	3	144	2 164
Lymphatic filariasis	0	0	41	227	0	0	91 031	549 244	0	0	11 066	58 770
Onchocerciasis	0	0	0	0	0	0	0	0	0	0	0	0
Intestinal nematode infections	**1**	**84**	**560**	**16 925**	**3**	**4 306**	**12 789**	**934 555**	**11**	**5 775**	**18 646**	**1 199 086**
Nutritional deficiencies	**10 479**	**1 362**	**737 572**	**267 159**	**79 052**	**16 260**	**6 384 534**	**2 477 615**	**38 277**	**6 390**	**2 698 720**	**1 510 097**
Protein-energy malnutrition	7 565	60	514 066	2 241	55 295	3 454	4 756 555	129 778	23 654	236	1 705 609	8 851
Iodine deficiency	359	85	38 454	4 389	4 133	1 115	296 729	43 620	4 059	933	277 587	36 325
Vitamin A deficiency	1 749	937	61 367	35 182	14 373	8 663	504 055	325 212	5 921	3 172	208 095	119 059
Anaemias	515	219	110 497	215 018	5 250	3 029	827 196	1 979 005	4 643	2 050	507 429	1 345 862
Other nutritional disorders	291	61	13 188	10 329	0	0	0	0	0	0	0	0

ANNEX Table 2: Disability and Nutritional Consequences of Helminth Infections & Treatment

Infection	Disability	PEM and Growth Retardation	Anemia	Treatment
Nematodes				
Ascaris lumbricoidis (Roundworm)	Intertwined worms may cause intestinal obstruction and single worms may obstruct bile duct	Growth faltering, reversible by intervention. May include protein loss and lactose malabsorption	n.a.	Mebendazole, albendazole
Trichuris trichiura (Whipworm)	Prolapsed rectum and chronic colitis; Moderate infections	Stunting associated with colitis.	Heavy infections can result in anemia	Mebendazole, albendazole
Ancylostoma duodenale (Hookworm)	Heavy infections cause fatigability, headache, numbness, tingling, dyspnea, palpitations, anorexia, dyspepsia, pedal edema, and sexual dysfunction.	Little effect on macronutrient absorption except some possible protein loss	Anemia is major consequence of hookworm infection	Mebendazole, albendazole
Necator americanus (Hookworm)	Heavy infections cause fatigability, headache, numbness, tingling, dyspnea, palpitations, anorexia, dyspepsia, pedal edema, and sexual dysfunction.	Anorexia with heavy infections	Major consequence of hookworm infection	Mebendazole, albendazole
Dracunculus medinensis (Guinea worm)	Mortality constraints for up to 30 weeks; cutaneous lesions	n.a.	n.a.	
Strongyloides stercoralis (Strongyloidiasis)	Autoinfection	Studies point to growth retardation and possible protein deficiency	n.a.	Mebandazole, albendazole, ivermectin
Trichuris trichiura (Whipworm)	Rectal prolapse	Substantial, reversible growth retardation	Probable anemia in heavy infections	Mebandazole, albendazole, ivermectin
Wuchereria bancrofti, brugia malayi (Filariasis)	Elephantiasis, Severe mobility constraints and discomfort from elephantiasis	n.a.	n.a.	Ivermectin, Diethylcarbamazine (DEC)
Onchocerca volvulus (River Blindness)	Blindness; severe sustained itching	n.a.	n.a.	Ivermectin, Diethylcarbamazine (DEC)
Trematodes				
Schistosoma japonicum, s. mansoni (Blood fluke)	Decreased work capacity in heavy infections; hepatosplenomegaly	Growth faltering due to *s. hematobium* and *s. japonicum*; mechanisms may include protein loss and altered endocrine function	n.a.	Praziquantel

Schistosoma hematobium (Blood fluke)	Decreased work capacity in heavy infections; Hydronephrosis	n.a.		Praziquantel
Cestodes				
Tenia solium (Pork tapeworm)	Long-term mental impairment, sometimes involving epilepsy, from neural cysticercosis	n.a.		Mebendazole, praziquantel

Source: (38;54).

ANNEX Table 3: Common Food Fortification Vehicles

Food item	Description
Fats with vitamin A and D	- Fats, oils and margarines are technologically feasible to fortify - Also relatively easy to fortify since oil-soluble vitamin are readily miscible with food oils - Most commonly used blend contains 1,000,000 IU of vitamin a and 100,000 IU of vitamin D_3 per gram - Twenty-four countries, both developed and developing, have implemented mandatory fortification of margarine with vitamin A and D
Salt with iodine and iron	- More than 50% of the world has access to iodized salt with many countries achieving universal salt iodization - More than 90 governments have budgeted for IDD elimination in national financial budgets - Work on iron fortification of salt has gone on in India and Thailand: if 5% of iron is absorbed and an average of 15g of salt consumed/day, slightly over 33% of the average daily iron requirement could be met with iron fortification of salt (MI doc, 1997). - While infrastructure required for salt iodization exists in developing countries, challenge is to find a formulation that is stable, bioavailable and does not affect the retention of iodine.
Sugar with vitamin A	- Fortification of sugar with vitamin A in Guatemala in 1970's cut deficiency in half. El Salvador, Guatemala, and Honduras have fortified sugar today. - National surveys in Guatemala and Honduras showed that pre-schoolers with low levels of plasma retinol were reduced from 40% to 13% in Honduras and from 27% to 15% in Guatemala. - Nicaragua, Bolivia, Brazil, Colombia, Costa Rica, Ecuador, Mexico, India, the Philippines, and Zambia have also made progress toward reaching this goal. - Sugar is fortified with vitamin A w/ a standard or refined sugar, retinyl-palmitate beadlets, vegetable oil, antioxidants, and a gelatin matrix. - Vitamin A pre-mix is diluted over the sugar in the final steps of production. This pre-mix has 1,000 times larger concentration than the expected final level of vitamin A that will be in the final product.

Source: (76)

ANNEX Table 4: Consequences of the three types of helminths on health & corresponding anthelmintic treatments

Organism	Common Name	Consequence of infection	Anthelmintic for Treatment
Nematodes			
Ascaris lumbricoidis	Roundworm	Malnutrition, growth deficit, impaired physical fitness. Intertwined worms may cause intestinal obstruction and single worms may obstruct bile duct	Mebendazole, albendazole
Trichuris trichiura	Whipworm	Heavy infections can result in anemia, prolapse of rectum and chronic colitis. Moderate infections colitis is associated with stunting.	Mebendazole, albendazole
Ancylostoma duodenale	Hookworm	Anemia	
Necator americanus	Hookworm	Anemia and hypoalbuminemia; worms attach to small intest. Mucosa & ingest 0.03-0.26 mil blood/day. Heavy infections cause fatigability, headache, numbness, tingling, dyspnea, palpitations, anorexia, dyspepsia, pedal edema, and sexual dysfunction.	Mebendazole, albendazole
Dracunculus medinensis	Guinea worm	Cutaneous lesions	
Enterobius vermicularis	Pinworm	Anal pruritus	Mebandazole, albendazole, ivermectin
Strongyloides stercoralis	Strongyloidiasis	Autoinfection	Mebandazole, albendazole, ivermectin
Trichinella spiralis	Trichinosis	Myositis	
Trichuris trichiura	Whipworm	Rectal prolapse	Mebandazole, albendazole, ivermectin
Wuchereria bancrofti, brugia malayi	Filariasis	Elephantiasis, Severe mobility constraints and discomfort from elephantiasis	Ivermectin, Diethylcarbamazine (DEC)
Onchocerca volvulus	River Blindness	Blindness, severe sustained itching	Ivermectin, Diethylcarbamazine (DEC)
Trematodes			
Clonorchis sinesis, opisthorchis viverrini, o. felineus	Liver fluke	Bilary obstruction	Praziquantel
Fasciola hepatica	Liver fluke	Hepatomegaly	Praziquantel
Fasciolopsis buski	Intestinal fluke	Diarrhea	Praziquantel
Paragonimus westermani	Lung fluke	Cough	Praziquantel
Schistosoma japonicum, s. mansoni	Blood fluke	Hepatosplenomegaly	Praziquantel
Schistosoma hematobium	Blood fluke	Hydronephrosis	Praziquantel
Encylostoma duodenale (hookworm)		Anemia	Mebendazole, albendazole

Organism	Common Name	Consequence of infection	Anthelmintic for Treatment
Cestodes			
Diphyllobothrium latum	Fish tapeworm	Anemia	Praziquantel
Echinicoccus granulosus	Hydatid	Cysts	Mebendazole, albendazole
Tenia saginata	Beef tapeworm	None	Mebendazole, praziquantel
Tenia solium	Pork tapeworm	Cysticercosis	Mebendazole, praziquantel

Source: (54)

(38)