Cost-Effectiveness of Micronutrient Interventions
A review of the literature and analysis of NGO-led interventions

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Table of Contents

Abbreviations used in text.

ALRI – Acute lower respiratory infection
ARI – Acute respiratory infection
DDM – dietary diversity and modification
NGO – non-government organization
RDA – recommended daily allowance
RDPT – Randomised double-blind placebo-controlled trial
U2s – children 6 months to 2 years; U3s = children 6 months to 3 three years, etc.
VAC – vitamin A capsule
VAD – vitamin A deficiency

NGO abbreviated names:

HKI – Helen Keller International
MIHV – Minnesota International Health Volunteers
RTCCD – Research and Training Centre for Community Development
WV – World Vision

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INTRODUCTION

The magnitude of the problem caused by micronutrient malnutrition is widely recognized; inadequate intakes of micronutrients affect more than one-third of the world's population, impairing growth, physical and intellectual development, activity and survival, predominantly among women, infants, and children in developing nations. At the joint FAO/WHO nutrition conference in Rome in 1992 participating nations adopted the World Declaration on Nutrition and Plan of Action for Nutrition, which includes numerous efforts to reduce or eliminate micronutrient malnutrition by the year 2000. Despite the resources and effort that have been poured into these interventions, there is little information available for policy makers comparing the costs and effectiveness of different approaches for reducing micronutrient deficiencies. Given that the Year 2000 goals were not reached and that micronutrient interventions will continue to be conducted for many years, it is important to understand the costs and impact of commonly employed interventions in various developing country settings.

In this report, we focus on vitamin A deficiency (VAD). Current estimates are that approximately 3.3 million children under the age of five years suffer from clinical VAD (that is, they exhibit clinical changes of the eye, xerophthalmia) and between 75 and 140 million children suffer from subclinical VAD (that is, they have low body stores of vitamin A and are at increased risk of sickness and death, but they do not exhibit xerophthalmia (MI, 1998)). Approximately 78 countries have significant levels of VAD in their populations, including 17 of 19 countries in East and Southern Africa, and 15 of 20 countries in West and Central Africa. Twenty-seven of these 32 affected countries have adopted national vitamin A policies, and their progress fighting VAD, while substantial and encouraging, has not been sufficient. This report may be an aid to policy makers, NGOs and international organizations in advocating for vitamin A programming.

Many people spent many hours contributing to this report. In particular, we thank the NGO project managers who graciously provided us with their cost and effectiveness data.

OBJECTIVES AND FRAMEWORK OF STUDY

The overall objective of this study is to assess the cost-effectiveness of various strategies for reducing micronutrient deficiencies, in particular vitamin A deficiency, in developing countries. The specific objectives of the study are:

(1) To review the literature on the costs and effectiveness of different strategies for reducing vitamin A deficiency;
(2) To collect and collate data on the costs and effectiveness of each strategy employed in three different categories of micronutrient interventions: (i) micronutrient capsule distribution, (ii) fortification of foods with micronutrients, (iii) dietary diversification and modfication (DDM), including promotion of home-gardening/livestock rearing, dietary education/promotion of alternative food choices, including breast-feeding;
(3) To develop a model for estimating the costs and benefits of the different strategies singly or in combination, at the national level.

We had planned on doing a detailed analysis of 25 ongoing vitamin A projects. However, as reported to Ms. Kirsten Bendixen in an email message sent by PATH Canada on 4 January 2000, the project has proceeded much differently than expected, with only seven of the twenty-five projects providing usable data. The project team decided instead to focus on a very detailed literature review, using data from a few of the vitamin A projects as supplementary and illustrative aids, rather than as the base of the project. Objective 1 (above) is now the focus of the report. A detailed and comprehensive literature review focusing on the effectiveness of vitamin A interventions and on the cost-effectiveness of different intervention approaches has been conducted using over 100 papers published since 1993 (the year of the comprehensive review and meta-analysis by Beaton et al.).

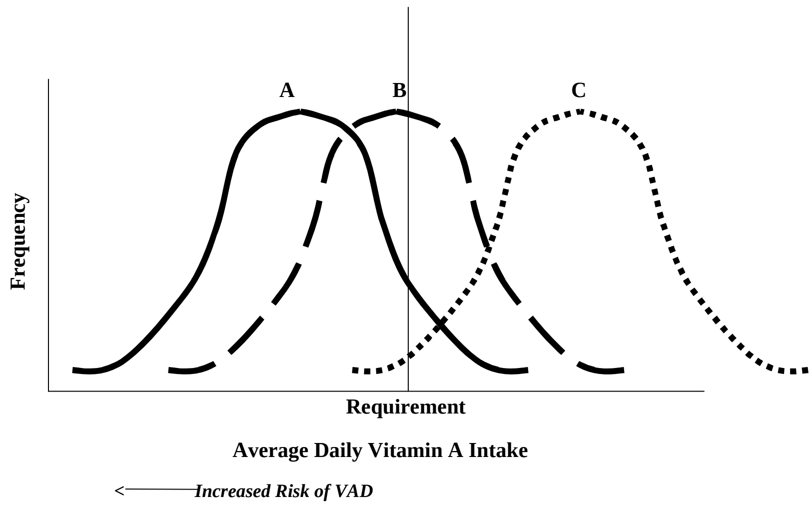
Only the first part of Objective 2 (re: micronutrient capsule distribution) has been met; there were insufficient data submitted by the 25 projects originally under consideration to address the other parts regarding DDM and food fortification. However the projects we were able to analyze did provide an opportunity to look at the effectiveness and cost-effectiveness of micronutrient interventions under field conditions, rather than the near-ideal conditions often reported in the literature.

Given the new focus of the project, Objective 3 could not be addressed.

BACKGROUND: VITAMIN A DEFICIENCY

The goal of micronutrient interventions is to increase the average daily intake of micronutrients to greater than the daily requirement, thereby improving the micronutrient status of high risk groups within populations, moving them from a state of deficiency to sufficiency (see Figure 1, using vitamin A as an example). With vitmain A, the shift in population intake can be achieved by increasing the intake every day or every few days (by changing the diet to include vitamin A rich foods), or by biannual megadose supplements. Because the liver can store approximately a four to five month supply of vitamin A, it does not matter if the vitamin A is ingested in daily, weekly, monthly or biannually, as long as the average daily intake is sufficient.

Figure 1. Hypothetical populations with (A) widespread clinical VAD; (B) widespread subclinical VAD; (C) little or no VAD. The goal of vitamin A programs is to move populations from A to C.



What is Vitamin A Deficiency?

The term "vitamin A" is used generically as a descriptor for retinoids exhibiting the biological activity of retinol. There are numerous sources of vitamin A in the human diet, including "preformed vitamin A", found in significant levels in animal livers, milk, eggs, some animal fats, and fortified foods, and "provitamin A carotenoids" contained in green, yellow, and orange vegetables and fruits, which need to be cleaved and modified to be biologically active as retinol. Humans require vitamin A for normal function; requirements vary from approximately 180 RE/day in infants to 300 RE/day in adults (FAO/WHO, 1988). Preferably, usual intakes will be greater than the requirements to enable the body to build up the liver stores of vitamin A. In a healthy adult, approximately 99% of the total vitamin A is stored in the liver as retinyl ester, and 1% circulates in the blood as all-trans retinol bound to RBP (retinol binding protein). Circulating levels are under homeostatic control, and liver vitamin A will be mobilized to maintain serum vitamin A (Olson, 1994). When vitamin A intake is lower than daily requirements liver vitamin A is mobilized and the liver stores will drop. Serum retinol levels (and vitamin A associated health risks) will be constant when liver stores are between approximately 20 and 300 ug/g. Serum retinol levels will drop when the liver stores are nearly depleted, making the individual subclinically deficient and placing the individual at increased risk of sickness and death. If vitamin A intake continues to be insufficient, retinol levels will continue to drop, leading to clinical deficiency, with overt damage to the eyes (Gibson, 1990). Vitamin A deficiency among children in developing countries remains the leading cause of preventable severe visual impairment and blindness. Approximately 2.8 million children under five years of age currently exhibit signs of clinical xerophthalmia (Micronutrient Initiative, 1998a). Continued insufficient intake will lead to death, but even subclinical deficiency places individuals, or at least young children, at an increased risk of death (Beaton, et al., 1993).

Individuals with low intakes of preformed vitamin A, or low intakes of carotenoids and dietary fat (fat is required for absorption of carotenoids) are at risk of vitamin A deficiency (VAD). This includes the children in most poor populations in most poor countries. As well, pregnant and lactating women, who have greater daily requirements of vitamin A, are also at increased risk (West et al., 1999), with some countries of Southeast Asia reporting prevalence of nightblindness of up to 10-20%. Current estimates are that 118 countries have clinical or subclinical vitamin A deficiency. Africa has the highest prevalence of clinical VAD, while the highest number of clinically and subclinically affected are in Southeast Asia ((Micronutrient Initiative, 1998a).

How is Vitamin A Status Assessed?

The approaches for measuring vitamin A status include (from Soleri et al., 1991) both direct (clinical and biochemical) and indirect (dietary) methods.

1. Direct
   - Biochemical indicators such as serum retinol, serum retinol binding protein (RBP), relative dose response, and breast milk retinol;
   - Morphological abnormalities such as conjunctival impression cytology;
   - Clinical manifestations of the eye such as xerophthalmia, including Bitot's spots and corneal destruction;
   - Assessment of dark adaptation (visual acuity at night).

2. Indirect
   - Dietary indicators such as food patterns, consumption of provitamin A-rich foods, and intrafamily distribution of these foods;
   - Community production and availability of dark green leafy vegetables, other provitamin A rich foods, or preformed vitamin A rich foods (e.g., eggs, and milk);
   - Self-report (or parent report) of nightblindness.

While the direct methods are more sensitive and accurate and are necessary for the unequivocal diagnosis of VAD as a public health problem, they are expensive, and require advanced technical or diagnostic skills and laboratory support. Indirect measures do not require the technical and infrastructural support necessary for direct assessment, and are less expensive. While direct methods are usually required for research, vitamin A programs usually use indirect methods.

Approaches for Reducing VAD

There are three categories of vitamin A interventions, broadly defined:
1. Vitamin A capsule distribution;
2. Food fortification;
3. Promotion of dietary diversification and modification (DDM).

The third category, DDM, is often considered as two separate categories: nutrition education to increase awareness (and therefore consumption) of vitamin A rich foods, and agricultural outreach to increase production of vitamin A rich foods.

The three categories are discussed below, and various issues, strengths, weaknesses and opportunities are discussed in Table 1.

VACs: The WHO protocol for vitamin A capsule distribution involves providing mega-dose vitamin A capsules (VACs) to children 6 months to 12 months of age (100,000 IU), children 1 year to 5 years of age (200,000 IU every six months), and to new, breast feeding mothers within eight weeks of giving birth (200,000 IU). There is also a protocol for VAC delivery to severely ill children (chronic diarrhea, measles or clinical VAD, respiratory disease, chickenpox, or other severe disease) or who live in the vicinity of severely ill children, directing 200,000 IU upon admission, 200,000 IU the following day, and a final 200,000 IU after 14 days (WHO, 1997). Large-scale VAC distribution programs have had great effects in reducing VAD and mortality in numerous countries (MI, 1998a). However, these programs do require massive efforts, typically with the mobilization of thousands of workers, and the motivation to receive the VACs of hundreds of thousands of parents in the target population.

Fortification: Food fortification is widely accepted as a sustainable and effective medium- to long-term intervention. Fortification has been used in numerous countries to virtually eliminate beri-beri, ariboflavinosis, pellagra, rickets and iodine deficiency disorders. The best fortification vehicles (that is, the foods to be fortified) are those that are widely consumed in relatively constant amounts nearly every day by the target population. With the proper vehicle chosen, widespread coverage can be quickly achieved at low cost. Sugar, milk, and oils have all been successfully used in vitamin A fortification programs, and there are recent efforts with rice, magi cubes and other novel vehicles.

Dietary diversification and modification (DDM): Changing the diet to include more micronutrient rich foods is often called "dietary diversification". While strictly speaking it would not be necessary to diversify the diet if a single, micronutrient rich food was identified, in practice it usually requires increasing the number of fruits, vegetables, and, when possible, animal products in the diet. Diversification programs usually include home gardening/animal rearing aspects, but programs to change consumer choice to healthier foods also fall in this category. Diversification is often preferred by nutritionists as the most holistic and sustainable approach, but, unfortunately, there are few documented successes with dietary diversification to support this bias. In food production projects, seeds, nutrition education and agronomic technical assistance are provided to participants (mostly families but also communities and schools) who themselves provide the labour and land. Unlike capsule programs, the impact of food production/education programs can be felt beyond the year in which the programs are implemented, if they are maintained. Home gardens and livestock rearing not only increase the intake of the micronutrient in question but also have the potential to improve caloric, protein and other micronutrient intakes. Gardening may also result in the generation of income from sale of produce (Marsh, 1998). Breast feeding promotion is often considered part of "dietary diversification". Continuing breast feeding, in addition to appropriate complementary feeding until 24 months of age is important to prevent nutritional deficiencies. Breast milk is virtually the only source of vitamin A in the first few months of life and often continues to be one of the most important sources until the age of two. Education programs are necessary to promote exclusive breastfeeding for the first 4-6 months of life, with appropriate complementary foods thereafter (Newman, 1993). Breast fed children are 65 to 90% less likely to develop clinical VAD (Sommer and West 1996).

The success of any nutrition intervention is dependent on nutrition education: "Nutrition education is an essential element in any strategy to reduce vitamin A deficiency; this includes promoting increased consumption of vitamin-A rich foods, suggesting new preparation techniques or food combinations, motivating acceptance of vitamin A capsules, and promoting purchase and use of vitamin A-fortified foods" (Cervinkas and Lofti, 1996). However, the scale of the education program varies between programs. For dietary change, massive education programs are required to elicit sustained behavioral change. For VAC programs, shorter term behavioural change is required (i.e., attending biannual VAC campaigns with young children), rather than permanent changes of daily diet. With fortification, the industry and regulatory agencies must be educated, if they are not already aware of micronutrient deficiencies and food fortification, but this is a fairly focused awareness raising that is required, not public education. Whether or not public education is required depends on the nature of the fortification. If staple food fortification is mandatory, universal and subsidized, then no behavioural change is required – in fact, the consumer need not even be aware that the food is fortified. If there are fortified and unfortified versions of the same food, or if the fortified food is more expensive, then large scale education/marketing campaigns will be required to encourage the purchase and consumption of the fortified food.

As a fourth category of intervention, non-diet related programs can also address VAD. Strengthening of other public health measures (e.g. parasite and diarrhoeal disease control, access to safe water and sanitation; EPI coverage) will have an impact on prevalence of VAD, by leading to improved absorption of vitamin A in the diet (with diarrhoeal disease control), or decreasing the rate at which vitamin A is used by the individual (e.g., measles causes accelerated vitamin A turnover).

Elements of a successful intervention:

Regardless of the intervention, or combination of interventions used, their success is more likely if they:

- are tailored to local circumstances;
- address the preventable causes of deficiency;
- are tailored to the country/region's capacity to implement and sustain
- have political support
- have community involvement, participation, and consumer demand
- make use of existing physical and administrative infrastructure
- incorporate good communication strategies
- have a monitoring and evaluation component built in

Some of the elements of a succesful intervention are summarized in Table 1 for each of VAC distribution, food fortification and DDM.

Table 1. Elements of a successful vitamin A intervention.

Issues	**Strengths**	**Weaknesses**	**Best suited when…**
	VAC Distribution		
1. Need to ensure coverage of at-risk groups, who may be the hardest to reach (e.g., rural, illiterate). 2. Need to ensure that supply	1. Possible to have mass distribution through add-on to existing campaigns (e.g. vaccination or deworming).	1. Requires cooperation of targeted population (i.e., they must appear at distribution centre and take a capsule). 2. Requires many motivated	1. It can be added on to an existing campaign that has high coverage of target population.

management is able to cope. This includes being able to: - procure supplements that look appealing, have helpful packaging and labeling, come in the correct dosage, and are available in time for every campaign; -store and transport them for maximal quality and preservation; -deliver them to well-selected distribution points in adequate numbers of doses at an appropriate frequency . 3. National level support or permission usually required.	2. Single contact with health worker can provide six months coverage. 3. Can target populations at high risk of VAD.	and well-trained workers (for distribution) and supervisory staff (for monitoring and surveillance).	2. Supply of VACs is ensured. 3. High number of trained workers available, and monitoring systems are in place. 4. There are acute VAD problems requiring immediate solutions. 5. A national VAC policy is in place.
Food Fortification			
1. Suitable food vehicle for fortification must be identified: -targeted group consumes food frequently and in relatively constant amounts; - the food is centrally processed or imported (so that food can be centrally fortified and monitored); -the food must be technically and economically feasible to fortify; - the fortified food must be culturally acceptable. 2. Industrial capacity for fortification should be locally available. 3. Government support and approval required. 4. There must be monitoring of industry compliance, and QA/QC must be in place to ensure quality. 5. Fortification has associated costs, which must be born by consumer, industry or government.	1. No behavioural change required in target population. 2. Often possible to have consumers pay for fortification premium (no donor requirement). 3. Existing distribution channels are used to reach all consumers of food. 4. Has been reported to be most cost-effective approach. 5. Relatively few trained people required for very large programs. 6. Multiple fortification (i.e., many vitamins and minerals in one food) can address numerous deficiencies simultaneously.	1. Can take months or years to launch fortification program (large initial investment required). 2. Not targeted to VAD population, so fortified food also consumed by non-VAD population, thereby incurring cost with no benefit. 3. Even when effective, not necessarily sufficient to eradicate deficiency. 4. May require modest changes in packaging, labeling and handling of food; shelf-life of fortified food may be less than unfortified.	1. Suitable vehicle identified. 2. Other programs are in place to address short-term needs. 3. Country is stable enough to support and justify the infrastructure investment.
Dietary Diversification and Modification *apply specifically to home gardening/livestock rearing or other food production programs.			
1. Government support not necessarily required. 2. Work can proceed on small scale. 3. Need to identify micronutrient-rich foods that are available and acceptable. 4. Need staff trained in agriculture and community development. 5. A much heavier community investment is required. 6. When there is little land available, dietary modification is	1. Home gardens/livestock rearing can lead to increase in intake of many micronutrients, calories, protein and fat*. 2. Gardening may also result in the generation of income from sale of produce*. 3. Production controlled by households rather than dependent on government goodwill and financial support.	1. Many trained staff needed to initiate and maintain program. 2. Few successful examples in developing countries from which to learn. 3. There may not be equitable distribution of food within the household. 4. Large training component required so that vitamin A rich foods are prepared in such a way to preserve vitamin A content.	1. Micronutrient deficiencies are not severe and widespread. 2. Many capable staff available. 3. Land available and cultural, climatic, and soil conditions suitable for agriculture*.

still possible, by combining income generating activities with nutrition education. 7. Household decision-making process and gender roles are much more pronounced in these programs.	4. Often more control by women on food production and distribution. 5. Promotes self-reliance and community participation.	5. Need to develop appropriate communication and training materials. 6. Hard to do if people are landless. Home gardens are often only feasible for households with access to fertile land with a good water supply.*	

LITERATURE REVIEW

The literature review includes two parts, a review of the effects of vitamin A interventions, and a review of cost-effectiveness of micronutrient interventions. In 1993, Beaton et al. published a comprehensive review and meta-analysis of vitamin A effects on mortality and morbidity. The effectiveness literature reviewed here includes all human studies on vitamin A and health reported between 1993 and June 2000, over 100 papers in total. It is a very rich literature, examining questions of ever finer detail on the exact health effects of VAD and vitamin A interventions. Following the review of the effectiveness literature, we discuss some program experiences and the potential of vitamin A programs. The cost-effectiveness literature is much less rich, with only a handful of reports to draw on. These reports are reviewed in detail and discussed.

Effectiveness of Vitamin A Interventions

Nutrition status influences susceptibility and immunity to various infectious diseases. Deficiencies of specific nutrients have been found to alter cell-mediated immunity both in humans and animal models (Shankar, 2000). Vitamin A deficiency is characterised by widespread immunological effects, including pathological alterations in mucosal surfaces, impaired antibody responses, changes in lymphocyte populations, and altered T- and B-cell function (Semba, 1994). In the last decade, much progress has been made in the elucidation of the role of vitamin A in immunity to infectious diseases and, although major gaps do exist, more is known for vitamin A than any other micronutrient. The impact of vitamin A deficiency on immunity is relatively well established for impairment of mucosal immunity, compromised function of neutrophils, macrophages and Natural Killer cells, altered immune responses and altered antibody responses (Semba, 1998). Vitamin A is therefore necessary for normal immune function and the effects of vitamin A supplementation in the reduction of childhood mortality in VAD children has been known for some time.   In the meta-analysis by Beaton et al. (1993) of eight vitamin A-mortality studies, the effectiveness of vitamin A interventions in reducing mortality and morbidity was analysed and described. The results of this analysis have been evaluated, replicated (Fawzi et al., 1993, Glasziou and Mackerras, 1993) widely disseminated, and used to justify (rightly so) countless vitamin A interventions.

The results of the meta-analyses consistently showed that vitamin A prophylaxis has a strong protective effect against mortality with overall mortality reduction of 23% (Beaton et al., 1993) to 30% (Fawzi et al., 1993, Glasziou and Mackerras, 1993). There was weaker (Glasziou and Mackerras, 1993) or no (Beaton et al., 1993) evidence of vitamin A prophylaxis reducing morbidity. In the Beaton meta-analysis, the protective effect of vitamin A is seen throughout a range of severity of vitamin A deficiency (prevalence of xerophthalmia from 0.7 to 13.2%) and control group mortality rate (as a proxy for baseline conditions, from 5.3 to 126.2 deaths per 1000 child-years), with the mortality reduction from 50% to 0% (Beaton has recently questioned his inclusion of the one study in which vitamin A did not have a protective effect (Sudan) because of possible problems with the study design and implementation (NGONut listserver, archived at http://www.univ-lille1.fr/pfeda/Ngonut/1999/ 9911e.htm)).

The reduction in overall mortality was considered to be due in large part to a reduction in diarrhea and measles-related mortality (RR=0.68 and 0.74 respectively), but not respiratory (RR=0.99). The lack of an effect on morbidity was surprising. Glasziou and Mackerras (1993) attributed this to insufficient sample size, but Beaton et al. (1993) interpreted it as a true biological phenomenon, proposing that vitamin A status modulated the child’s response to infection, but did not change the actual susceptibility to getting the infection.

Since 1993 research has focussed on refining our understanding of the biological effects of vitamin A. In the remainder of this section, the relationship between vitamin A and mortality, morbidity or other health indicators as described in research post-1993 is summarized. The effectiveness of vitamin A supplementation is considered in HIV/AIDS (transmission and disease progression), respiratory disease, diarrheal disease, malaria, measles, maternal mortality and “all cause mortality”. Details of the studies summarized in the next section can be found in Appendix A.

HIV/AIDS
Much of the early work on vitamin A and HIV/AIDS (mostly 1990 to 1996) showed that there was an association between HIV and vitamin A status, with VAD being associated with greater viral load, worse symptoms and more rapid progression of symptoms (Rwangabwoba et al., 1998; Phuapradit et al., 1996; Periquet et al., 1995; Karter et al., 1995; Baum et al., 1994; Coodley et al., 1993; Nduati et al., 1995; *contra* Semba et al. 1997). Most of the recent vitamin A related research has been on disease transmission (almost exclusively mother-to-child transmission, with very little work on adult-to-adult transmission) and disease progression, and is summarized below.

HIV/AIDS Transmission
Observational studies:
Most of the vitamin A-HIV/AIDS research has been on vertical (mother-to-child) transmission. One study in Malawi, where VAD prevalence is high (Semba et al., 1994), and one in the US with VAD mothers (Greenberg et al., 1997), observed a relationship between maternal vitamin A status and mother-to-child transmission , but three other studies did not (Burns et al., 1999; Wiratchai et al., 1999; Burger et al., 1997). However, in these three negative studies, the prevalence of VAD was probably not high, and therefore VAD was not an important risk factor for HIV transmission. Transmission rates would not be correlated with vitamin A status, if the population had adequate vitamin A status. It has been observed that vaginal shedding of HIV infected cells is greater in VAD women, which could lead to higher transmission rates (John et al., 1997; Mostad et al., 1999). The one study on adult-to-adult transmission showed that vitamin A status was not associated with becoming infected (Moore et al., 1993).

Prophylactic VACs:
One of the studies which did not see a vitamin A effect on transmission, did observe that VAD was associated with higher risk of premature births (Burns et al., 1999), and elsewhere (Coutsoudis et al., 1999), vitamin A supplementation was observed to reduce the incidence of premature birth, and to reduce the transmission rate in the prematures. However, in three, as yet unpublished, trials in South Africa, Malawi, and Tanzania vitamin A supplementation to mothers in an area with VAD did not have a protective effect on mother-to-child transmission (Humphrey, 2000; Fawzi, 2000).

While an association between vitamin A status and mother-to-child transmission is plausible, there is also conflicting evidence. If there is a benefit to vitamin A supplementation, it is generally weak, and would only apply in certain, as yet unspecified, situations (e.g., premature babies of severely VAD mothers).

HIV/AIDS Progression
There is ample evidence supporting an association between vitamin A status and HIV/AIDS progression, including both observational studies and interventions with VAC prophylaxis.

Observational studies:
The studies are usually prospective observational (e.g., vitamin A status at baseline as a predictor of disease progression and mortality). The association between vitamin A status and progression is consistently reported and reveals faster progression and more severe disease with poorer vitamin A status (Rich et al., 2000; Kelly et al., 1999; Camp et al., 1998; 1995; Baum et al., 1995; Semba et al., 1995; Tang et al., 1993; Semba et al., 1993). Two studies which did not observe such a relationship did not include VAD individuals (Read et al., 1999; Tang et al., 1997). Other work has shown that the infants of HIV+ VAD moms were lighter by 8% and shorter by 2% at 12 months than children of HIV+ non-VAD mothers (Semba et al., 1997a).

Therapeutic VACs:
There have been three supplementation clinical trials of the form of supplements (or placebos) taken by HIV+ individuals and disease progression tracked. The evidence on the effect of supplementation on disease progression are mixed, with two studies showing strong benefits (decreased mortality of HIV+ children (Fawzi et al., 1999), decreased diarrheal disease in HIV+ children (Coutsoudis et al., 1999)), and one study not showing any benefits (Kelly et al., 1999).

In summary, the HIV research supports the standard WHO protocol of VAC supplementation in VAD areas. The benefit of supplements to non-VAD individuals is uncertain, but unlikely.

Respiratory Disease
In the meta-analyses of 1993 (Beaton et al., 1993), it was concluded that respiratory-related disease was not associated with vitamin A status, and outcome from respiratory disease was not improved by vitamin A supplementation. A number of

studies have been published since 1993 and, although the results are inconclusive, it appears there is a relationship between vitamin A and respiratory health status.

Observational studies:
In observational studies, children with ARI had lower serum retinol than healthy cohorts (Kucukbay et al., 1997), and, similarly, children with VAD had a higher incidence (Pandey and Chakraborty, 1996) and severity (Dudley et al., 1997) of ARI. In a dietary study, dietary intake of vitamin A was inversely related to the incidence of cough with fever, but directly related to the incidence of cough alone (Fawzi et al., 1995).

Prophylactic VACs:
There have been numerous supplementation trials with children since 1993, with mixed results on respiratory disease outcome. In two studies (Humphrey et al., 1996; Lie et al., 1993) prophylactic supplementation has led to decreased incidence of respiratory disease, but most studies (Bandari et al., 1994; Barreto et al., 1994; Biswas et al., 1994; Fawzi et al., 1998b; Ghana VAST Study Team, 1997; Kartasasmita et al., 1995; Ramakrishnan et al., 1995; Venkatarao et al., 1996) did not observe a decreased incidence, and one study observed an increased incidence in the two week period following supplementation (Stansfield et al., 1993). Supplementation of children has decreased the duration of respiratory disease when delivered prophylactically to children (Rahman et al., 1996; Kartasasmita et al., 1995) or to breastfeeding children's mothers (Roy et al., 1997) who later go on to develop respiratory disease. Two studies reported an increased incidence of respiratory disease in normal weight children, but a decreased incidence in underweight children (Dibley et al., 1996, Sempertegui et al., 1999).

Therapeutic VACs:
When administered to children with pneumonia, two studies (Julien et al., 1999; Si et al., 1997) reported a decreased duration of the disease, and one did not (Fawzi et al., 1998). Therapeutic VACs did not change respiratory disease-related mortality rate in children with pneumonia (Fawzi et al., 1998; Nacul et al., 1998), but did increase the incidence of other adverse effects (lower blood oxygen saturation, higher incidence of requiring supplementary oxygen) (Stephensen et al., 1998). In a trial with U4s (of unknown vitamin A status, but probably little or no VAD) with ALRI, there was no difference in any of the outcome indicators between placebo and supplemented when both groups otherwise received standard treatment (Kjolhede et al., 1995).

In summary, the prophylactic use of vitamin A does generally not decrease the incidence of respiratory disease (and may even increase it), but, for children who develop respiratory disease, the disease duration is shorter in supplemented than unsupplemented children. The therapeutic use of VACs decreases duration, but, consistent with Beaton et al., 1993, it does not affect the respiratory-related mortality rate.

Diarrhea
In the meta-analyses of 1993 (Beaton et al., 1993; Glasziou and Mackerras, 1993) the strongest protective effects of vitamin A were related to reduction in diarrhea-related mortality (RR=0.68). However, vitamin A supplementation was not observed to affect diarrhea-related morbidity (duration or incidence). Research since 1993 has focused on diarrhea morbidity, while the strong protective effect of vitamin A supplementation for diarrhea related mortality is generally accepted.

Observational studies:
The evidence from observational studies is inconclusive. High serum retinol levels have been associated with lower faecal levels of eggs of some species of helminths in U5s (Curtale et al., 1994), and in schoolers, but not preschoolers (Friis et al., 1997). In preschoolers, persistent diarrhea was associated with lower serum retinol levels (Kucukbay et al., 1997). High dietary intakes of vitamin A had a strong protective effect against diarrhea in U6s (Fawzi et al., 1995).

Prophylactic VACs:
The prophylactic use of VACs has been observed to decrease the duration of diarrhea by approximately 40% (Walser et al., 1996; Biswas et al., 1994). A number of studies have observed decreased incidence of diarrhea, in at least some ages and conditions (Sempertegui et al., 1999; Coutsoudis et al., 1995; Barreto et al., 1994; Bhandari et al., 1994; Lie et al., 1993). No effect on incidence was seen in other studies, regardless of age (Venkatarao et al., 1996; Ramakrishnan et al., 1995.), even in those studies which measured a decrease in duration (Walser et al., 1996; Biswas et al., 1994). An increase in incidence has been observed in one study of U7s in the two weeks following supplementation (Stansfield et al., 1993). This increase has been observed elsewhere in children less than 30 months of age, whereas a decrease was observed in those greater than 30 months (Dibley et al., 1996).

Therapeutic VACs:
There was a slight decrease in duration of diarrhea in one study (Faruque et al., 1999), but not another (Rollins et al., 2000).

Overall, there is evidence that VACs decrease diarrhea morbidity. However, the inconsistency with which an effect is observed suggests that the vitamin A effect on diarrhea morbidity is not large and is specific to certain (not well defined) conditions of the child (e.g., age, disease state, severity of VAD) and does not apply in all situations. This is consistent with the 1993 understanding of vitamin A and diarrhea.

Malaria
In the meta-analyses of 1993, vitamin A and malaria was only briefly discussed, as there was only one relevant vitamin A and mortality study (the Ghana VAST study (Binka et al., 1995)), which showed no benefit of vitamin A supplementation. Since then, more research has been done, with results largely contradictory to the VAST study.

Observational studies:
A number of cross-sectional studies found an inverse relationship between malaria parasitemia and vitamin A levels, suggesting a possible increased utilization of vitamin A during infection or depressed plasma retinol concentration, during clinical and sub-clinical malaria (Adelekan et al., 1997; Das et al., 1996; Davis et al., 1994; Filteau et al., 1993; Galan et al., 1990; Hautvast et al., 1998; Thurman and Singkamani, 1991). In one study, effects on serum retinol were seen only in pre-school children with malarial parasitemia, who would likely not have yet developed any immunity to the disease (Friis et al., 1997). In this setting, parasitemia did not have any effects on vitamin A status in primary school children who would likely have developed some malaria immunity. In this same study, elevated serum levels of C-reactive protein and malaria parasitemia were significant predictors of serum retinol, suggesting that this may be due to the acute phase response. This is substantiated by the knowledge that retinol is bound to the negative acute phase proteins, retinol binding protein and transthyretin (Thurman and Singkamani, 1991). This suggests that the behaviour of retinol during infection involves a rapid release from the liver, distribution into extravascular fluids, and increased availability throughout the body, although there is still much to be learned about the interactions between vitamin A and acute infections. A causal relationship is not established, nor is it clear whether the VAD state preceded the malaria or occurred as a result of it.

Prophylactic VACs:
There have been only two studies on the malaria-related health effects of VACs prophylaxis. In the VAST Study in northern Ghana (including a Survival Study on 21,906 U8s and a Morbidity Study on 1455 U5s), no difference was found between vitamin A supplemented and non-supplemented children's malaria mortality rates or fever incidence, based on reported symptoms (Binka et al., 1995). However, these results were weakened as there was no longitudinal surveillance of slide-confirmed malaria in this study (Shankar, 1995).

In an RDPT of VAC supplementation of U5s in Papua New Guinea, supplementation resulted in a 30% reduction in *Plasmodium falciparum* clinical episodes and a 36% reduction in parasite density. Children who began receiving the supplements at 12-36 months of age benefited the most, having 35% fewer malaria episodes, 26% fewer enlarged spleens and a 68% decrease in parasite density (Shankar et al., 1999).

Therapeutic VACs:
Some practitioners now recommend the use of vitamin A supplementation in cases of malaria, however there have been no reported studies on its efficacy, although it is very unlikely that VAC supplementation to malarious individuals would be harmful.

In summary, as many malarious areas also have high incidence of VAD (Young and Berti, 2000), and there is likely prophylaxis against subsequent malaria infection, prophylactic VAC should be continued.

Measles
Beaton et al.'s meta-analysis suggests that vitamin A prophylaxis reduces measles mortality (RR=0.74, 95% CI=0.53-1.04), but the number of cases was too small to be confident in the magnitude of the protective effect. Also reviewed were three clinical trials and one retrospective review on vitamin A used therapeutically for measles. All report positive effects on various indicators of measles morbidity, and one of the trials and the review also report reduced mortality (the other two did not include mortality as a study outcome) (Beaton et al. 1993).

Since Beaton et al.'s review there have been only a few additional studies on the vitamin A – measles relationship. There have been six studies on the effect on seroconversion when VACs are given at measles vaccination – five of the studies reported no adverse effect (Bhaskaram and Rao, 1997; Bahl et al., 1999; WHO/CHD, 1998; Benn et al., 1997; Semba et al., 1997b); one reported reduced seroconversion (Semba et al., 1995). The relationship between depleted vitamin A levels and measles status, long observed in developing countries, was also observed in developed countries, where VAD is assumed to be uncommon in the general population (Frieden et al., 1992; Caballero and Rice 1992; Arrieta et al., 1992). Also, therapeutic use of VACs was beneficial in non-VAD populations in developed countries (Kawasaki et al., 1999; Butler et al., 1993). The research in developed countries was not all positive, with one study showing some benefits to therapeutic VACs (Ogaro et al., 1993), but three studies showing no benefit (Rosales et al., 1996; Rosales, Kjolhede, 1994; Bandari et al., 1994). Elsewhere, the fatality rate in children with post-measles complications was decreased from 32 to 16% by supplementing with VACs, in addition to antibacterials and other supportive care (Madhulika, 1994). Vitamin A supplementation may have benefits in addressing measles, but it is more important to give VACs to prevent post-measles VAD.

Maternal Mortality

In many countries VAD during pregnancy is a widespread problem. As the fetus/breast feeding child acquires all of its vitamin A from the mother, VAD mothers have VAD children. The health effects of VAD on children are well documented. A recent study indicates severe health effects of VAD on mothers too. In an RDPT in Nepal ~20,000 mothers were given weekly doses of either vitamin A, beta-carotene or placebo. The two supplemented groups had pregnancy related mortality rate 44% lower than the placebo group (West et al., 1999). While this research has been criticized (Ronsmans et al., 1999; Sachdev et al., 1999; Vijayaraghavan and Krishnaswamy, 1999), it seems reasonable and likely that improving vitamin A status of mothers does improve maternal survival.

All Cause Mortality

Outside of the disease/situation specific studies summarized above, vitamin A supplementation and vitamin A status are strongly associated with overall mortality rates. Therapeutic (Fawzi et al., 1999) and prophylactic (Pant et al., 1996, Humphrey et al., 1996, Ghana VAST Study Team, 1993; Ross et al., 1995) VACs studies showed 40 to 65% lower mortality rates in supplemented children, and mortality rates were also lower in children with better vitamin A status as shown in dietary (Fawzi et al., 1994) and serum retinol status (Semba et al., 1998) surveys.

Summary of Effectiveness

The conclusions about mortality reduction reached in the 1993 meta-analyses (Beaton et al., 1993, Fawzi et al., 1993, Glasziou and Mackerras, 1993) still stand and are widely accepted. VAC prophylaxis dramatically reduces U5 mortality. In this report, studies published since 1993 were reviewed to enable a more complete understanding of the conditions and illnesses in which vitamin A has an effect on mortality and morbidity. For a number of conditions and illnesses, the benefits of vitamin A are less clearly defined than they are for reducing U5 all-cause mortality.

<u>Respiratory disease:</u> As was the case in 1993, vitamin A supplementation does not reduce *mortality* from respiratory disease, nor does it affect respiratory disease *incidence*, although both prophylactic and therapeutic administration of VACs does reduce *duration* of respiratory disease.
<u>Diarrhea:</u> Beaton et al. (1993) did not observe an effect on diarrhea morbidity, only mortality, but research since 1993 has observed prophylactic VACs decreasing diarrhea *duration* by approximately 40%, with a smaller and less frequently observed reducing in *incidence* rates. The effect of therapeutic VACs on diarrhea is uncertain (although the WHO recommendation of giving VACs to individuals with diarrhea is still valid, as vitamin A absorption can be impaired during diarrhea, placing the sufferer at increased risk of VAD (WHO/UNICEF/IVACG, 1997)). The greatest effects of supplementation still appear to be in reducing *mortality* from diarrheal disease.
<u>Measles:</u> Beaton et al.'s meta-analysis suggests that vitamin A prophylaxis reduces measles mortality, but the sample size was too small to be confident in the magnitude of the protective effect. Other reviewed literature on therapeutic VACs report positive effects on measles morbidity and mortality (Beaton et al., 1993). Since 1993, research has been done showing the benefits of therapeutic use of VACs in non-VAD populations in developed countries, but ironically the results have been mixed in developing countries. Nonetheless, as measles places children at increased risk of VAD, supplementation with VACs, as recommended by WHO (WHO/UNICEF/IVACG, 1997) is still valid.
<u>HIV/AIDS:</u> There was very little work done on vitamin A and HIV/AIDS before 1993. Given the current AIDS epidemic and the importance of AIDS as a cause of illness and death in Africa and elsewhere, the benefits of vitamin A supplementation in AIDS indicates the potential to change the accepted ~23% reduction in U5 mortality with VAC prophylaxis. Given maternal HIV+ prevalence of 20 to 30%, and mother-to-child transmission of 20 to 30%, the prevalence of HIV/AIDS in U5s in some African countries may be as high as 10%. If vitamin A had no protective effect (i.e., those children with AIDS will die whether or not they are supplemented) the mortality reduction for VAC prophylaxis could be lowered to, say, ~ 20%. However, it appears that therapeutic VACs do markedly affect HIV/AIDS progression (although vitamin A status and VAC prophylaxis or treatment do not affect HIV mother-to-child transmission), reducing all cause mortality of HIV+ children by as much as 60% (Fawzi et al., 1999). More work is needed to determine how vitamin A will affect all cause mortality of U5s in populations with high levels of HIV/AIDS.

Malaria: Reduction in malaria-associated mortality was not observed in the earlier VAST study, but there were some methodological problems with that study. Work since 1993 indicates that VAC prophylaxis does markedly reduce malaria-associated morbidity by ~30% (Shankar et al., 1999). Given the reductions in parasite density and clinical episodes associated with VAC prophylaxis, a proportionate reduction in U5 mortality of may be expected, although this has not yet been measured. VAC prophylaxis may be able to dramatically reduce the approximate one million young child deaths from malaria annually in Africa.
Maternal mortality: Prenatal weekly VACs were observed to reduce post-natal maternal mortality by 44% in Nepal (West et al., 1999). Despite criticisms of this work (Ronsmans et al., 1999; Sachdev et al., 1999; Vijayaraghavan and Krishnaswamy, 1999), the evidence indicates that improving vitamin A status of mothers does improve maternal survival.
All cause mortality: While the effects of vitamin A supplementation on any single disease may be imperfectly known, it is clear that VAC supplemented children in VAD populations have mortality rates approximately 23% lower than unsupplemented children.

Finally, relationships between numerous other conditions and vitamin A status/VACs have been observed. Some of those that could be of importance for reducing burden of disease in developing countries are summarized below.

Positive Effects

VAC supplementation:

- VAC improved growth rates in severely VAD children (West et al., 1997; Ramakrishnan et al., 1995)
- Giving VACs to breastfeeding moms decreased incidence of febrile illness in their infants (Roy et al., 1997)
- 50,000 IU given at birth to child, with follow-up at 4,6 and 12 months). Placebo group sought medical attention for fever 51% more often (Humphrey et al., 1996)

Vitamin A Status:

- VAD had more rapid progression from cervical dysplasia to cervical cancer (Nagata et al., 1999)
- 100% of children with meningicoccal disease in Rwanda were VAD (Semba et al., 1996)
- Serum vitamin A and B-carotene were lower in women with pre-eclampsia and eclampsia (Ziari et al., 1996)

No Effects

- No effect of VAC on growth in VAD population (but effect on mortality and morbidity) (Kirkwood et al., 1996; Lie et al., 1993)
- No relationship between serum retinol and otitis media (but all the children were moderately VAD or worse, so dose response not necessarily expected) (Durand et al., 1997)

Conclusions:

When vitamin A has an effect, it appears to be protective to the individual for roughly the number of days worth of vitamin A given (e.g., 200,000 IU lasts for at least 5 months). In other words, if a child at risk of VAD receives only 1 VAC per year, their risk of dying will be lower for the ~6 months following receipt of the VAC, and the population to which the child belongs will therefore have a decreased mortality risk for the whole year.

In considering the effect of vitamin A supplementation on health outcomes at the population level, it is necessary to consider (1) the vitamin A status of the study populations; (2) the difference between disease progression and disease transmission; and (3) the difference between giving VACs prophylactically versus therapeutically.

1. Vitamin A Status: In most of the studies, vitamin A status of the populations is assessed, but in many of the studies listed the vitamin A status of the study population is not known, but is either assumed to be VAD (or not), or is not mentioned at all. Other than the studies showing benefits of VACs to developed country (presumedly non-VAD) children with measles, supplementation to a non-VAD population should not be expected to have any benefits. Often when the observed effects of VAC supplementation is weak it may be because a large percentage of the study population (i.e. all those not VAD) will be “non-responders”.

2. Progression versus Transmission: Beaton concluded that improving the vitamin A status of VAD populations reduces mortality not morbidity. Similarly, varying for each disease/condition, vitamin A status may affect disease transmission or susceptibility to some diseases (maybe with HIV/AIDS, malaria), while affecting progression in other diseases (HIV/AIDS, diarrhea, respiratory disease). Often therapeutic VAC supplementation is important to prevent VAD, rather than (or as well as) improving recovery (measles, diarrhea).

3. Prophylactic versus Therapeutic: When VACs have a prophylactic effect on a disease it does not necessarily follow that there will be a therapeutic effect (e.g., with diarrheal disease). And alternatively, when there is a therepeutic effect, it does not necessarily follow that there will be a prophylactic effect (e.g., with measles).

In this review of the relationship between vitamin A status, vitamin A interventions and health, the research on the specific relationships in various conditions and diseases has been documented. There is still uncertainty about some aspects of the consequences of VAD in certain conditions, about the exact magnitude of the health benefits of vitamin A interventions. But it is absolutely clear that VAD is a serious health risk for the overall health of the individual. It is equally clear that vitamin A interventions bring tremendous health benefits to vitamin A deficient populations. It is one of the most powerful public health interventions available. It is no longer a question of whether, in VAD populations, vitamin A interventions should be carried out or not, but rather how they should be done to ensure effective, efficient and sustainable change.

Vitamin A Programs…. How effective are they?

The demonstration of the effectiveness of vitamin A interventions on mortality and morbidity has been done mostly in very tightly controlled studies in which vitamin A capsules were administered in double-blind placebo controlled trials, so that the effects of vitamin A can be isolated from other nutritional and environmental variables. In "real world" programs, usually the *process* is monitored, not biological effectiveness. This reflects the difficulty and expense of measuring morbidity, mortality and vitamin A status. Vitamin A programs are often add-ons to other programs, which do not have improving vitamin A status as a goal. Program managers therefore choose to dedicate their limited resources to increasing coverage, rather than incorporating intensive monitoring of effectiveness. Program Managers reason that if the process is in place, the effectiveness should follow. While this is reasonable program management, it lends to a rather sparse literature on vitamin A program effectiveness.

A more pertinent question is actually "*How effective can "real world' vitamin A programs be?*" A review of all program experience is really not feasible, as most goes unreported or underreported. However, we can consider the effectiveness that has been achieved in the field and, integrating this with what we know from the controlled studies of the health effects of vitamin A, we can estimate the range of effectiveness of Vitamin A programs. We will not discuss the "lower end" of the range of effectiveness – poorly run programs that do not improve the vitamin A status of the population obviously have no health benefits. On the other hand, programs that achieve complete coverage (100% of target population) should be expected to have health benefits of the magnitude observed in the controlled trials, for example, ~23% reduction in U5 mortality rates.

VAC Supplementation: Coverage rates of U5s with VACs of over 90% have been reported in national and subnational programs in the Philippines, Bangladesh, Nepal, Vietnam, and Brazil (Sanghvi and Murray, 1997). Some of the GVAI projects summarized in the next section also achieved coverage of over 90%. With such high coverage, health effects like those observed in the controlled trials should be expected.

Fortification: The fortification of multiple staple foods can achieve near 100% coverage. Vitamin A fortification of foods has virtually eliminated VAD in North America and Europe, and although it has not been measured as such, has certainly contributed to the low U5 mortality rate in these regions. Most developing countries are in the early stages of developing food fortification programs. There has been progress, but such progress is usually with single foods, not with the multiple food fortification that is common in North America and Europe. The success of some of these efforts (usually in terms of process, not effectiveness) is documented in various reviews (e.g., Micronutrient Initiative, 1998b, Nestel, 1993). Fortifying single food items is often not sufficient to reach most of the target population.

Dietary Diversification and Modification (DDM): Process indicators for DDM (e.g., knowledge of sources of Vitamin A, number of households with gardens) are often used in programs, but critical evaluation of outcome indicators such as vitamin A status, or maternal or child health are rare. There are unresolved issues regarding the evaluation of DDM programming: outcome is strongly influenced by assumptions about whether goals should be short term or long term, and narrow (e.g. vitamin A nutritional status of children) or broad (e.g., improved overall nutritional status of children). In general, the longer the term and the broader the focus, the greater will be the observed benefits of DDM.

One of the few DDM programs that measured change in vitamin A status was conducted in Indonesia in the 1990s. A very intensive social marketing campaign promoting dark green leafy vegetables and eggs raised the vitamin A intake in the target population from 335 to 371 RE/d (from 67% to 74% of RDA) for mothers and from 130 to 160 RE/d (from 32% to 40 % of RDA) for children, and concomitant increases in serum retinol were observed (de Pee et al., 1998). While these are important and positive changes, this may be the maximum change that can be expected in this setting through DDM without the promotion of fortified foods.

In summary, we should expect supplementation and fortification programs to have health benefits similar to those observed in the controlled trials. The benefits from home gardening and nutrition education will usually be broader than supplementation and fortification (i.e., not limited to vitamin A), but not as large, with respect to vitamin A.

Cost-Effectiveness of Vitamin A Interventions

Introduction

Throughout the public health literature there are repeated references to the cost-effectiveness of micronutrient interventions and, in particular, the cost-effectiveness of Vitamin A interventions relative to other health interventions. In this section we review the post 1985 literature on the cost-effectiveness of Vitamin A interventions identified from the National Library of Medicine on-line databases, references in papers, discussions with experts in the field, files held by PATH Canada, and conference abstracts. Despite the repeated references to the cost-effectiveness of Vitamin A very few studies were identified. For example, a search of PubMed on 1 June 2000 using the search terms "Vitamin A" and "cost-effectiveness" identified only seven papers of which only four were relevant.

In addition to these studies three guides on how to assess the cost-effectiveness of micronutrient interventions have been published.

- The Practitioner's Guide to Cost-Effectiveness Analysis of Nutrition Interventions. 1996. Maternal and Child Health Interorganizational Nutrition Group (Splett, 1996).
- Methods for Assessing the Cost-Effectiveness of Micronutrient Programs. (Opportunities for Micronutrient Interventions, 1996).
- The Economic Analysis of Nutrition Projects: Guiding Principles and Examples. (Phillips and Sanghvi, 1996).

This section is divided into three parts. The first part summarizes data from country specific projects in Guatelemala, Nepal, the Philippines and South Africa, and the second part summarizes modelling efforts. The final part summarizes the costs (but not effects) of food fortification.

Costs and Effects: Projects in Four Countries

1. Guatemala: Phillips et al., 1996.

Phillips et al. (1996) provide data comparing three interventions in operation in Guatemala in 1991/1992. Table 2 summarizes the study and methods used to collect data and Table 3 summarizes the results.

The study found that in Guatemala, sugar fortification was the most attractive option. The cost was estimated to be US$ 0.98 per high risk beneficiary reached. These costs were substantially lower than the costs of capsules (US$ 1.68) and food production/education (US$ 3.91). Fortification and food production also had benefits to other than those at high risk. These results, however, were sensitive to the level of vitamin A fortificant found in sugar supplies; lower concentrations resulted in fortification lowered cost-effectiveness.

Table 2. Summary of the Guatemala study.

Problem/ Evaluation Objective	1. To assess how best to deliver Vitamin A to the national population of Guatemala. 2. To test a framework for identifying the most efficient approach to delivering Vitamin A in a given country context.
Background	Vitamin A deficiency is a serious public health problem in Guatemala affecting an estimated 22% of U5s.
Interventions considered	Three broad options were considered; the focus however was on 1 and 2, as 3 is a longer term option and likely to take several years. 1. Fortification of sugar with Vitamin A; 2. Periodic distribution of high dose Vitamin A capsules to women and children under 6 years; 3. Food production/education designed to encourage the establishment of home gardens and consumption of Vitamin A rich foods.
Other issues addressed:	Does "wastage" suggested by the untargeted nature of fortification render it less cost-effective than a targeted supplementation program?
Type of analysis	Review of data from on-going interventions.

Data sources	Study drew on secondary data provided by donors, implementing and collaborating agencies.
Cost Data	Cost data collected for a single year of operation for each program after it had moved beyond start-up mode into more routine operation (1991 for fortification and 1991/2 for capsule and food production/ education) • Data on all capital and recurrent costs collected. Data on recurrent costs mainly come from expenditure records. Where these records were not sufficient, costs were calculated based on quantities of inputs and unit prices; • Value placed on donations as well as purchased supplies; • All activities including management and supervision and field level operations costed; • Start up costs excluded; • Discount rate set at 10%.
Effectiveness Data	Two different indicators were used to assess the effectiveness of the interventions: a) Number of person-years for which individuals with inadequate access to Vitamin A satisfy their needs as a result of the intervention b) Number of mothers and children protected from vitamin A deficiency • Effectiveness of supplementation was based on data from a study in 24 communities through a campaign of mobile clinics. • Effectiveness of fortification was based on sugar consumption patterns by quintile determined from national expenditure data, estimates of vitamin A levels in sugar, and 24 hour recall diet surveys. • Effectiveness of food production/education was based on data from an evaluation conducted in the study area. In the evaluation it was found that 87% of the households that received inputs had established gardens and that households that had established gardens consumed adequate levels of vitamin A in the year.
Time Horizon	For supplementation and fortification one year time horizon. For Food production/education two assumptions made: (1) that once inputs are halted 50% of gardens operating in one year drop out the next year, indefinitely, and (2) that 50% of gardens drop out in year 1, 40% in year 2, etc., until the number of gardens stabilizes at about 15%.

Table 3. Summary of the estimates of the effectiveness, costs and cost-effectiveness of Vitamin A programs in Guatemala. (All costs in 1991 US$)

	Fortification	Capsules	Food production/ education
Location	Nationwide	2 Departments	2 Departments
Delivery system	Retail sales	Rural health centres, community contacts	Agricultural extension workers
Implementing agencies	Sugar industry, Gov't of Guatemala	Project Hope, Ministry of Health	Project Hope, Ministry of Agric.
Population covered	8,280,000	47,000	53,000
Potential beneficiaries	5,496,000	47,000	53,000
Beneficiaries	5,4960,00[1]	43,000[2]	50,000[3]
High risk beneficiaries	2,418,000[1]	43,000[2]	22,000[3]
Annual cost	$ 2,380,000	$ 71,556	$ 82,284
Cost per beneficiary	$ 0.43	$ 1.68	$ 1.72
Cost per high risk beneficiary	$ 0.98	$ 1.68	$ 3.91

[1] Assumes that all urban and rural household with an annual income less than 2400 quetzales benefit, of whom 44% are high risk, and that sugar is fortified at 7.3 ug across the country.
[2] Assumes that children receiving one dose are protected for 6 months.
[3] Assumes 50% of houses drop out every year after program investment stops.

2. Nepal: Pant et al., 1996 (also quoted in Pokharel et al., 1998)

Pant et al. (1996) report data from an intervention trial conducted in seven districts in the Terai and mid-hill areas of Nepal. A total of 40,000 children were enrolled in the study and assigned to one of three groups:

1. Vitamin A supplementation: semiannual distribution of 100,000 IU to children between 6 and 12 months of age and 200,000 IU to children between 1 and 10 years.
2. Nutrition education: education targeted at increasing consumption of vegetables and increasing access to selected public health activities (deworming, promotion of ORS and immunizations, and antibiotics for acute respiratory infections).
3. Control group: received treatment during examinations only.

The study was completed in 1992 after a follow up period of 24 months. Two different criteria were used to compare the interventions – cost (both as a project and extrapolated to different levels of program intensity) and impact on health status, primarily xerophthalmia and wasting malnutrition.

Cost estimates for the inputs for each intervention were based on accounts of transfers and unit prices of physical resources and personnel. Table 4 records the projected 5 year costs of covering a district in Southern Nepal with a population of 200,000 of whom 60,000 are children under the age of 11. The nutrition education program was broken down into two groups – nutrition education only and nutrition education plus maternal literacy.

Table 4 also records the projected changes in health status and cost-effectiveness of the three interventions. All three of the interventions were highly cost-effective in comparison to other interventions when death was used as the measure of effectiveness. The cost per death averted ranged from US$73 (capsule distribution) to US$252 (nutrition education plus literacy). For each of measure of health status investment capsule distribution was the most cost-effective. The capsule distribution program also benefited from high coverage rates (estimated at 80% at 24 months).

Table 4. Estimated costs for a district in southern Nepal and the associated improvement in health status and cost-effectiveness. (All costs in 1992 US$)

	Capsules	Nutrition Education	Nutrition Education + Maternal Literacy
Program costs			
Investment cost	$ 10,000	$ 33,000	$ 33,000
Operating cost	$ 75,000	$ 240,000	$ 370,000
Training	$ 2,000	$ 11,000	$ 11,000
Supplies	$ 10,000	$ 29,000	$ 29,000
Supervision	$ 2,000	$ 5,000	$ 5,000
Miscellaneous	$ 1,000	$ 0	$ 0
Adult literacy	$ 0	$ 0	$ 29,000
Total program cost for 5 years	$ 85,000	$ 273,000	$ 403,000
Health status of district after 5 years*			
n Bitot’s spots prevented	2,535	2,340	3,510
n deaths prevented	1,160	1,085	1,600
n cases wasting prevented	4,000	6,000	7,000
Cost-effectiveness			
Cost per Bitot’s spot prevented	$ 33.53	$ 110.26	$ 114.81
Cost per death avoided	$ 73.28	$ 237.79	$ 251.88
Cost per wasted child prevented	$ 21.25	$ 43.00	$ 57.57

Source: Pant et al, 1996.

* In the absence of an intervention it was assumed that each year 780 children would develop Bitot’s spots, 540 would die and 14,000 would show signs of wasting.

A reference to the cost-effectiveness of Vitamin A supplementation in Nepal can also be found in the discussion of a paper by Daulaire et al., 1993. This paper reported information on the consequences of a Vitamin A supplementation program introduced in the Jumla district of Nepal targeted at all children under 5 years of age (single high dose capsule of retinyl palmitate: 200,000 IU to children 12-59 months, 100,000 IU to children 6-11 months, and 50,000 IU for children < 6 months). The authors stated that “The extra cost of the supplementation program (capsules, staff and management time) was less than $0.20 per dose. Based on our calculation of deaths averted, this indicates a total marginal cost of less than $11 per death averted making vitamin A supplementation a highly cost-effective strategy for increasing child survival which should be sustainable over an extended period. Of course, our estimate of cost per death averted is particularly low because of the extremely high underlying mortality and vitamin A deficiency among the population and the existence of a viable delivery system on which to add vitamin A distribution; these factors will vary in other settings". These estimates are substantially less than the figures quoted by Pant et al (e.g., US$ 11 vs US$ 73.28 per death averted). Unfortunately, the authors provided no information on how the cost estimates were made and, as a result, it was not possible to assess how much these differences reflect the type of cost data collected or other program differences (e.g. the tighter age range of the program (under 5 vs under 11) and the higher rate of xerophthalmia in the community.

3. Philippines: Loevensohn et al. 1997, Fiedler et al., 2000

Two papers provide data on the cost-effectiveness of different strategies for reducing vitamin A deficiency in the Philippines. The paper by Loevinsohn et al. focused on targeting strategies for supplementation while the paper by Fiedler et al. compared supplementation to a hypothetical scenario of flour fortification.

Loevensohn et al.'s (1997) study examined the relative merits of different options for targeting vitamin A capsules delivered during the national campaigns linked to routine immunization and polio eradication from the perspective of the Department of Health. The three options explored were:

1. VACs given to all children 6-59 months of age (universal distribution),
2. VACs given only to children mildly, moderately or severely underweight (broad targeting; 30% of children fall in this category),
3. VACs given only to those suffering from moderate and severe malnutrition (narrow targeting; 5% of children fall in this category).

The only difference between the universal and targeting approaches was that during the latter children were weighed and classified before being supplemented if necessary (weighing and classifying was assumed to take 3 minutes; while the time to give and record vitamin A was assumed to take 1.25 minutes).

The study was conducted from the perspective of the Department of Health and, as a result, only those costs borne by the Department of Health were considered. Table 5 provides more information on some of the assumptions underlying the analysis. The results indicated that universal distribution of vitamin A to all pre-schoolers was the most effective method for preventing deaths and the most efficient in terms of cost per death averted. The first year average cost of the universal approach was US$67 per death averted compared to $144 and $257 for the broad and narrow targeting approaches respectively. This the authors argued is "because vitamin A is very effective, relatively inexpensive to purchase and deliver universally, and because the cost of defining high risk groups is relatively costly and inaccurate." It should be noted, however, that universal distribution was not the least expensive approach --the total cost of the universal approach was 12% more than narrow targeting (which was the cheapest) but that it resulted in a 327% increase in the number of deaths averted.

Table 5. Assumptions underlying the analysis on the relative costs and benefits from targeting supplementation activities in the Philippines.

Effectiveness Estimates	• Indicator used was number of deaths averted; • Coverage rates were assumed to be the same regardless of targeting strategy and were based on 1993 National Immunization Days data (93%); • Vitamin A supplementation was assumed to reduce overall mortality by 23%; • Effect of Vitamin A distribution of blindness prevention and reduction in morbidity was not taken into account; • Owing to problems in measuring weights assumed that 20% of malnourished children were misclassified as normal; • Moderately and severely malnourished children were assumed to comprise 19% of all deaths preventable by vitamin A and mildly, moderately and severely malnourished children 55% of the total.

Cost Estimates		• All costs calculated as the incremental costs incurred by the Department of Health due to the introduction of vitamin A supplementation;
		• Costs were measured for the first year of the program only (1993);
		• Costs were based on actual expenditures in the Philippines;
		• Cost included were:
		  • Procurement and distribution of vitamin A capsules (capsules assumed to cost US$ 0.028)
		  • Training health workers
		  • Public information, education, and communication
		  • Time health workers spent weighing, classifying, and supplementing children (US$ 0.64 per hour);
		• Volunteer labour time was not included.

Source: Loevensohn et al., 1997

Fiedler et al.'s (2000) paper presented an economic evaluation of the Philippines National Vitamin A Supplementation Program (NVASP) in 1996/7 (the third year of the program) and compared this to a hypothetical program of vitamin A fortification of wheat flour. Table 6 summarizes the assumptions underlying their analysis. Based on their estimates of the costs of the two programs the authors suggested that fortification is more efficient in reducing inadequate vitamin A intake compared to the NVASP. The authors estimated that fortification of hard wheat flour at 490 RE/100 grams would cost half as much as the current NVASP (see Table 7). It should be noted, however, that the cost figures presented in the paper include volunteer labour time which accounted for 30% of the total costs of the program. If these costs are removed – the total cost of a supplementation program with a coverage of 88% falls to 583.7 million pesos, and the cost per person year of sufficiency obtained to 211 pesos.

Due to the nature of food consumption patterns, however, fortification of hard flour at 490 RE/100 grams of hard flour would leave 29% of Filipino children, or 2.2 million children, suffering from inadequate vitamin A. Increasing the level of 710 RE/100g reduced the number of children with inadequate intake by a third but increased costs by 48%. To compensate for this the authors proposed that the Philippines should restructure their Vitamin A supplementation program and introduce a combined fortification-supplementation program targeted by geographic area.

Table 6. Assumptions underlying the analysis of the relative costs and benefits from universal supplementation and fortification of wheat flour

NVASP Program	
Effectiveness Estimates	• Coverage estimates for 1996 (ranged from 78 to 88%) used to estimate the number of person years of vitamin A gap reduction (one capsule = 6 months of intake).
Cost Estimates	• Data based on questionnaires sent out to different administrative units and extrapolated to the national level; • Volunteer labour time valued at minimum wage (80% of personnel who work on NVASP are volunteers); • Share of national polio immunization campaign day costs were based on the proportion of time spent delivering Vitamin A.
Fortification Program	
Effectiveness Estimates	• Based on food consumption survey data. Impact of fortification was calculated as the increase in the number of children with adequate vitamin A intake due to fortification of flour.
Cost Estimates	• Analysis includes only the incremental production costs, the promotion of the program, and monitoring costs (internal and external). Start up costs were not included; • Costs for procurement and monitoring based on data from 2 flour millers and interviews with other millers; • Promotion and external monitoring costs estimated from data obtained in interviews with representatives of the government and the Philippines Baker's Association.

Source: Fielder et al., 2000

Table 7. Cost and effectiveness of the Philippines vitamin A program interventions. (All costs in January 1998 Pesos)

Scenario	Total Cost	Cost per person year of adequate VA intake achieved	% of children who still have inadequate Vitamin A intake
Fortification (REs per 100g)			
Hard flour (490)	P 149,244	P 152	29%
All flour (490)	P 227,195	P 221	28%
Hard flour (600)	P 181,710	P 141	25%
Hard flour (710)	P 221,465	P 131	20%
Hard flour (820)	P 270,143	P 143	17%
Supplementation			
Twice yearly–coverage= 88%	P 833,819	P 302	5%
Twice yearly–coverage=78%	P 829,647	P 339	9%
Combined	P 818,658	P 368	12%
Fortification (hard flour at 490 REs); universal supplementation in urban areas; and targeted supplementation in worst affected rural areas			

Source: Fielder et al., 2000

4. South Africa: Hussey and Klein, 1993

Only one published study from Sub-Saharan Africa was identified providing cost-effectiveness data. This paper focused on the provision of Vitamin A supplementation to children hospitalized with measles. In the study, hospital records of children under 15 years of age admitted with measles to the City Hospital for Infectious Diseases in Cape Town, South Africa were reviewed retrospectively for two non-consecutive two year periods. 1,061 of these children had not received Vitamin A and 651 had received a high dose (400,000 IU of oral vitamin A -- half given on admission and half given the following day). The study demonstrated an impressive reduction in measles morbidity and mortality in hospitalized children who received Vitamin A: mortality was reduced by 64%, ICU admissions by 62% and hospital stays by 2.9 days on average (from 13 to 10.1). While no detailed data on costs of Vitamin A supplementation were provided in the paper the authors state that high dose Vitamin A therapy cost R 1.00 (US$ 0.35) per patient and resulted in an estimated saving to the hospital of R 580 (US$ 203) per case. The authors do not provide estimates of the cost per death prevented – but using their figure for the death rate in children hospitalized with measles (5%) and the reduction in death following high dose Vitamin A therapy (64%), the cost per death prevented from high dose Vitamin A therapy was R 31.25 or US$ 10.94.

Costs and Effects: Modeling

The figures most widely quoted in the literature are from a paper by Levin et al. produced for the 1993 World Development Report (Levin et al., 1993; World Bank, 1994). The authors based their estimates of the costs and effectiveness of two interventions – supplementation of U5s and food fortification - on published data. Table 8 records the epidemiological assumptions underlying their estimates, Table 9 the data upon which their cost estimates were based, and Table 10 the results of their analysis. Note, there are some differences in the results presented in the two papers – the following tables are based on the revised figures published in 1994.

The authors concluded that supplementation was more cost-effective in terms of number of deaths prevented and DALYs than fortification (US$ 9.3 versus US$ 29 per DALY, and US$ 325 versus US$ 1000 per death averted, for supplementation and fortification, respectively).

Table 8. Epidemiological assumptions.

U6s with VAD (%)	15
U6s with severe VAD (%)	0.27
U6s with severe VAD dying (%)	0.16
U6s partially blind (%)	0.60
U6s totally blind (%)	0.28
Degree of disability if partially blind	25%
Degree of disability if totally blind	50%

Source: World Bank, 1994

Table 9. Data on which estimates of costs of different interventions were based (see Levin et al., 1993, for references to the original papers). Fortification costs include: micronutrient compounds, as well as personnel, equipment and special packaging required for the preparation and delivery of the fortified food. Supplementation costs include: cost of supplements as well as transportation and personnel for distributing supplements.

Country	Year	Type of Intervention	Estimated cost per person (1994 US$)	Estimated cost per person year of protection (1994 US$)
Guatemala	1976	Fortification – sugar	0.17	0.17
Haiti	1978	Supplementation	0.55-0.81	0.55-0.81
Indonesia/ Philippines	1975	Supplementation	0.50	0.50

Source: World Bank, 1994

Table 10. Costs and effectiveness of vitamin A interventions.

	VACs supplementation (semi-annual mass dose)	Vitamin A fortification
Description of program		
Target group	Children under 5	Entire population
Number	13,000	100,000
Per capita cost per participant (US$)	0.50	0.20
Program costs (US$)	6500	20000
Program effectiveness (%)	75	75
Outcome		
Deaths averted	20	20
Total blindness averted	4	4
Partial blindness averted	8	8
DALY gained	696	696
Cost-effectiveness		
Cost per DALY (US$)	9.3	29
Cost per death averted (US$)	325	1000

Source: World Bank, 1994

An earlier paper by Grosse and Tilden (1988) looked at program costs and effects of the three main classes of interventions: (1) supplementation, (2) fortification of processed foods; and (3) diet modification. The model contained sub-models which dealt with the resource requirements of the alternative program configurations, the health benefits associated with that activity (rates of specific eye pathologies associated with vitamin A deficiency and mortality), and the consequences of specific budgetary allocations over time. Costs incorporated included personnel, equipment, training, and facility construction both to set up and to run the program. Data from the province of West Java in Indonesia were used to explore the implications of the different interventions over a 20 year time frame using a discount rate of 10%. Table 11 summarizes some of their assumptions. Unfortunately, no data are presented on the cost-effectiveness of the different interventions, and the use of a 20 year time frame for the analysis makes it difficult to compare results with other studies.

The authors found that fortification of monosodium glutamate (MSG) yielded the highest level of health benefits. Under constrained budgets, however, the preferred strategy varied. Table 12 reports their preference ranking of the three alternatives under their base case scenario. It should be noted, however, that different groups bore the costs in each of the different interventions. For example, the costs of dietary modification tend to be borne by families and supplementation by governments and donors.

Table 11. Assumptions underlying the estimates of the costs and effects of different Vitamin A interventions in the province of West Java.

Intervention	Assumptions

Supplementation	• Capsules distributed twice a year to children from 6 months to 6 years of age by community health post system (capsules cost US$ 0.03 per capsule); • Program estimated to reduce by 80% all signs and subclinical VAD in target population; • Coverage is a function of budget intensity.	
Fortification	• Fortification of all monosodium glutamate produced in West Java (fortificant costs US$ 25 per kg); • At a level of 0.003 kg per person per year, 80% reduction in all signs and symptoms is achieved; • Efficacy is a function of fortification level.	
Diet Modification	• Program encourages consumption of green leafy vegetables by children and pregnant or lactating women and is delivered by community health post system; • Assumed efficacy of program in altering dietary patterns is 50%; • Cost of sources of beta-carotene resulting from increased consumption caused by the program was included in total cost; • Coverage and range of health messages is a function of budget intensity.	

Source: Grosse and Tilden, 1988

Table 12. Preference ranking of alternative strategies given different levels of budgetary resources committed to VAD control over a 20 year period. Cost estimates in 1988 US$.

Budget level ($/capita/ 20 years)	Preference ranking First	Second	Third
< 0.25	Diet modification	Fortification	Capsules
0.25-0.42	Diet modification	Capsules	Fortification
0.43-0.87	Capsules	Diet modification	Fortification
0.88-1.25	Capsules	Fortification	Diet modification
>1.25	Fortification	Capsules	Diet modification

Source: Grosse and Tilden, 1988

Costs of Fortification

A number of different food products have been fortified with Vitamin A in different parts of the world. Table 13 reports data from a number of studies that were presented at a conference in 1997 (Micronutrient Initiative, 1998b) on the costs of fortifying different products. In general, the incremental costs of fortificant, marketing and quality assurance, are a small percentage of the final price and are either passed along to the consumer or absorbed by food companies.

Table 13. Costs of fortifying different food products with Vitamin A (from Micronutrient Initiative, 1998b).

Product fortified	Country	Results	Ref:
Margarine	Multiple	Cost of fortifying margarine at 33,000 IU/kg vitamin A is US$ 0.0018/kg (typical serving ~ 15mg).	Johnson
	Philippines	In early 1990s estimated that fortifying margarine added US$ 0.01 /100 g margarine (<3% of sale price of $ 0.37).	Solon
Vanaspati (cooking oil used by 90% of households in India)	India	Fortification became compulsory in 1953 at 25 IU/g. Average consumption in country is 3 g/day (up to 10g/day), therefore providing ~ 4% (up to 12%) of RDA (consumption is much lower in rural areas than urban). Cost is 90 rupees per ton (Hindustan Lever, Ltd) or 0.3% of product cost.	Sridhar

Corn starch	Latin America	Fortification levels set so that each serving provides approx. 25% of RDA. Based on manufacturer's experience, cost of fortification is less than 1% of total plant costs (defined as sum of raw material, packaging material, and manufacturing expenses).	Roden-stein
Sugar	Guatemala	Estimated cost of sugar program in mid 90s was US$ 3,654,000 to fortify 350,000 MT of sugar, and of these costs 95% are the cost of the fortificant. In addition, cost of monitoring ($60,000) and of program evaluation ($100,000) need to be included. Estimate yearly cost of coverage per person at risk US$1.01. Note that about 30% of sugar goes for industrial use in which much of fortificant is lost.	Dary
Flour	Philippines	Added cost of fortificant per kg of flour was 8.8 centavos or US$ 0.0034.	Solon

Discussion

Cost-effectiveness analysis is a tool for systematically comparing the costs and outcomes of two or more competing interventions. It has been used widely in the health field to help make decisions between different treatment and prevention methods. Cost-effectiveness analysis, is only one component of a full economic evaluation – other elements that need to be examined include the total cost of the project, who will bear the costs (e.g. governments, consumers or industry), and foreign exchange requirements.

The relative cost-effectiveness of micronutrient interventions depends upon a number of factors including the level of micronutrient deficiency, demographics and the health care system. An intervention that is reported to be more cost-effective under one set of circumstances may not be in different circumstances. For example, nationwide fortification programs for Vitamin A are likely to be more cost-effective than capsule delivery at reducing deficiency when deficiency is widespread and targeted capsule delivery more cost-effective when deficiency is localized.

The relative ranking of the different ways of reducing VAD is not clear and varies widely depending upon a number of factors including the prevalence of VAD, the health care system, and the suitability of food commodities for fortifying. In practice, a combination of interventions may well be the best approach for reducing VAD, and countries would be well advised to continue (or initiate) a range of interventions including supplementation, fortification, and nutrition education as part of their efforts to improve health and nutrition status.

A small number of studies were identified that provide data on the costs and effectiveness of two or more interventions for reducing VAD. The most widely quoted figures are from a paper published in 1993 by Levin et al. in a book titled "Disease Control Priorities in Developing Countries". The results from their study suggest that supplementation is superior to fortification. These results, however, were based on data from studies conducted in the 70s. More recent country studies, including those from Guatemala and the Philippines, suggest that – provided there is a suitable food vehicle for fortification – fortification is a less costly way to improve Vitamin A status at the population level than nutrition education or supplementation. Fortification, however, will not meet the needs of all of the population and should be complemented by appropriately targeted capsule distribution programs.

Comparisons between the different studies are fraught with difficulties as, in general, the studies have not collected similar data on the costs and/or effectiveness of their interventions and do not provide detailed enough information on what was and was not included to be able to adjust their figures accordingly. In addition, the type of project evaluated (research project, on-going intervention, or hypothetical scenario) and the time frame of the projects vary which further compounds the difficulties in comparing results.

The focus of the published literature has been on vitamin A supplementation and fortification. There is a marked shortage of information on the costs and effectiveness of home gardening and nutrition education as related to Vitamin A deficiency. Both of these need to be looked at in more detail while also taking into consideration that the benefits from home gardening and nutrition education may extend beyond their impact on VAD, into food security, income generation, and self-sufficiency issues.

Information on the cost-effectiveness of Vitamin A interventions relative to other public health interventions is also limited as few studies provide data that can be easily compared to other interventions. Three studies provide data on the cost per death averted: In Nepal Pant et al.'s (1996) estimates ranged from US$ 73 for capsule distribution to US$ 252 for nutrition education and maternal literacy; in the Philippines, Loevensohn et al. (1997) estimates ranged from US$ 67 to US$ 257 for targeted supplementation and varied depending on which population group was targeted, and in Levin et al.'s (1993) modeling work estimates ranged from US$ 325 for fortification to US$ 1000 for supplementation. In addition, Daulaire et al. (1993) quoted a cost per death averted of US$ 11 but provided no information in the paper on what was included in their estimates. All of these figures compare favorably to the cost per death averted for other public health interventions for reducing deaths in U5s. Data on the cost per DALY, unfortunately, are even more limited; the only data are from the study by Levin et al where they estimated that a cost per DALY ranging from US$ 9.3 (fortification) to US$ 29 (supplementation).

ANALYSIS OF VITAMIN A INTERVENTIONS

Introduction

The existing literature on the cost-effectiveness of Vitamin A and other micronutrient interventions is limited. Given the public health importance of micronutrient deficiencies there is clearly a need for more economic research focused on exploring the implications and sustainability of different approaches for reducing micronutrient deficiencies. In this research project we have generated some additional information from community vitamin A interventions in Africa and Asia conducted by NGOs in collaboration with government agencies. Initially we had hoped to be able to compare the cost-effectiveness of vitamin A capsule distribution, home gardening and nutrition education in a number of different projects. This proved not to be possible owing to the limitations of the data available on the effectiveness side and we have had to restrict our analysis to a comparison of the costs of vitamin A capsule distribution. The data we do have are from a retrospective review of the costs and effectiveness of the projects based on accounts routinely provided by the project and a retrospective questionnaire, completed by project staff. The use of retrospective data and lack of site visits clearly limited the quality of the data upon which our estimates are based.

Methods

Selection of projects:

From 1997 to 1999, PATH Canada, supported by the Micronutrient Initiative, coordinated the Global Vitamin A Initiative (GVAI), a network of 14 NGO-led vitamin A interventions in 11 countries in Asia and Africa. These projects formed the core of the analysis. In addition, PATH Canada linked with World Vision Canada (WVC) and Helen Keller International (HKI), both of whom have numerous vitamin A projects. Three WVC and two HKI projects were identified as potential projects to be included in the analysis.

Of the fourteen GVAI projects, four were excluded from the analysis in the first pass through, as they had either dropped out of the network or had not met reporting requirements. The remaining projects (see Table 14) were then screened and, based on the quality of their reporting, a decision was made to include or exclude them from the cost-effectiveness study. For each study selected a questionnaire was developed to collect both cost and effectiveness data. These questionnaires were similar in structure but tailored to each project based on the monitoring and financial reports submitted to PATH Canada to improve completion rates. This cost-effectiveness study was an add-on to the projects' work, and no funds were available to the projects for collecting supplementary data.

For the WVC and HKI projects data were collected from the project reports submitted to their North American headquarters.

Table 14. Vitamin A projects considered for inclusion in the study

	Project	Status*
GVAI	Uganda – MIHV	1
	Vietnam - RTCCD	1
	Bangladesh - WV	1
	Bangladesh – Initiatives	1
	Yemen - ADRA	2
	Indonesia – WV	3
	Kenya – CARE	3
	Malawi – CPAR	3
	Nepal – HKI	3
	Niger – HKI	3
Helen Keller International	Philippines	2
	Niger	2
World Vision	Tanzania	1
	Senegal	1
	Ghana	1

* Status: 1=used in the final analysis, 2= key information missing, 3=no questionnaire returned

Assessment of effectiveness

Estimates of the number of VACs distributed and VACs coverage rates were based on the information drawn from project reports and the retrospective questionnaires. Where there were discrepancies in the reported figures contact was made with the project staff to clarify the situation.

Estimates of the number of VACs distributed were used to estimate the number of child years of coverage. In doing this we have assumed that the important variable for our analyses is the total amount of vitamin A delivered to the population by the project. For example, it is assumed that 200,000 IU given to 100 children twice in a year at six monthly intervals (=40,000,000 IU) has the same population health benefits as 200,000 IU given to 200 children once in a year (=40,000,000 IU). From our knowledge of the pharmacokinetics of vitamin A this appears to be a reasonable assumption and means that estimates can be made of the health benefits of VAC distribution without information on the frequency (once or twice per year) children received VACs.

Using the total vitamin A delivered by each project, project specific estimates of child-years of "useful" coverage were based on the number of child-years of coverage and the prevalence of VAD in the target population. Child-years of coverage figures came from VAC distribution data reported from the project, and prevalence of VAD was taken from published national estimates (Micronutrient Initiative, 1998).

Number of deaths averted were calculated from the estimated figure for child years of "useful" coverage using national estimates of under-five and under-one mortality rates, and the relative risk of death in children receiving VACs. Owing to a lack of specific information on mortality rates in each population group, the estimates are based on national data (UNICEF, 1999). The estimated mortality reduction as a result of vitamin A supplementation (i.e., 23%) was based on Beaton et al. (1993).

Assessment of costs

Data on the costs of the GVAI projects came from two sources – the annual accounts submitted by the project and a self-completed questionnaire. The questionnaire asked for information on the quantities of goods used and actual expenditures under selected cost categories for two years. The cost categories included: personnel (which covered expatriate costs, local personnel costs paid for directly by the project), per diems, training, IEC materials, supplies, transport, monitoring and office costs. Project staff were also asked to provide estimates of the costs of goods not paid for (e.g. local personnel provided by other organizations and volunteers), and to allocate project expenditures to the different interventions being supported.

Data on the costs of the WVC and HKI supported projects were based on a review of the records held at their headquarters.

The cost data are for the Years 1997 to 1999 and we have not adjusted the costs to take into account inflation. We have also used the exchange rate figures provided by the projects.

Assessment of cost-effectiveness

Estimates of the costs and effects of the projects were combined to generate for each project three different cost-effectiveness ratios:

1. cost per child year of coverage
2. cost per child year of 'useful' coverage
3. cost per death averted

Data were generated for each of the years that we had both cost and effectiveness data for. Where the data collected were for different time periods we linearly extrapolated the data. For example, the World Vision Ghana project had information on the number of VACs delivered over 6 months whilst the cost data referred to a 16 month period. To estimate the cost per VAC delivered we assumed that that the rate of delivery of VACs remained unchanged.

Results:

Selection of projects

Ten GVAI projects were selected for inclusion in the study.   Of these projects, only five returned a completed questionnaire despite a number of reminders. The quality of the returned information varied, and after further clarifications from project staff a decision it was decided to drop one of the projects owing to changes in the project structure and difficulties in interpreting the data (see Table 14).

Owing to missing information and the difficulties in interpreting the data from the HKI projects which were part of large Child Survival Projects we were not able to generate estimates for either HKI project.

More information on the seven selected projects can be found in Appendix B.

Assessment of effectiveness

Table 15 records for each project our estimates of child-years of coverage, child-years of "useful coverage", and number of deaths averted.   The calculatons are explained in the footnote to Table 16.

Table 16 illustrates how changing some of our estimates affects the number of deaths averted using the data from the Bangladesh – Initiatives project. The first row repeats the "actual" scenario, as also shown in Table 15. In Scenario 1 mortality rates are modeled 25% higher in than the national average mortality rate which was used in Table 15. The project targeted a relatively poor region of the country, so mortality rates at the project site higher than the national average are not unexpected. With a higher mortality rate the number of deaths averted would be proportionately higher.   In Scenario 2 the prevalence of VAD in the target population is modeled 25% higher than the national average, which, again, is not unexpected. Accordingly, the child-years of useful coverage is 25% higher.

Paradoxically, in these scenarios, number of deaths averted is independent from the prevalence of VAD, which is calculated as a simple multiple of the mortality rate. The reality would be more complicated – in this location, if the prevalence of VAD were higher, it would be reflected in a higher mortality rate (which in turn would yield more deaths averted). VAD is (obviously) not independent of mortality rate, as modeled in this exercise.

Note the various sensitivities in the calculations. Obviously child-years of VACs coverage is an important variable, but the mortality rates and VAD prevalence are also very important.   For example, in World Vision – Senegal the child-years of coverage was 50% less than in World Vision – Bangladesh, but because the prevalence of VAD was more than twice as high in Bangladesh, the number of child-years of "useful coverage" is four times higher in Bangladesh. However, because of the higher 1 to 5 mortality rate in Senegal, an equal number of deaths were averted. The differing effectiveness (in terms of deaths averted or useful coverage) of the various projects is not necessarily due to more effective project implementation, but, at least in part, due to the differences in VAD prevalence and mortality rates.

Table 15.. Effectiveness of VAC distribution in children under 5 years old in seven projects.

A	B	C	D	E	F	G	H	I	J	K
Project	**Total VACs**	**Child-Years of VACs Coverage**	**U5MR (est)**	**U1MR (est)**	**E2-E1 = 1-5MR (est)**	**Subclin+ clin VAD**	**N child-years of "useful coverage"(N child-years moved from VAD to non-VAD)**	**N deaths expected per year at baseline (in children in D) if coverage was 0**	**N child deaths expected with coverage in C**	**Deaths averted**
<u>GVAI Projects</u>										
Bangladesh – Initiatives										
Year 1	30,050	15,025	106	79	27	0.275	4,132	101	78	23
Year 2	37,381	18,691	106	79	27	0.275	5,140	126	97	29
Total	67,431	33,716	106	79	27	0.275	9,272	228	175	52
Uganda – MIHV										
Year 1	14,000	3,500	134	84	50	0.234	819	44	34	10
Year 2	19,000	4,750	134	84	50	0.234	1,112	59	46	14
Total	33,000	8,250	134	84	50	0.234	1,931	103	79	24
Vietnam – RTCCD										
Year 1	2,696	1,348	43	32	11	0.108	146	3.7	2.9	0.9
Year 2	2,767	1,384	43	32	11	0.108	149	3.8	2.9	0.9
Total	5,463	2,732	43	32	11	0.108	295	7.5	5.8	1.7
Bangladesh - WV										
Year 1	23,032	11,516	106	79	27	0.275	3,167	78	60	18
Year 2	21,542	10,771	106	79	27	0.275	2,962	73	56	17
Total	44,574	22,287	106	79	27	0.275	6,129	150	116	35
<u>World Vision Projects</u>										
Tanzania										
Actual for 6 months	2,351	1,176	143	92	51	0.162	190	15	12	3
Estimated for 22 Months	8,620	4,310	143	92	51	0.162	698	55	42	13
Senegal										
Actual for 6 months	6,246	3,123	124	72	52	0.122	381	41	31	9
Estimated for 23 Months	23,943	11,972	124	72	52	0.122	1,461	156	120	36
Ghana										
Actual for 6 months	3,100	1,550	107	72	35	0.158	245	14	10	3
Estimated for 16 Months	8,267	4,133	107	72	35	0.158	653	36	28	8

See Footnote of Table 16 for Explanation of Columns.

Table 16. Scenarios based on the estimates of the effectiveness of the Bangladesh-Initiatives project, demonstrating some of the sensitivities in the calculations. The first cases uses the “actual” estimates as in Table 15. Scenario 2 uses a higher mortality rates. Scenario 3 uses 25% higher prevalence of VAD. The differences in Scenarios 2 and 3 are bolded.

A	B	C	D	E	F	G	H	I	J	K
Project	**Total VACs**	**Child-Years of VACs Coverage**	**U5MR (est)**	**U1 MR (est)**	**E2-E1 = 1-5MR (est)**	**Subclin+ clin VAD**	**N child-years of "useful coverage"(N child-years moved from VAD to non-VAD)**	**N deaths expected per year at baseline (in children in D) if coverage was 0**	**N child deaths expected with coverage in C**	**Deaths averted**
Actual	67,431	33,716	106	79	27	27.5%	9,272	228	175	52
Scenario 1	67,431	33,716	**132.5**	**99**	**34**	27.5%	9,272	**284**	**219**	**65**
Scenario 2	67,431	33,716	106	79	27	**34.5%**	**11,590**	228	175	52

Explanation of Columns.

B. These numbers are from project reports, and are for 1 to 5 year old children only, although many projects also distributed to U1s, mothers, and older children.

C. C=B/2 (except Uganda-MIHV = B/4). Based on two 200,000 IU capsules providing 1 year of coverage. For Uganda, where only half a capsule was given, four capsules provide one year of coverage

D and E. Estimated Mortality Rates per 1000 children under 1 and under 5 years old. From Unicef (1999).

F. Estimated mortality rate for children 1 to 5 years old (the target group for the U5 VACs campaigns)

G. From Micronutrient Initiative (1998a). It includes both clinical and subclinical VAD.

H. Calculated as C x G, assuming that VAC distribution not targeted to VAD children (as is the case in mass campaigns).

I. Calculated as: (C*F/1000)/4 (Divided by 1000, because Mortality Rates are given per 1000 children. Divided by 4 because the mortality rate in F is for a four year period (from age 1 to age 5 yrs)

J. Calculated as: (C*F*.77/1000)/4 0.77 is the estimated RR for children receiving VACs

K. Calculated as I - J

Assessment of costs

Detailed information on the costs of the 7 projects are recorded in Appendix B. The projects collected and reported information in different ways. For example, in some projects VACs were provided free of charge and in other projects they were paid for. We have attempted to adjust the figures to reflect some of the major differences (see details in appendix B). The costs of the projects varied considerably depending upon how the project was linked to the existing health care system or to other on-going projects. The figures we have been given are the additional costs incurred by the various projects in delivering vitamin A.
In addition to providing data on the costs of the whole intervention we have also tried to break the costs down by route of delivery when more than one route has been used (e.g. delivery through National Immunization Days and through measles immunization contacts.

It should be noted that the projects were dependent to a large extent on labour. We did ask people to provide an estimate of the level of volunteer labour time but apart from the Ugandan project this information was not provided.

Assessment of cost-effectiveness

Table 17 records the estimates for the cost per child year of coverage, the cost per child year of "useful" coverage and the cost per death averted for each of the projects. The figures show considerable variations between the different projects. For example, the cost per child year of coverage ranged from US$ 0.14 in the Bangladesh – WV project to US$ 5.56 in Year 1 of the Uganda – MIHV and the estimated cost per death averted from US$ 90 in Bangladesh-WV project to US$ 3,383 in the first year of the Vietnam-RTCCD project. These differences reflect differences in the cost of delivering VACs, the underlying mortality rates, the estimated level of VAD in the different study areas, and also differences in the quality and type of information collected.

Table 17. Estimates of the cost-effectiveness of the different projects (US$)

Project		Cost per child year of coverage	Cost per child year of "useful" coverage	Cost per death averted
Uganda – MIHV [1]	Year 1	5.56	23.76	1933.91
	Year 2	3.66	15.64	1273.04
Vietnam – RTCCD [2]	Year 1	2.14	19.81	3383.40
	Year 2	2.08	19.26	3288.54
Bangladesh – WV [2]	Year 1	0.14	0.51	90.18
	Year 2	0.14	0.51	90.18
Bangladesh – Initiatives [2]		0.49	1.78	315.62
Tanzania – WV [3]		2.13	13.15	726.34
Senegal – WV [3]		1.08	8.85	361.20
Ghana – WV [3]		0.86	5.44	427.33

1 Based on all three delivery routes and both actual and estimated in-kind expenses. If "in-kind" labour expenses are excluded the cost per child year of coverage drops by US$ 0.99 in Year 1 and US$ 0.75 in Year 2
2 Includes estimated cost of VACs
3 Includes estimated costs of VACs + 40% of staff time, village worker allowances, and travel and supplies associated with supplementation activities

Table 18 compares the cost per child year of coverage for different routes of delivering VACs for those projects where the information was available. We opted not to use the same approach as in Table 17 to calculate the cost per child year of "useful" coverage or death averted. To do this would in a meaningful way would require information on the comparative levels of VAD in the populations targeted by each of the delivery routes.

Table 18. Comparison of the cost per child year of coverage of different routes for delivering Vitamin A

Project		Cost per child year of coverage
Uganda – MIHV [1]: Year 2	National immunization days	7.12
	Immunization outreach	6.41
	Health Unit immunization sessions	3.63
Vietnam – RTCCD [2]: Year 2	National Vitamin A capsule distribution days	1.16
	Follow up	15.91
Bangladesh – WV [2]: Year 2	National Vitamin A weeks – 1 to 6 years	0.13
	NIDs– 1 to 6 years	0.14
Bangladesh – Initiatives [2]	Measles immunization contact	2.11

Vitamin A administration week	0.32

1. Based on all three delivery routes and both actual and estimated in-kind expenses
2. Includes estimated cost of VACs

Discussion

Data on the costs and effectiveness of delivering Vitamin A to communities at need outside of a research setting are very limited. In this study we collected and collated data from a number of NGO projects. The project, however, was an add-on to an existing project looking at the effectiveness of different routes for delivering Vitamin A. Projects were invited to participate, and owing to the timing of the add-on study, All of the cost figures are based on project staff reviewing existing records.

Retrospective reviews of existing records are not an ideal way of collecting cost data, especially when the records are very much linked to a donor funded project. Donated goods, volunteer labour time, funds provided by other sources are likely to be under reported. In addition, the projects were all involved in doing more than one thing (e.g. vitamin A supplementation was only one component of a larger child survival project) and, as a result many of the projects had problems allocating their expenses. For some of the projects this was further compounded by the cost data and the effectiveness data referring to different time periods.

Ideally, we would have collated the cost data prospectively and could have looked more carefully at what contributed to the costs of the different projects and played with different scenarios. However, owing to the nature of the data and the fact that we were not able to visit the sites in person to discuss it we did not feel that this level of analysis was appropriate.

There was also uncertainty in the effectiveness data. Assessment of effectiveness in these reports includes two components: measurement of coverage of a given aspect of the project, and then estimation of program effectiveness given the coverage. The general objective of the projects is to shift the population distribution of vitamin A intakes rightward, as depicted in Figure 1. The best indicators for CEA purposes, therefore, are those that allow an estimation of how the vitamin A intake distribution has shifted. The projects used in these analyses all had intensive monitoring components, with the indicators designed to specifically match the projects' objectives, however the indicators were most often "process indicators" (e.g., number of nutrition classes given, number of gardens cultivated), rather than "outcome indicators" (e.g., change in vitamin A intake). It was only for VAC distribution, where one indicator was always "number of VACs distributed", that we were able to make valid estimates of project effectiveness. There is, of course, error about the vitamin A status of the target population, and the estimates of the numbers of VACs distributed. There is also uncertainty about the magnitude of effect vitamin A supplementation has on the health of a VAD population. The reduction in young child mortality is about 23%, but has been estimated as high as 30% (Fawzi et al., 1983), and in certain situations could be much higher or lower. Also, change in mortality does not capture the full health benefit of vitamin A supplementation. VAC supplementation also affects morbidity, but the magnitude of this effect is difficult to quantify, and has not been explicitly included in our estimates of program effectiveness.

The uncertainties in our estimates of the effectiveness of the different projects and in our estimates of their costs mean that the confidence intervals around our cost-effectiveness estimates are large. Having said that the costs of the projects themselves and our estimates of the cost per death averted suggest that the delivery of vitamin A capsules through NGO projects in areas with Vitamin A deficiency is a cost-effective way or reducing under 5 mortality.

CONCLUSIONS

An adequate intake of vitamin A is required for good health, and vitamin A deficiency remains a major public health problem in many countries. There are a variety of different strategies for addressing vitamin A deficiency (food fortification, VAC distribution, DDM), and the strategy (or combination of strategies) appropriate for a given situation are variable – the various strategies are not mutually exclusive, and in fact combinations are often most appropriate.

Data on the relative cost-effectiveness of the various strategies is limited, and the confidence interval about our estimates of cost-effectiveness is quite broad. There are problems in measuring both effectiveness (e.g., difficulties in quantifying the many benefits from home gardening other than increased vitamin A intake, difficulty in quantifying the morbidity reducation of vitamin A supplementation) and costs (very little data collected prospectively from large scale projects). Nonetheless, it is clear that vitamin A projects (and nutrition projects in general) have a key role to play in improving health and reducing mortality and morbidity. There is a need to do more nutrition interventions and to do them better. Nutrition interventions should *not* be put on hold while waiting for more cost-effectiveness data. We know that nutrition interventions (and vitamin

A in particular) have an important role to play in improving health, and from the published literature and our own review, such interventions will be cost-effective in terms of lives saved and DALYs in comparison to many other commonly implemented public health interventions.

The challenge is to ensure that vitamin A programs are introduced in a way that best uses scarce resources available, and is sustainable. Such decisions may best be made considering local opportunities and constraints, rather than cost-effective analyses done in other settings with different opportunities and constraints which, given the low precision of these cost-effectiveness estimates, can not be easily applied to other, different situations. Decision makers may take comfort in the knowledge that a logically designed and efficiently implemented vitamin A intervention *will* be relatively cost-effective, even if the exact cost-effectiveness is unknown.

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Annex A: Summary of literature on effectiveness of vitamin A interventions.

Explanation of Table Columns:
1. Study Design: For most supplementation studies, usually a randomized, double-blind, placebo controlled trial (RDPT). Also commom were observational studies: cross-sectional (XObs), retrospective (RObs), prospective (PObs) and cohort (CObs). For supplementation trials, unless otherwise stated, WHO protocol for VAC supplementation was used (and in the placebo controlled trials, placebos were given at the WHO protocoled schedule).
2. Country: Country or countries where study conducted.
3. Age: The age of the study subjects. U2s = children 6 months to 2 years; U3s = children 6 months to 3 three years, etc.
4. Vit A Status: not reported (NR), not measured, but VAD assumed to be present in significant numbers (VAD-Asm) or not (No VAD-Asm), or measured, reported and VAD present (VAD) or not (no VAD).
5. Therapeutic/Prophylactic: For VAC studies, VACs given either before disease onset (Prophylactic), or after disease onset, as treatment (Therapeutic). For non supplementation studies it is left blank.
6. Results: +, - or =. For clinical trials: + indicates VACs were beneficial; - indicates harmful; and = indicates no effect. For observational studies: + indicates that vitamin A status is directly related to health outcome; - indicates that vitamin A status is inversely related to health outcome; = indicates there was no relationship. The number following is the sample size.
7. Summary: A brief description of study and results.
8. Reference.

The tables are sorted by "Therapeutic/Prophylactic/neither", "Results" (+, =, -), and Reference.

Table A1. HIV/AIDS – Transmission and Disease Progression

Study Design	Age	Country	Vit A Status	Therapeutic/ Prophylactic	Results, n	Summary	Reference
HIV/AIDS – Transmission							
RDPT	Mothers/ infants	South Africa	VAD-Asm	Prophylactic	+/=, 728	Supplement of 5000 IU/d retinyl palmitate and 30 mg/d beta-carotene during the 3^{rd} trimester and 200,000 IU at delivery. No overall reduction in mother-to-child transmission, except reduced incidence of premature birth (17% vs 11%), and reduced transmission in premature infants (34% vs 17%).	Coutsoudis et al., 1999
RDPT	Mothers/ infants	Malawi, Tanzania, S.Afr	VAD-Asm	Prophylactic	=	VAC supplements did not decrease the rate of mother-to-child transmission. (review of new, unpublished studies by various teams)	Humphrey 2000
RDPT	Mothers/ infants	Tanzania	NR	Prophylactic	=, 1083	Mothers assigned to vitamin A, multi-vitamin, vit A + mulit-vitamin, or placebo. Infants were followed to six weeks of age, or death. There was no difference in HIV transmission between groups.	Fawzi et al., 2000
Pobs	Mothers/ infants	US	VAD		+, 133	In HIV+ mothers mother-to-child HIV transmission higher (adjusted odds ratio =5.05) when mother was VAD.	Greenberg et al., 1997
Pobs	Mothers/ infants	Malawi	VAD		+, 338	The mother-to-child transmission rate of HIV from HIV+ mothers with serum retinol (umol/l) of (1) ≤ 0.70, (2) 0.70-1.05, (3) 1.05-1.40, (4) ≥ 1.40 were 32.4%, 26.2%, 16.0%, and 7.2%, respectively.	Semba et al., 1994

Pobs	Women	Kenya Kenya	VAD		+, 417 +, 318	Detection of vaginal HIV-1 DNA was associated with, among other things, VAD. Vaginal shedding of HIV+ cells may be important for HIV transmission.	John et al., 1997; Mostad et al., 1997
Case control	Adult women	Rwanda	VAD?		=, 119	Non-infected, sexually active women were followed for 2 yrs; some became HIV+. The baseline vitamin A levels did not differ between those who became infected and those who did not.	Moore et al., 1993
Pobs	Mothers/ infants	US	VAD		=, 449	Maternal vit A status during pregnancy not a predictor of mother-to-child transmission (although it was a predictor of premature birth).	Burns et al., 1999
Pobs	Mothers/ infants	Thailand	VAD		=, 67	Maternal vitamin A status during pregnancy was not a predictor of mother-to-child transmission when mothers also receive short-course zidovudine therapy.	Wiratchai et al., 1999
Pobs	Mothers/ infants	US	no VAD		=, 95	Third trimester vit A levels in HIV+ moms not related to mother-to-child transmission.	Burger et al., 1997
HIV/AIDS Progression							
RDPT	U5s	Tanzania	VAD	Therapeutic	+, 687	U5s hospitalized with pneumonia. In HIV+ children, VAC supplementation reduced all-cause mortality over ~2 yrs by 63%.	Fawzi et al., 1999
RDPT	infants of HIV+ women	South Africa	No VAD-Asm	Therapeutic	+, 728	VACs or placebos given to children of HIV+ women at 1,3,6,9,12 and 15 months of age (n=28 HIV+, 57 HIV-). Diarrhea morbidity was reduced in HIV+ children (OR = 0.51), but not the HIV- children.	Coutsoudis et al., 1995
RDPT	Adults	Zambia	VAD	Therapeutic	+/=	Initial vitamin A status IS a predictor of mortality in HIV+ individuals, but vitamin A supplementation does not change progression, nor reduce diarrhea.	Kelly et al., 1999
Pobs	men	US	VAD		+, 108	In HIV+ men tracked for 18 months, development of VAD was associated with a decline in CD4 cell count, while normalization of vitamin A was associated with higher CD4 cell counts.	Baum et al., 1995
PObs	Mothers/ infants	US	VAD		+, 122	Maternal vitamin A status during pregnancy was an independent predictor of infant disease progression in those infants who became infected.	Rich et al., 2000
PObs	men	US	VAD		+, 179	In intravenous drug using men, HIV+ men had lower plasma vitamin A than HIV- men. In HIV+ men, VAD was associated with increased mortality rate (RR =6.3.)	Semba et al., 1993
PObs	Women	Rwanda	VAD		+, 30	Serum vitamin A decreased more rapidly in those whose HIV progressed more rapidly (ie ~4 yrs from diagnosis to death) then in those whose HIV progresses slowly (asymptomatic 8 years post-diagnosis).	Camp et al., 1998
PObs	infants of HIV+ women	Malawi	VAD		+, 474	The mortality rates of children of 474 HIV+ mothers with serum vitamin A (umol/L) of (1) <0.35, (2) 0.35-0.70, (3) 0.70-1.05, (4)1.05-1.40, (5)1.40-1.75, (6) >1.75 were 93.3%, 41.6%, 23.4%, 18.5%, 17.7%, and14.2%, respectively.	Semba et al., 1995
PObs	children	US	VAD		=, 207	Serum retinol in HIV+ children was measured and tracked for a year. There was no association between baseline vitamin A, or change in Vitamin A, and morbidity or mortality, but there was little VAD.	Read et al., 1999
PObs	Men	US	No VAD		=, 311	Serum Vitamin A level at year 0 was related to progression from HIV diagnosis through AIDS over 9 years. There was no relationship.	Tang et al., 1997
RDPT	Women	US	NR		=, 40	HIV+ women were given VAC or placebo. Study was designed to test hypothesis that vitamin A may worsen HIV (clinically or immunologically). It did not.	Humphrey et al. 1999.

Table A2. Respiratory Disease

Study Design	Age	Country	Vit A Status	Therapeutic/ Prophylactic	Results, n	Summary	Reference
RDPT	U6s	Mozambique	NR	Therapeutic	+, 164	VACs given at admission to children with ALRI. There was a moderate reduction in duration of disease (3 vs 4 inpatient days).	Julien et al., 1999
RDPT	U6s	Vietnam	VAD-Asm	Therapeutic	+, 596	VACs given upon hospital admission for pneumonia. VACs decreased time in hospital, especially for girls (> 1 yr).	Si et al., 1997
RDPT	U5s	India	NR	Therapeutic	+, 900	VAC to U5s with acute diarrhea. There was no difference in ARI incidence during 90 days following supplementation.	Bhandari et al., 1994
RDPT	U4s	Guatemala	No VAD-Asm	Therapeutic	=, 263	Standard care plus VAC to U4s with ALRI. There was no difference between the groups in any of the outcome indicators (duration of hospitilization, mortality, clinical scores, etc.)	Kjolhede et al., 1995
RDPT	children	Tanzania	VAD	Therapeutic	=, 687	Children admitted to hospital with nonmeasles pneumonia were administered VAC. There was no difference between groups in the pneumonia outcome.	Fawzi et al., 1998b
RDPT	U4s	Brazil	VAD (marginal)	Therapeutic	=	Children with pneumonia given VACs of 200K IU (6-12m) or 400K IU (12m-5yrs). There was a 16 wk followup, with no difference in outcome.	Nacul et al., 1998
RDPT	U10s	Peru	NR	Therapeutic	-, 95	VACs given to U10s admitted to hospital with severe pneumonia. There was a higher incidence of adverse effects in supplemented than in placebo group.	Stephensen et al., 1998.
RDPT	infants	Bangladesh	VAD	Prophylactic	+, 165	Infants received 15 mg of vit A or placebo at 2.5, 3.5 and 4.5 months. Incidence of ARI was unchanged but duration was less in VACs group, and, within the VACs group, greater in those who remained VAD despite the supplementation.	Rahman et al., 1996
RDPT	U3s	China	NR	Prophylactic	+, 172	VACs given at 3 and 9 months after baseline, with followup until 12 m. The risk of respiratory disease was 3.4 times higher in control group.	Lie et al., 1993
RDPT	infants	Indonesia	VAD-Asm	Prophylactic	+, 2097	50,000 IU to neonates, with follow-up at 4,6 and 12 months. Placebo group sought medical treatment for cough 73% more often. (Also mortality RR =0.36)	Humphrey et al., 1996
RDPT	U5s	Indonesia	VAD	Prophylactic	+, 269	VAC at time 0 and 6 months to U5s. Morbidity data collected every 2 weeks. VACs decreased slightly the duration of ARI, but did not effect severity or incidence.	Kartasasmita et al., 1995
RDPT:	infants	Bangladesh	VAD-Asm	Prophylactic	+, 50	VACs to breastfeeding moms. Infants of supplemented moms had slightly decreased duration of respiratory tract infection.	Roy et al., 1997
RDPT	U5s	Indonesia	VAD-Asm	Prophylactic	+/-, 1,407	VAC given to U5s. A morbidity survey was carried out every second day. Supplemented children had increased overall ARI (8%) and ALRI (39%), mostly in adequately nourished children. In chronic malnourished ARI was reduced by 29%.	Dibley et al., 1996
RDPT	U3s	Ecuador	VAD-Asm	Prophylactic	+/-, 400	Weekly supplementation of 10,000 IU. The RR of ALRI was 0.38 in those with weight-for-age Z-score <-2, but in those with WAZ >-2 the RR=2.21.	Sempertegui et al., 1999
RDPT	U4s	Brazil	VAD-Asm	Prophylactic	=, 1240	VAC given every 4 months with follow-up morbidity for 1 year. There was no difference in incidence of ALRI.	Barreto et al., 1994

RDPT	U6s	India	VAD-Asm	Prophylactic	=, 174	VAC given once, with morbidity follow-up for 6 months. There was no difference in ARI incidence.	Biswas et al., 1994
RDPT	U8s	Ghana	VAD	Prophylactic	=, 21,906	VACs given every four months for up to 24 months. There was no difference in the prevalence of ARI and no differences in respiratory related mortality.	Ghana VAST Study Team, 1994.
RDPT	U3s	India	VAD	Prophylactic	=, 583	Moderately and mildly malnourished U3s were given VACs of 200K IU every 4 months, with a 1 year follow up. Severely malnourised and xerophtalmic children were excluded. All children had access to health care and immunization coverage was good. There was no difference in respiratory morbidity incidence.	Ramakrishnan et al., 1995.
RDPT	mothers/ infants	India	NR	Prophylactic	=, 909	VACs or placebos to mothers and infants (both, mother only, neither). There was no reduction of ARI in infants.	Venkatarao et al., 1996
RDPT	U7s	Haiti	NR	Prophylactic	-, 11,124	VAC or placebo given to U7s every 4 months, followup for two weeks after each administration. During this two week period, supplemented children had increased rhinitis (RR = 1.02), cold/flu symptoms (RR = 1.04), cough (RR = 1.07), and rapid breathing (RR =1.18).	Stansfield et al., 1993
PObs	U6s	Sudan	VAD		+ 28,753	A high vitamin A intake was inversely associated with cough+fever (top quintile vs bottom quintile RR=0.60), but for cough alone RR=1.69, possibly indicative of healthy respiratory epithelium when vitamin A intake is adequate.	Fawzi et al., 1995
CObs	children	South Africa	VAD		+, 131	Children seeking treatment for ARI (classified as severe and mild) and controls. Vitamin A status in children at time of admission for ARI was directly related to ARI severity.	Dudley et al., 1997
PObs	U5s	India	VAD		+, 200	Children with signs of VAD had more ARI.	Pandey, Chak-raborty, 1996
Xobs	U5s	Turkey	VAD		+, 91	Serum B-carotene and retinol were lower in pre-school children with ARI, compared to healthy cohorts.	Kucukbay et al., 1997

Table A3. Diarrheal Disease.

Study Design	Age	Country	Vit A Status	Therapeutic/ Prophylactic	Results, n	Summary	Reference
RDPT	U2s	Bangladesh	NR	Therapeutic	+, 684	Hospitilized children with diarrhea were given 4500ug vitamin A per day for 15 days. Treated group had slightly reduced duration of diarrhea (p=.09).	Faruque et al., 1999
RDPT	U7s	Bangladesh	VAD-Asm	Therapeutic	+, 83	VACs given to children with Shigellosis, but not clinical VAD. VAC improved clinical recovery but not bacteriological recovery, measured five days after supplementation.	Hossain et al., 1998
RDPT	infants of HIV+ women	South Africa	No VAD-Asm	Prophylactic	+, 85	VACs or placebos given to children of HIV+ women at 1,3,6,9,12 and 15 months of age (n=28 HIV+, 57 HIV-). Diarrhea morbidity was reduced in HIV+ children (OR = 0.51), but not the HIV- children.	Coutsoudis et al., 1995
RDPT	U5s	India	NR	Therapeutic	+, 900	VACs were given to U5s with acute diarrhea or ARI There was no difference in diarrhea incidence during the 90 days following the VAC, but there was a significant reduction in diarrhea+fever in children >2 years.	Bhandari et al., 1994

RDPT	U5s	South Africa	VAD	Therapeutic	=, 68	VAC given to young children with diarrhea either at admission, or after diarrhea resolved. There was no change in biochemical or clinical recovery from diarrhea, although the VAC did improved vitamin A status.	Rollins et al., 2000.
RDPT	U4s	Brazil	VAD-Asm	Prophylactic	+, 1240	VAC given every 4 months with follow-up morbidity for 1 year. Overall diarrhea RR= 0.94, for severe diarrhea RR=0.80.	Barreto et al., 1994
RDPT	U3s	China	NR	Prophylactic	+, 172	VACs given at 3 and 9 months after baseline, with followup until 12 m. The risk of diarrheal disease 2.5x higher in control	Lie et al., 1993
RDPT	U6s	India	VAD-Asm	Prophylactic	+, 174	VAC given once, with morbidity follow-up for 6 months. There was no difference in diarrhea incidence but a 30% decrease in duration.	Biswas et al., 1994
RDPT	U3s	Ecuador	VAD-Asm	Prophylactic	+, 400	Weekly supplementation of 10,000 IU. The RR of diarrhea incidence was 0.26 (in 18-23 month old only).	Sempertegui et al., 1999
PObs	children	Brazil	VAD-Asm	Prophylactic	+	Comparing diarrhea for 2 to 3 weeks before and after supplementation with VAC, duration of diarrhea decreased from ~7 to 4 days, incidence unchanged.	Walser et al., 1996
RDPT	U5s	Indonesia	NR	Prophylactic	+/-, 1,407	VAC given to U5s. A morbidity survey was carried out every second day. VAC decreased incidence of diarrhea in children > 30 months of age, BUT increased in children < 30 months.	Dibley et al., 1996
RDPT	U3s	India	VAD	Prophylactic	=, 583	Moderately and mildly malnourished U3s were given VACs of 200K IU every 4 months, with a 1 year follow up. Severely malnourised and xerophtalmic children were excluded. All children had access to health care and immunization coverage was good. There was no difference in diarrhea morbidity.	Ramakrishnan et al., 1995.
RDPT	mothers/ infants	India	NR	Prophylactic	=, 909	VACs or placebos to mothers and infants (both, mother only, neither). There was no reduction of diarrhea in infants.	Venkatarao et al., 1996
RDPT	U7s	Haiti	NR	Prophylactic	-, 11,124	VAC or placebo given to U7s every 4 months, followup for two weeks after each administration. During this two week period, supplemented children had increased diarrhoea (RR =1.09).	Stansfield et al., 1993
XObs	U5s, 9-17y	Kenya	VAD		+, 159 (U5s), 695 (9-17)	Serum retinol and various helminths measured in preschoolers and schoolers. In preschoolers, helminth infections were not predictive of retinol levels. In schoolers *S. manoni* egg output was a predictor of serum retinol. It is not known if VAD increases susceptibility to *S. mansoni*, or if the infection causes VAD.	Friis et al., 1997.
PObs	U6s	Sudan	VAD		+ 28,753	A high vitamin A intake was inversely associated with diarrheal mobidity (top quintile vs bottom quintile RR=0.58).	Fawzi et al., 1995
Xobs	U10s	Nepal	VAD		+, 510	Ascaris lumbricoides eggs, but not hookworm eggs, associated with lower levels of serum retinol in U5s. Children who received at least one course of mebendazole during the past 12 months had higher serum retinol levels.	Curtale et al., 1994
Xobs	U5s	Turkey	VAD		+, 91	Serum B-catoene and retinol were lower in pre-school children with recurrent diarrhea, compared to healthy cohorts.	Kucukbay et al., 1997

Table A4. Malaria

Study Design	**Age**	**Country**	**Vit A Status**	**Therapeutic/ Prophylactic**	**Results, n**	**Summary**	**Reference**

RDPT	U5s	Papua New Guinea	VAD-Asm	Prophylactic	+, 480	200,000 IU every 3 months for 13 months to U5s. The incidence of fever + parasite ≥8000/ul were reduced in the supplemented group (RR=0.70). In 12m-3 yr group there was also a reduction in spleen enlargement (RR=0.74) and lower parasite density (RR=68%)	Shankar et al., 1999
RDPT	U8s	Ghana	VAD	Prophylactic	=, 22,000	Children assigned to VAC or placebo. For mortality study, 22,000 children visited every 4 mo for 2 yrs; for morbidity study, 1500 children visited every wk for 1 yr. There was no difference in malaria mortality rates or fever incidence, parasitemia rates, parasite densities in children with a positive blood smear, and rates of probable malaria illness. No correlation between baseline retinol and subsequent parasitemia in children who received placebo.	Binka et al., 1995
XObs	children		VAD		+, 150	Serum retinol and RBP measured in children with severe and mild malaria, and controls. RBP and retinol levels varied inversely with severity of malaria.	Das et al., 1996
XObs	U5s, 9-17y	Kenya	VAD		+, 159 (U5s), 695 (9-17)	Serum retinol and malaria parasatemia (and other parasites) measured in preschoolers and schoolers. In preschoolers, malaria was predictive of retinol levels, but not in schoolers. The difference was attributed to the non-immunity of preschoolers vs semi-immunity of schoolers.	Friis et al., 1997.
PObs	Adults	Vietnam	VAD		+, 18	Adult patients with severe malaria had serum retinol levels monitored through one week of their recovery. The retinol levels were initially low, but increased with treatment (not VACs).	Davis et al., 1994.
XObs	U2s	Zambia	VAD		+, 210	Dietary intake of vitamin A, serum retinol and malaria parasetemia measured in U2s. Intake was low and serum retinol was inversely proportional to parasite count.	Hautvast et al., 1998
self as control	U5s	Congo	VAD		+, 454	Serum retinol measured in preschoolers during normal health and during malarial attacks. Retinol levels were lower during malaria attacks.	Galan et al., 1990
XObs	U8s		VAD		+, 65	Measured serum retinol in malarious and non-malarious U8s. Retinol levels were lower in malarious children, independent of WAZ.	Adelekan et al., 1997
CObs	Adults	Thailand	VAD		+	Urban and rural adults with malaria and controls had serum retinol measured. Retinol levels were low with malaria, despite normal caratenoid levels.	Thurnham and Singkamani, 1991
CObs	U5s	Ghana	VAD		+	Serum retinol and malaria parasite density measured in U5s. There was a negative correlation between parasite density and serum retinol	Filteau et al., 1993

Table A5. Measles

Study Design	**Age**	**Country**	**Vit A Status**	**Therapeutic/ Prophylactic**	**Results, n**	**Summary**	**Reference**
RObs	U15s	South Africa	NR	Prophylactic	+, 1720	Outcomes of children hospitalized during two non-consecutive 2 year periods (1985-6 (not given VACs) and 1989-90 (given therapeutic VACs)). Those receiving VACs had shorter hospital stays, lower requirement for intensive care, and lower death rate (1.6 vs 5 %)	Hussey and Klein, 1993

RDPT	children	Kenya	NR	Therapeutic	+	Therapeutic VACs given to children with measles upon admission. Diarrhea was shorter and less severe, and otitis media was less frequent with VACs, but there was no difference in pneumonia or diarrhea incidence, or mortality rate.	Ogaro et al., 1993
RDPT	U8s	Ghana	NR	Prophylactic	=, 25,433	Prophylactic VAC or placebo given to U8s every six months for three years. There was no difference between VAC and placebo, in measles incidence or measles fatality.	Dollimore et al., 1997
RDPT	U17	Zambia	NR	Therapeutic	=, 200	VAC given to non-hospitalized measles patients. The incidence of pneumonia and cough, did not differ between the VAC and placebo (all CIs include 1.0) and there was no difference in immune response (as measured with cutaneous delayed-type hypersensitivity tests).	Rosales et al., 1996; Rosales, Kjolhede, 1994
RDPT	U5s	India	NR	Therapeutic	+, 900	VACs were given to U5s with acute diarrhea or ARI. During the 90 days following VAC, the RR for measles was .06.	Bandari et al., 1994

Table A6. All cause mortality

Study Design	Age	Country	Vit A Status	Therapeutic/ Prophylactic	Results, n	Summary	Reference
RDPT	U5s	Tanzania	NR	Therapeutic	+, 600	VACs were given to non-HIV U5s hospitalized with pneumonia. Follow-up was for ~2 years. Vitamin A group had a 42% reduction in mortality over ~2 yrs	Fawzi et al., 1999
Controlled Random trial	U5s	Nepal	VAD-Asm	Prophylactic	+, ~40,000	U5s randomly assigned to VACs, Nutrition Education or Control: After two years the RR for VACs =0.57 and for Nutrition Education=0.64.	Pant et al., 1996
RDPT	infants	Indonesia	VAD-Asm	Prophylactic	+, 2097	50,000 IU to neonates, with follow-up at 4,6 and 12 months. After 1 year, VAC group had mortality rate reduced by 65%. The impact was stronger in boys and in those with normal birth weight.	Humphrey et al., 1996
RDPT	U8s	Ghana	VAD	Prophylactic	+, 21,906	U6s were given VAC or placebo every four months for up to 24 months. The supplemented children had fewer attendances at clinics (RR=0.88), fewer hospital admissions (RR=0.62), and fewer deaths (RR=0.81).	Ghana VAST Study Team, 1993
RDPT	U5s	Ghana	VAD-Asm	Prophylactic	+	VACs every ~4 months . Supplementation reduced severe illnesses (esp. diarrhea with dehydration), clinic attendances, hospital admissions, and mortality.	Ross et al., 1995
RDPT	U0.5s	Nepal	VAD-Asm	Prophylactic	=, 11918	Placebo or 50,000 IU given to children < 1 month old, and placebo or 100,000 IU given to children 1-5 months old. There was no effect on mortality.	West et al., 1995
POBs	U6s	Sudan	VAD		+ 28,753	In U6s the dietary vitamin A intake was a predictor of mortality. High vitamin A intake (top quintile vs bottom quintile) was protective: After adjusting for confounding socioeconomic variables, RR= 0.53.	Fawzi et al., 1994

PObs	Mothers/ infants	Malawi	VAD		+, 377	HIV-negative mother-child pairs. Mothers of infants who died had lower serum vitamin A levels during pregnancy (0.74 +/- 0.13 mumol/l) than mothers of infants who did not die (1.02 +/- 0.03 mumol/l). Infants of lowest quartile women (< 0.32 mumol/l) had three-fold mortality rate of infants of higher quartile women.	Semba et al., 1998

ANNEX B. Summary of NGO Interventions

Country: Uganda:
NGO: Minnesota International Health Volunteers (MIHV), GVAI

Project Location: Ssembaule district
Target population: over 160,000

Start Date: 28/02/97
End Date: 28/02/99

Background to project:
- MIHV initiated a USAID funded community-based Child Survival Project in Ssembabule District (1993 to August 2000).
- In 1997 funds from GVAI enabled MIHV to integrate into its Child Survival initiative a health education and volunteer training component designed to increase access to, and consumption of vitamin A.

Partners:
- Uganda: Ministry of Health and the District Health Office (DHO) and communities.
- External: MIHV, USAID, UNDP, Rotary International

Overall Objective of GVAI project:
- To reduce vitamin A deficiency in women of childbearing age (approximately 30,935) and children under five (approximately 33,196) in the district of Ssembaule by increasing their consumption of vitamin A rich foods and supplementing the target groups with VACs

Effectiveness data:

- ***VAC supplementation to children under 5***
  AIM: to increase coverage from 8% to 35%

Table B.1.1 Coverage data for VAC supplementation of children under 5			
Date	Delivery route	# VACs distributed	# children treated*
Year 1			
August 1997	NID (2 sessions of 2 days)	2500	4500
September 1997	NID (2 sessions of 2 days)	2500	4500
ongoing	Immunization outreach	3500	6300
ongoing	Immunization sessions	5500	10000
Total		14000	25300
Year 2			
August 1998	NID (2 sessions of 2 days)	5000	9000
September 1998	NID (2 sessions of 2 days)	5000	9000
ongoing	Immunization outreach	3500	6300
ongoing	Immunization sessions	5500	10000
Total		19000	34300

* based on 2 dose capsules and 10% wastage due to cutting capsules for proper dosing. The "roundedness" of the totals probably reflects some rough estimations made in the program monitoring.

Cost data

- Data based on questionnaires completed by the project. Information provided for the two years separately. All figures quoted in US$.
- The cost data (US$) provided are specifically for the costs associated with distributing VACs to children under 5 through (1) national immunization days, (2) immunization outreach sessions, or (3) health unit immunization sessions

Table B.1.2 Actual expenditures by cost category for all three interventions combined. All cost estimates provided by project in US$		
	Year 1	Year 2
Personnel Costs	8602	8602
Per diems	558	558
Training	441.25	601.25
Supplies (includes VACs but not shipping or insurance)	500	1000
IEC Materials	4060	2150
Transport	4692	6850
Office Costs	8119	3265
TOTAL	26973.25	23028.25

Table B.1.3 Breakdown of actual expenditures by delivery route based on information provided by the project

	Year 1	Year 2
national immunization days	45.5%	47.5%
immunization outreach sessions	28.7%	28.7%
health unit immunization sessions	25.8%	23.8%

Table B.1.4 In-kind support not included in actual expenditures. All cost estimates provided by project in US$		
	Year 1	Year 2
Volunteer immunizers[1] (40 @ 4 days per month)	3430	3430
Health Unit Staff[2] (22 @ 3 days per month)	2830	2830
DMO (3.6 days per year)	55	55
Rent (valued at 150/ month)	1800	1800
Shipping and insurance of VACs[3]	100	200
TOTAL	8216	8317

[1] have assumed volunteer immunizers time is valued at half the rate of Health Unit Staff
[2] salary for health unit staff = US$ 857 per year;
[3] valued at 20% of value of goods (paid for by UNICEF)

Cost-effectiveness estimates

Table B.1.5. Cost-effectiveness estimates for distributing Vitamin A to children under 5 . All costs in US$.				
	Year 1		Year 2	
Assumptions	Cost/child treated	Cost per child year of coverage	Cost/child treated	Cost per child year of coverage
All 3 routes together				
• Actual expenditures	1.07	4.26	0.67	2.69
• Actuals + in-kind	1.39	5.56	0.91	3.66
Route 1: National immunization days				
• Actual expenditures	1.36	5.45	0.61	2.43
• Actuals + in-kind	1.78	7.12	0.83	3.31
Route 2: Immunization outreach				
• Actual expenditures	1.23	4.92	1.05	4.20
• Actuals + in-kind	1.60	6.41	1.43	5.71
Route 3: Health Unit immunization sessions				
• Actual expenditures	0.70	2.78	0.55	2.19
• Actuals + in-kind	0.91	3.63	0.75	2.98

Notes: Cost per child year of coverage = 4 * cost per child treated as 100,000 IU units used

Country: Vietnam
NGO: Hanoi Research and Training Center for Community Development (RTCCD), GVAI

Project Location: Cao Loc and Ninh Son districts in Ninh Son District
Target population: 9,526

Start Date: 01/08/97
End Date: 01/07/99

Background to project:

- RTCCD was established in May 1996 to assist in increasing the capacity and the quality of human resources at district and commune levels. It functions primarily as a training and research institution, and also implements projects. The purpose of the GVAI project was to reduce VAD in pilot communes. Vitamin A is only one component of the whole RTCCD project.

Partners:

- Vietnam: Ministry of Health, National Institute of Nutrition (provided technical support to the project) and the Committee for the Protection and care of Children (CPCC, is a national committee).

Overall Objective:
To reduce VAD in three pilot communes in each target district with a focus on women of childbearing age and children under 5.**Effectiveness data:**

- ***VAC supplementation of children 6 to 60 months of age***

Table B.2.1 Coverage data for VAC supplementation of children 6 to 60 months of age			
Date	Delivery route	# VACs distributed	# VACs received by children 6 to 60 months
Year 1	National VAC day	2541	2586
	At home by CHWs	155	102
Year 2	National VAC day	12842595	12722485
	At home by CHWs	172	172

- Data based on questionnaires completed by the project. Information provided for the two years separately.
- The cost data are specifically for the costs associated with distributing VACs to children under 5 through (1) National Vitamin A capsule distribution days and (2) follow up of children missed during campaign days by Health care workers.
- Breakdown of costs between two approaches from data provided was 50:50
- No cost data were provided for VACs
- Project depends upon infrastructure being provided for other activities; Improving Vitamin A status is only a small component of the more general project and only Vitamin A specific data was provided by the study

Table B.2.2 Breakdown of actual expenditures by cost category (excluding VACs). All cost estimates provided by project in VND. Exchange rate in Year 1 according to the project was 14000 VND = 1 US$ and in Year 2 13800 VND = 1 US$		
	Year 1	Year 2
Personnel Costs	15945600	18494400
Per diems	3928252	4137600
Training	7600000	1600000
IEC Materials	4677000	4917000
Transport	2942820	4800000
Office Costs	3263850	3600000
TOTAL	38357522	37549000

Table B.2.3 Breakdown of actual expenditures by intervention in US$		
	Year 1	Year 2
Excluding VAC charges		
• Combined programme	2740	2720
• National Vitamin A capsule distribution days	1370	1360
• Follow up	1370	1360

Including VAC charges (assuming VAC costs US$ 0.05 and 10% wastage rates)		
• Combined programme	2889	2872
• National Vitamin A capsule distribution days	1510	1503
• Follow up	1379	1369

Cost-effectiveness estimates:

Table B.1.* Cost-effectiveness estimates for distributing Vitamin A to children 6 to 60 months. All costs in US$ and assuming VACs cost US$ 0.05 and 10% wastage rates.

	Year 1		Year 2	
Assumptions	Cost/child treated	Cost per child year of coverage	Cost/child treated	Cost per child year of coverage
2 Routes together	1.07	2.14	1.04	2.08
Route 1: National Vitamin A capsule distribution days	0.59	1.19	0.58	1.16
Route 2: Follow up	8.90	17.80	7.96	15.91

Notes: Cost per child year of coverage = 2* cost per child treated

Country: Bangladesh
NGO: World Vision, GVAI

Project location: Peri-urban wards of Chittagong city
Target Population: 58,0589 (13,353 children under 5 and 11,362 women of child bearing age)

Start Date: 01/04/97
End Date: 01/03/99

Background to project:

- The GVAI grant allowed World Vision Bangladesh (WVB) to integrate a Vitamin A component into WVBs existing Health and Development Program

Partners:

- Bangladesh: World Vision Bangladesh, Neighbourhood Health Committees, Ministry of Health, Institute of Public Health Nutrition
- External: World Vision Canada, CIDA, Canadian Public Health Association

Overall Objective:

- To improve the vitamin A status of children under 6 years of age and lactating mothers through VA supplementation, kitchen gardening, changes in feeding practices and inter-house food distribution among vulnerable groups, and formation of Women Development Groups to enhance family income.

Effectiveness data:

- ***VAC supplementation to children 12 to 71 months through National Vitamin A weeks***
  AIM: to increase VAC coverage from 94% to 95% of children 12-71 months (200,000 IU)
- ***VAC supplementation to children 12 to 71 months through NIDs***
  AIM: to increase VAC coverage during NIDs for 12-59 months (200,000 IU) from 94 to 97%
- ***VAC supplementation to children under 12 months***
  AIM: to increase VAC coverage in under 12 months (25,000 IU) from 83% to 100%

Table B.3.1 Coverage data for VAC supplementation of children		
	# children treated	
	Year 1	Year 2
National Vitamin A weeks – 1 to 6 years	16021	14485
NIDs– 1 to 6 years	7011	7057
Supplementation - under 12 months	4501	2860

Cost data

- All data based on questionnaires completed by the project. Information provided for two years separately.
- Data available breaking expenses down by type of cost (not shown)
- All figures quoted in Taka (44 Taka = 1 US$)
- VACs not included in initial cost estimates

Table B.3.2 Breakdown of actual expenditures by intervention (in Taka) not including costs of VACs		
	Year 1	Year 2
National Vitamin A weeks – 1 to 6 years	7359	7366
NIDs– 1 to 6 years	4367	4397
Supplementation - under 12 months	10089	10580
Total	21827	22345

Table B.3.3 Breakdown of actual expenditures by intervention in US$ and assuming VACs cost US$ 0.05 and 10% wastage		
	Year 1	Year 2
National Vitamin A weeks – 1 to 6 years	1048	964
NIDs– 1 to 6 years	485	488
Supplementation - under 12 months	477	398
Total	2011	1852

Cost-effectiveness data

Table B.3.4. Cost-effectiveness estimates for distributing Vitamin A to children 1 to 6 years . All costs in US$ and assuming VACs cost US$ 0.05 each and 10% wastage				
	Year 1		Year 2	
Assumptions	Cost/child treated	Cost per child year of coverage	Cost/child treated	Cost per child year of coverage
2 routes together	0.07	0.14	0.07	0.14
National Vitamin A weeks – 1 to 6 years	0.07	0.13	0.07	0.13
NIDs– 1 to 6 years	0.07	0.14	0.07	0.14

Notes: Cost per child year of coverage = 2 * cost per child treated

Country: Bangladesh
NGO: Initiatives, GVAI

Target Population: 233,150 in 10 participating unions

Start Date: 14/03/97
End Date: 14/03/99

Background to project

- Debidwar Vitamin A project in Chittagong was implemented in 10 of 16 unions of the district where the Local Initiatives Program (LIP) funded by USAID was supporting ongoing projects. Funds from GVAI allowed them to integrate into existing family planning/ MCH activities a variety of interventions aimed at reducing the prevalence and severity of VAD among children.

Partners (GVAI, present & previous partners):

- Bangladesh: Government of Bangladesh, community leaders, BRAC
- External: USAID, HKI, World Vision, Radd Barnen

Overall Objective:

- To reduce VAD among children from birth to 15 years of age and post partum women by (a) increasing VAC coverage; (b) improving knowledge of proper breastfeeding and infant feeding practices; (c)increasing houses with home gardens with VA rich foods; (d) to increase consumption of VA rich foods.

    - *VAC to infants 9-11 months at measles immunization contact*
      AIM: to increase VAC coverage from 44% to 85% in children 9-11 months through EPI
    - *VAC to children 12-71 months at twice a year during Vit A administration week*
      AIM: to increase VAC coverage twice a year from 57% to 90% in children 12-71 months

Effectiveness data

Table B.4.1 Coverage data for VAC supplementation of children			
	# children treated		
	Year 1 (12 months)	Year 2 (6 months)	Combined period (18 months)
Measles immunization contact	5282	1738	7020
Vit A administration week	30050	37381	67431

Cost data

- All data based on questionnaires completed by the project. Information provided for the period March 6 1997 to August 31 1999 combined.
- Data available breaking expenses down by type of cost (not shown)
- All figures quoted in Taka (exchange rates given by project: 30 Taka = 1 CDN$ or 44 Taka = 1 US$)
- VACs not included in initial cost estimates

Table B4.2 Breakdown of expenditures by route of VAC delivery. All cost estimates provided by project in Taka for the period March 6 1997 to August 31 1999.	
	Costs in Taka
Measles immunization contact	308,635
Vit A administration week	308,635
Total	617,270

Table B.4.3 Breakdown of actual expenditures by intervention in US$ and assuming VACs cost US$ 0.05 and 10% wastage	
	Costs in US$
Measles immunization contact	7400
Vit A administration week	10723
Total	18123

Cost-effectiveness estimates

Table B.4.4 Cost-effectiveness estimates based on 18 month period. All costs in US$ and assuming VACs cost US$ 0.05 each and 10% wastage

	Combined period	
Assumptions	Cost/child treated	Cost per child year of coverage
2 routes together	0.24	0.49
Measles immunization contact	1.05	2.11
Vit A administration week	0.16	0.32

Notes: Cost per child year of coverage = 2 * cost per child treated

Country: Tanzania
NGO: World Vision (not GVAI)

Target Population: 197,797

Start Date: 01/06/97
End Date: 5 year project

Background to Project:

- World Vision (WV)- Tanzania is part of World Vision Canada's MICAH program (Micronutrient and Health Program). This program is directed at addressing the "hidden hunger" of micronutrient malnutrition and aims to reduce child diseases and infant mortality rates

Overall Objective:

- To increase coverage of VAC among children under 5 and post-partum mothers and to improve primary health care and laboratory services

Effectiveness data:

- Number of children under 5 receiving VAC during May to October 1998 (6 month period): 2351.
- Note, only have data on VACs distributed and/ or children treated for a 6 month period

Cost data:

- All data based on review of data at headquarters in Canada. All cost data were provided in US$.
- Total actual expenditures between June 97 (inception of the study) to March 1999 under the Micronutrient and Health Program was US$ 303,386
- Of this total 6.0 % (US$ 18,210) was allocated to "Supplementation activities" which included Vitamin A and Iron, and 26.6 % (US$ 80,710) to overhead. Other cost headings included: Primary Health Care (12.4%), Dietary Diversification (11%), Fortification (3.2%), Capacity Building (29.7%), and Surveys (14.1%)
-
-

Table B.5.1. Breakdown of costs linked to Supplementation Activities. All costs in US$.

Activity	Total US$
Iron Tablets	3,892
Vitamin A Tablets	8,647
Village worker allowance	195
Salaries	3,807
Travel and supplies	1,669

- Vitamin A tablets were used to treat both children under 5 and post partum mothers. In the period we have data on number of tablets distributed -- 80% of the people treated were under 5 years of age

Cost-effectiveness estimates

- Based on data on number of children treated between May and October 1998 (6 months) and assuming numbers distributed remain constant over the time for which we have cost data (may not be a valid assumption) we can guestimate that 8620 children were treated.
- Other assumptions:
  - All of the capsules were distributed over the 22 month period
  - The proportion of the costs of the tablets given to children = 80% of the total costs of the tablets (based on proportion of tablets given to children under 5 during 6 month period May to October 1998 – other tablets went to post partum mothers)

Table B.5.2 Cost effectiveness estimates for Vitamin A distribution to under 5s. Cost estimates in US$.

Assumptions	Cost/child treated	Cost per child year of coverage
a) costs of capsules only	0.80	1.61
b) costs of capsules + 40% of staff time, village worker allowances, and travel and supplies associated with supplementation activities	1.07	2.13

Notes: Cost per child year of coverage = 2 * cost per child treated

Country:	Senegal
NGO:	World Vision
Project location:	Central Senegal
Population target:	500,000 people
Start Date:	01/02/97
End Date:	5 year project

Background to project:
- World Vision (WVV- Senegal is part of World Vision Canada's MICAH program (Micronutrient and Health Program). This program is directed at addressesing the "hidden hunger" of micronutrient malnutrition and aims to reduce child diseases and infant mortality rates

Partners:
- Senegal: Faculty of Medicine, University of Dakar, Ministry of Health,
- External: World Vision, BASICS

Overall Objective:
To improve the micronutrient and health status of mothers and children under 5 and of school children by reducing prevalence of deficiency and reducing the prevalence of diseases which affect micronutrient status.

Effectiveness data:

- Number of children under 5 receiving VAC during July to December 1998 (6 month period): 6,246
- Number of schoolchildren receiving VAC during July to December 1998 (6 month period): 5,608
- Note, only have data on VACs distributed and/ or children treated for a 6 month period

Cost data

- All data based on review of data at headquarters in Canada. All cost data were provided in US$.
- Total actual expenditures between February 97 (inception of the study) to December 1998 under the Micronutrient and Health Program was US$ 495,146 (23 months).
- Of this total 8.3% (US$ 41,072) was allocated to "Supplementation activities" which included Vitamin A and Iron, and 39.8% (US$ 197,193) to overhead. Other cost headings included: Primary Health Care (17.3%), Dietary Diversification (1.2%), Social Marketing (9.7%), and Surveys (9.0%)
-

Table B.6.1. Breakdown of costs linked to Supplementation Activities. All costs in US$.

Activity	Total US$
Iron Tablets	958
Vitamin A Tablets	7,166
Staff Time	19,082
Travel and supplies	13,865

- Owing to a lack of data it was not possible to break cost estimates down by population group targeted (i.e. childern under 5 and school children)

Cost-effectiveness estimates
- Based on data on number of children treated between May and October 1998 (6 months) and assuming numbers distributed remain constant over the time for which we have cost data (may not be a valid assumption) we can guestimate that 45,440 children were treated (23,943 under 5 and 21,497 school children).
- Other assumptions:
  - All of the capsules were distributed over the 23 month period
  - The proportion of the costs of the tablets given to children = 94 % of the total costs of the tablets (based on proportion of tablets given to children during 6 month period – other tablets went to postpartum mothers)

Table B.6.2 Cost effectiveness estimates for Vitamin A distribution to under 5s and school children . Cost estimates in US$.

Assumptions	Cost/child treated	Cost per child year of coverage
a) costs of capsules only	0.18	0.37
b) costs of capsules + 40% of staff time and travel and supplies associated with supplementation activities	0.54	1.08

Notes: Cost per child year of coverage = 2 * cost per child treated

Country: Ghana
NGO: World Vision (not GVAI)

Project Location: Nadowli Area Development, Upper West region of Ghana.
Population Target: 131,155

Start Date: 01/09/97
End Date: 5 year project

Background to project:

- World Vision (WVV- Ghana is part of World Vision Canada's MICAH program (Micronutrient and Health Program). This program is directed at addresseing the "hidden hunger" of micronutrient malnutrition and aims to reduce child diseases and infant mortality rates

Partners:

- Ghana: Area Development councils (District Assembly), WV Ghana
- External: CIDA, World Vision Canada

Overall Objective:

- To improve the micronutrient and health status of mothers and children under 5 by reducing prevalence of deficiency and reducing the prevalence of diseases which affect micronutrient status. Specific projects included provision of VACs and support for home gardening.

Effectiveness data:

- Note, only have data on VACs distributed and/ or children treated for a 6 month period (May to October 1998)
- Number of children under age of 5 years receiving VAC: 3,100
- Number of children six years of age and older receiving VAC): 7,500
- Number of children 6 to 12 months receiving VAC: 545

Cost data

- All data based on review of data at headquarters in Canada. All cost data were provided in US$.
- Total actual expenditures between September 97 (inception of the study) to December 1998 (ie. 16 months) under the Micronutrient and Health Program was US$ 348,400
- Of this total 8.9% (US$ 31,007) was allocated to "Supplementation activities" which included Vitamin A and Iron, and 40.0 % (US$ 139,360) to overhead. Other cost headings included: Primary Health Care (25.4%), Dietary Diversification (4.6%), Social Marketing (0.7%), Fortification (3.3%), Capacity Building (10.9%), and Surveys (6.2%)
- Supplementation activities did not include the costs of purchasing Vitamin A as the capsules were donated.

Table B.7.1. Breakdown of costs linked to Supplementation Activities. All costs in US$.

Activity	Total US$
Iron Tablets	20560
Vitamin A Tablets	--
Staff Time	4711
Travel and supplies	5736

- Owing to a lack of data it was not possible to break cost estimates down by population group targeted (i.e. childern under 5, school children, and children 6 to 12 months)

Cost-effectiveness estimates

- Based on data on number of children treated between May and October 1998 (6 months) and assuming numbers distributed remain constant over the time for which we have cost data (may not be a valid assumption) we can guestimate that a total of 29,720 children were treated (8,267 to U5s; 20,000 to 6 years+; and 1,453 to children between 6 and 12 months of age).
- Other assumptions:
  - All of the capsules were distributed over the 16 month period
  - Cost of a vitamin A capsule = US$ 0.05 and there is 10% wastage

Table B.7.2 Cost effectiveness estimates for Vitamin A distribution to under 5s and school children. All costs in US$ and assuming VACs cost US$ 0.05 each and 10% wastage

Assumptions	Cost/child treated	Cost per child year of coverage
a) costs of capsules only	0.05	0.11
b) costs of capsules + 40% of staff time, village worker	0.43	0.86

alloowances, and travel and supplies associated with supplementation activities		

Notes: Cost per child year of coverage = 2 * cost per child treated