Insecticide Treated Nets and Vitamin A Supplementation:

An integrated approach to control malaria and micronutrient deficiency

Literature Review Paper and Malawi Case Study

Prepared for:
The Micronutrient Initiative

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PATH Canada began working on VAD and ITN interventions when both were in the early stages of experimentation. With support from the Canadian government, PATH Canada worked with partners in sub-Saharan Africa to conduct research on key operational aspects of these important public health interventions. In 1998, Dr. Anuraj Shankar, of Johns Hopkins School of Hygiene and Public Health, presented a thought-provoking paper at the IVACG meeting in Cairo proposing community-based integration of these two interventions. By this time, both interventions had become generally recognized as cost-effective public health interventions that should be implemented on a national scale, although admittedly there is still considerable debate over the feasibility of implementing ITNs on a large scale. Given the existing technical expertise in these two interventions, PATH Canada was well-placed to design and implement, on a pilot scale, a controlled integrated community-based intervention. PATH Canada initiated discussions with Dr. Shankar, as well as with Dr. Martin Bloem of Helen Keller International, on the possibility of a partnership for such an endeavour. In 1999, PATH Canada began exploring the possibility of working with CPAR in Malawi, which resulted in a workshop held earlier this year in Lilongwe to outline the details of an integrated program.

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1 Introduction:

The health effects of vitamin A deficiency (VAD) and malaria are particularly severe in young children and women of reproductive age. Approximately half a million children become blind each year due to VAD, of which two thirds die within months of going blind. Another 231 million children are more vulnerable to infectious disease because of inadequate vitamin A intake [WHO, 1995]. Improving intake of vitamin A in areas where deficiency is common has shown to result in an average of 23 percent reduction of young child mortality [Beaton et al., 1993]. Malaria deaths are estimated at 1.5 to 2.7 million a year, most of which are among children under five years and pregnant women [WHO, 1994]. Ninety percent of these deaths occur in sub-Saharan Africa (SSA).

There is widespread recognition of VAD and malaria as two widely distributed public health problems in the developing world. Each has a tremendous impact on health, particularly on those living in sub-Saharan Africa, causing high morbidity and mortality. In SSA, VAD and malaria often co-exist, each exacerbating the health consequences of the other.

At the World Summit for Children in 1990, and again in the FAO/WHO International Conference on Nutrition held in Rome in 1992, the elimination of vitamin A deficiency (VAD) was set as a goal to be achieved by the year 2000. As that date has come and gone, VAD remains an important public health problem in much of the developing world, and there are renewed global efforts at VAD control. In 1998, Gro Bruntland, the new Director General of the World Health Organization announced a plan to "Roll Back Malaria". In a speech delivered to the World Bank, Dr. Bruntland stressed the need for malaria control to become a priority. She emphasised the important role of NGOs in this process.

In the recent past, malaria control in sub-Saharan Africa and has generally focused on the early treatment of clinical malaria. However, the emergence of resistant strains has stimulated the search for alternative methods of malaria control and prevention. Mosquito nets, impregnated every 6-12 months with pyrethroid insecticides, are proving to be an effective (and cost-effective) intervention (Lengeler et al., 1996). When used regularly, insecticide treated nets (ITNs) have an impact on both the frequency of episodes of malaria in children and on the parasite load within the mosquito population [IDRC/WHO, 1996]. Also in recent years, several studies have reconfirmed sizeable health benefits of vitamin A supplementation [Ramakrishnan and Martorell, 1998]. In recognition of the health impact of vitamin A deficiency, in most countries in SSA ministries of health have incorporated distribution of vitamin A capsules (VAC) into their national health plans.

Research into the understanding of malaria and micronutrient deficiencies and the search for more effective means to control and prevent both problems is continuing. Existing strategies are modified and re-evaluated with significant, but incomplete, success while novel strategies are developed, implemented and evaluated. In this paper, we review malaria and VAD epidemiology and programming, examine the biological relationship

between malaria and vitamin A, and explore the rationale for integrating malaria and vitamin A programs. Two other micronutrients, iron and zinc, will be considered as well. Iron deficiency is of significant public health importance in SSA and it is the only other micronutrient for which many countries have national supplementation programs currently in place. Although the prevalence of zinc deficiency is under review, it is likely widespread as well, and there is emerging evidence the beneficial effects of zinc on childhood morbidity.

The "paper" considers the global context with a special emphasis on SSA and Malawi. We have reviewed recent micronutrient and malaria research, particularly in sub-Saharan Africa (esp. Malawi), in view of the interrelationship between the biology and epidemiology of vitamin A deficiency and malaria, the effects of malaria infection or prevention (e.g. ITNs) on vitamin A and immune system status, and the effects of vitamin A (and other micronutrient) supplementation on the health outcome of malaria. Much is known about the impact of vitamin A (and zinc) supplementation on diarrhea, respiratory disease, and, more recently, HIV infection. However little is known about the impact of vitamin A, zinc or iron on malaria infection and the public health importance of linking these strategies.

The integration of micronutrient and malaria control strategies would ideally be conducted in an area where there is a large population at risk for both vitamin A (and other micronutrient) deficiency and malaria, and where there is already an existing infrastructure for vitamin A supplementation and/or ITNs. Malawi, for example, is significantly affected by both vitamin A deficiency and malaria. Recent surveys have found that the majority of children under five are at risk of VAD. Malaria infection is also endemic in the country, so that Malawi has over one million children at risk of both micronutrient deficiency and malaria infection.

Recently, detailed mapping of the populations at risk of malaria in the Africa have been developed by MARA (*Mapping malaria risk in Africa* - a collaboration between the South African Medical Research Council and the Kenyan Medical Research Institute). The final section of this review describes African countries, as well as a detailed consideration of Malawi, with regard to the number and proportion of children at risk for both vitamin A deficiency and malaria. This will assist in the location of areas where integrating malaria prevention (ITNs) and VAC/micronutrient supplementation programs may be most effective.

2 Rationale of integrating ITN and vitamin A/micronutrient activities:

2.1 Effectiveness of approaches in morbidity/mortality reduction:

In Asia and Africa, a significant reduction in morbidity and mortality has been achieved through vitamin A supplementation. Similarly, there is sufficient evidence that suggests a considerable reduction in malarial morbidity and mortality among children protected by insecticide treated nets. Both interventions are proven to be cost effective and many

country level national programmes utilising ITNs and vitamin A capsule (VAC) distribution are in place.

The existing body of knowledge and field experience regarding the use of vitamin A supplementation and ITNs, and the results achieved respectively, are sufficient to encourage public health managers and persuade policy makers. As a result, both strategies are being adapted by an increasing number of countries and incorporated into the general health delivery and primary health care programmes. In reality, the question now is not the effectiveness of ITNs or vitamin A capsules (VAC), but how to maximise the health benefits by delivering them effectively and efficiently. For other micronutrients such as iron and zinc, the information on the effectiveness of operational programs is either not completely known (iron) or non-existent (zinc).

2.1.1 Micronutrients:

Vitamin A:

In the meta-analysis by Beaton et al. (1993), 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. Supplementation with VA resulted in an average reduction of 23% in overall mortality for children aged 6-60 months. This mortality effect was most pronounced for diarrheal disease and measles, but was not seen specifically in respiratory disease or malaria. The effect of VA supplementation on morbidity was less pronounced. VACs appear to affect a child's ability to respond to infection and has more of an impact on the course of an illness, rather than in reduction of incidence or prevalence, and the evidence did not differentiate effects on morbidity related to different types of illness.

Zinc:

The importance of zinc for growth and development [Nishi, 1996] is recognized, as documented in research in developing countries [Rohaghy et al., 1974; Walrevens et al., 1983; Castillo-Duran et al., 1994]. Perhaps even more important for the children of Africa are the recent studies which have indicated the positive effects of a reduction in the length and severity of diarrheal disease in zinc supplemented children [Sachdev et al., 1988; Simmer et al., 1988; Behrens et al., 1990; Sazawal et al., 1996; Rosado et al., 1997], including a pooled analysis of 10 clinical trials [Bhutta et al., 1999], and a reduction in malaria episodes in both The Gambia [Bates et al., 1993] and PNG [A. Shankar - personal comm.].

Iron:

Iron deficiency anaemia is the most common nutritional disorder in the world, affecting over two billion people [WHO/UNICEF/UNU, 1995]. It causes impairment in cognitive development and immune mechanisms and is associated with increased morbidity and

mortality in children [Brown et al., 1967; Enwonwu, 1990; Lozoff, 1989; Scrimshaw, 1990; Walter et al., 1983; Walter et al., 1986]. Iron deficiency anaemia (IDA) during pregnancy increases perinatal risks for mothers and new-borns and increases overall infant mortality [Murphy et al., 1986; Scholl et al., 1992; Worthington-Roberts, 1990]. Infants, young children, adolescents and pregnant women are the population groups that are particularly vulnerable [WHO/UNICEF/UNU, 1995]. The World Health Organization estimates that in 1992 about half of the children and women in developing countries were iron deficient and that the prevalence of anaemia in pregnant women is presently about 52% in Africa.

Despite the widespread problem, most current national level iron supplementation programs involve only women during pregnancy. Although supplementation with iron has been shown to be efficacious in improving iron status and reducing anaemia in numerous studies, the effectiveness of operational programs is still in question.

2.1.2 Insecticide Treated Nets (ITNs):

The use of ITNs substantially reduces the frequency and severity of clinical episodes of malaria. In the ITN studies completed this decade in Africa, a 20-63% (median = 45%) reduction in malaria disease rates following the introduction of ITNs was found [IDRC/WHO, 1996], as well as a corresponding substantial (up to 63%) reduction in mortality as a result of ITN use [Alonso et al., 1991; Binka et al., 1996; D'Alessandro et al., 1995; Nevill et al., 1996]. This reduction in "all-cause" mortality exceeds the reduction that is predictable from current understanding of malaria-specific mortality, implying that ITNs also have impact on mortality from causes other than malaria [IDRC/WHO, 1996]. More recently, an analysis was done on the ITN studies which found the absolute (rather then relative) impact to be 3.8 to 6.9 lives saved per 1000 children protected per year, without a significant difference between low and high transmission sites [Lengeler et al., 1998]. This emphasises the contribution of malaria to childhood mortality in Africa and the potential benefits from effective control programs in all countries, even in areas where endemicity may be low.

2.2 Target Group Similarities:

Both malaria infection and vitamin A deficiency are particularly threatening to children under five years and pregnant women [IDRC/WHO, 1996; WHO/UNICEF, 1995]. For malaria infection, this is particularly true for areas of stable, high transmission, which covers most of the central and east Africa region, including Malawi. Malaria and vitamin A deficiency (VAD) are often found in the same poor, economically depressed areas.

Recent estimates for sub-Saharan Africa indicate that about one million people die each year from malaria, with about three-quarters of these being children under the age of five years, the group at greatest risk from the disease in areas of stable transmission [Snow et al., 1999a]. Estimates of VAD in the region indicate that about one million pre-school children are affected by clinical VAD with a further 20-30 million suffering from sub-clinical forms of the deficiency [MI/Tulane/UNICEF, 1998]. Women and young children

are the most vulnerable segments of African society due to economic and other socio-cultural factors, as well as physiologically, and therefore most at risk for dietary deficiencies and illness [Bezner-Kerr, 1998; UNICEF/GOM, 1987].

The epidemiology of VAD and malaria, with particular reference to age patterns and risk groups, will be further described in section 3 below.

2.3 Periodicity:

The delivery mechanisms of the two strategies may be complementary, as the scheduling of net retreatment with pyrethroid, and vitamin A capsule distribution, take place approximately every six months. Research has shown that pyrethroid insecticides lose their effectiveness in vector control over time, and with repeated washings, and it is recommended to retreat nets at least every 6 months for maximum effectiveness [Miller et al., 1999a, 1999b]. Some of the newer synthetic pyrethroids may have a longer duration of action, up to 12 months, but this needs to be further explored.

The recommended twice-yearly VAC supplementation protocol [WHO, 1997] (100,000 IU for children under 1 year of age, 200,000 IU for children 1 year and over, 200,000 IU for post-partum women within 8 weeks of delivery), is the norm for most country-level programs.

2.4 Synergism?:

The existing research and field experience findings regarding the use of vitamin A and ITNs are sufficient to persuade public health managers of the benefit of additional investigation. Both strategies are being incorporated by an increasing number of developing countries into their general health services.

The success and experience from the field on the use of ITNs and vitamin A supplementation raises questions as to whether an intervention that integrates the two strategies together will bring an added health advantage which exceeds the health benefits from each intervention implemented in parallel fashion, i.e. would a "synergistic action" be seen?

There is an abundance of Vitamin A deficiency and malaria research. However, little has been done to study the actual impact on the health of individuals and populations when the two occur simultaneously. The health effects of treated nets on vitamin A status and vitamin A supplementation on the health outcome of malaria is incompletely known. There are few data on whether the two conditions (vitamin A deficiency and malaria infection) are independent or in some way modify each other, so the outcome of such an integrated intervention, synergetic or antagonistic, is open to exploration. There is growing evidence that VAC supplementation, and zinc supplementation, can reduce the frequency and severity of malaria infection, although the mechanism of action is not clear. This will be further discussed below in section 4.

3 Distribution (Epidemiology) of vitamin A/micronutrient deficiency and malaria:

3.1 Malaria:

3.1.1 General:

Although malaria-related death rates are falling in many regions, particularly Latin America and Asia, the rates are in fact rising once again in Africa [WHO, 1999]. This reflects the emergence of drug resistant strains of the parasite, changes in climate, population movements and a relative reduction in public health capacity within many National Health Ministries.

It is estimated that 0.5-2 million deaths occur each year in Africa due to malaria infection, but estimates are coarse. More detailed estimates have been recently published [Snow et al., 1999a]. By integrating malaria prevalence data with ecologic data (temperature, precipitation, altitude, latitude), the authors have calculated the risk of malaria transmission throughout Africa. On the basis of these calculations it is concluded that, in SSA, malaria is responsible for about 1 million deaths and over 200 million episodes of clinical disease each year.

There are various levels of malaria transmission intensity, or endemicity, in Africa (Table 1). Although virtually all of the continent between the latitudes of 15 degrees North and 20 degrees South suffers from intense and stable malaria transmission (hyperendemic to holoendemic), there are areas that have epidemic outbreaks of the disease. Clinical disease and mortality are concentrated primarily in young children, with adolescents and adults generally having acquired some form of immunity through repeated and recurrent childhood infections. Even in areas of stable, intense transmission, the risk of infection can vary considerably from urban to rural areas. Under holoendemic conditions (much of sub-Saharan Africa), morbidity and mortality is concentrated in the youngest age groups. Under these conditions the risk of severe anemia is high, although the occurrence of life-threatening cerebral malaria is relatively low. As transmission becomes less intense, reaching characteristics of epidemic malaria, overall life-threatening disease risk is spread across a wider age group and cerebral malaria is increasingly common [Snow et al., 1997].

Other factors that can increase the risk of malaria infection include: poor diet, repeated systemic infections, pregnancy (primarily, first and second pregnancy), and low socio-economic status.

Table 1 - Levels and Characteristics of Malaria Endemicity [IDRC/WHO, 1996]

Level of Endemicity	Characteristics
Hypoendemic	Little transmission. Malaria does not affect the general population to a great extent. Spleen rates in children (2-9 yr.) is less than 10%.
Mesoendemic	Typically found in rural communities with varying intensity of transmission. Spleen rate in children is 11-50%.
Hyperendemic	Intense but seasonal transmission where immunity is insufficient to prevent effects in all age groups. Spleen rates in children usually >50%. Spleen rates in adults often >25% .
Holoendemic	Perennial, high-degree transmission producing immunity in older age groups. Spleen rates in children usually >75%. Spleen rates in adults generally low.

3.1.2 Malawi specific:

In Malawi, malaria infection is hyper- to holoendemic, resulting in perennial transmission in all but a few mountainous areas of the country. A warm rainy season runs from November to May and the highest transmission period runs from February to May. During this time, prevalence of parasitemia is estimated at 70-80% in children under 5 years of age [A. Macheso, Malawi National Malaria Control Program - pers. comm]. Point prevalence during the dry season (June to October) is estimated at 40%. It is further estimated that more than 80% of malaria in Malawi is caused by *Plasmodium falciparum* (Pf), which is responsible for the most severe forms of the disease [Tambala et al., 1992]. Apart from the morbidity and mortality effects of malaria, the economic impact of the illness in Malawi is substantial.

Malaria is the leading cause of morbidity and mortality in children under 5 years of age in Malawi. Over 40% of deaths in children under 2 years of age are caused by Malaria. Malawi has the eighth highest childhood mortality rate (223/1000) in the world, and a high MMR (about 800 per 100,000 live births) [GOM, 1995]. Many of these deaths are malaria related [NSO, 1997; Wirima, 1996]. Malaria has been the most common cause of admission to children's wards and to female wards in the country for the past four years, and is the most common problem among all outpatients [CHSU, 1995], often leading to anaemia, a major contributor to morbidity and mortality in children and pregnant women [Young, 1998a].

During 1997 at Ekwendeni Hospital, serving about 120,000 people in northern Malawi, almost 9,000 outpatients (25-30% of all patients) were seen with a medical problem relating to malaria infection. In 1997 there were 631 admissions to the children's ward

due to malaria and 24 deaths as a result of this disease among admitted children [Ekwendeni Hospital, 1997]. Many more children die as a result of malaria infection at the community level without ever coming to the attention of the health system. Parasitemia rates (the presence of malaria parasites in the blood) are almost 50% in children under the age of five [Young, 1997].

Malaria is very high in Nkhata Bay, one of the lakeshore districts, and in Lilongwe, the capital city of Malawi. Fifty-three percent of children tested positive for malaria parasites and seven percent of families had a family member die in the past year due to malaria [CPAR, 1999]. Two key points learned for a project that seeks to control malaria by promoting the use of impregnated bed-nets are: 1) 60% of mothers know that malaria is transmitted through a mosquito bite, and 2) 17% of households currently have a bed net [CPAR 1999].

In the Blantyre area, located in more densely populated southern Malawi, 38% of surveyed children had malaria within the previous week [Coombes et al., 1998], and 33% of adult respondents reported a malaria infection in the previous two weeks [NSO, 1997].

Not only does malaria contribute to high mortality but it also contributes to high morbidity and over-burdening of health facilities. Children under five years suffer on average 9.7 malaria episodes per year while adults suffer on average 6.1 episodes of malaria per year [NSO, 1997; Wirima, 1996]. Malaria episodes contribute to a general decline in overall health status, making individuals more susceptible to other illnesses and diseases. In addition to the cost of consultation, treatment, hospitalisation and travel, the economic costs of malaria include low productivity and potential loss of income through days of work lost. It has been estimated that the total annual cost of malaria to the average Malawian household is US$35, this amounts to 7.2% of average household income. For very low income households (i.e. <$167 per year which accounts for 52% of households) the annual cost of malaria is $22 which is equivalent to a staggering 32% of annual household income for this group [Ettling et al., 1996].

Table 2 - Top 5 Causes of In-Patient Admission in Malawi (All Patients): 1992

	Malaria	Pneumonia	**Anemia**	Diarrhoeal Disease	Ill-Defined	All Other Diagnoses
Attendance's	**34,793**	15,520	**13,946**	13,174	8,798	80,509
% of Total	**20.9%**	9.3%	**8.4%**	7.9%	5.3%	48.3%

Table 3 - Top 5 Causes of In-Patient Admission in Malawi (Under-5 yr.): 1992

	Malaria	**Anemia**	Pneumonia	Diarrhoeal Disease	Measles	All Other Diagnoses
Attendance's	**16,034**	**9,845**	6,758	3,879	3,842	12,816
% of Total	**30.2%**	**18.5%**	12.7%	7.3%	7.2%	24.1%

Source for both tables: CHSU, 1995

It is difficult to estimate the overall burden of malaria in developing countries such as Malawi, due to the lack of reliable national statistics for morbidity and mortality, particularly at the community level. Recently, by integrating malaria prevalence data (where available) with ecologic data (available for all of Africa) at a small scale, it is possible to estimate malaria risk at a national and sub-national level [Craig et al., 1999; Snow et al., 1998a, 1998b, 1999c]. It is estimated that, in tropical Africa, malaria is responsible for about 1 million deaths and 200 million episodes of clinical disease. The mortality estimates developed by MARA have been combined with the country-specific morbidity estimates described above [NSO, 1997; Wirima, 1996] to produce estimates for the burden of disease in Malawi (Table 4).

Table 4 - Estimated number of malaria deaths and clinical attacks in Malawi

Age Group	Mortality (rate per 1000)	Morbidity (attacks/person/year)
0 -4 years	17,894 (9.9)	17,532,461 (9.7)
5 -9 years	3,269 (2.17)	12,049,811 (8.0)
10 -14 years	1,004 (0.8)	8,786,306 (7.0)
15 years and older	711 (0.13)	33,382,967 (6.1)
Total	22,878	71,751,545

*Morbidity rate for 5-14 year olds has been interpolated from the existing rates for young children and adults, by the authors. Population is based on 1998 census data.

3.2 Micronutrient Deficiency:

Women and, particularly, children in Africa are currently at risk of, or are suffering from, chronic energy deficiency and micronutrient malnutrition [UNICEF, 1999]. This follows from a diet with limited intake of animal products, fruits, vegetables and fortified foods and high intake of anti-nutrients (phytates). The adverse effects of deficiencies in vitamin A, iron, folic acid, zinc, and the B vitamins include night blindness, anaemia, impaired immune function, impaired nervous system function and impaired growth. Ultimately the deficiencies result in increased morbidity and mortality in the population groups at risk, primarily young children.

3.2.1 Vitamin A

Prevalence of VAD for Eastern and Southern Africa is estimated as 530,000 pre-school children with clinical VAD and 10-18.6 million affected by sub-clinical deficiency. For West and Central Africa, the figures are 450,000 and 9.4-17.4 million pre-school children, respectively [MI/Tulane/UNICEF, 1998]. Most countries in SSA have a greater than 10% estimated prevalence of VAD among young children with a number of countries, such as Mozambique, Angola, Uganda and Malawi having prevalence estimates greater than 20%. The prevalence of VAD globally is decreasing, however it remains an enormous problem in SSA.

For Malawi in particular, studies in various parts of the country between 1983 and 1989 found the prevalence of xerophthalmia to range from 0.6% to 3.0%, with the highest rates in the most southerly region [WHO/UNICEF, 1995]. Xerophthalmia rates of 8.7% in Chinteche and 7.5% in Lilongwe were found in community surveys conducted last year [CPAR, 1999] (see figure 3). The clinical prevalence of VAD in children 0-60 months is now estimated to be 2.2%, and sub-clinical prevalence 31.3% [MI/Tulane/UNICEF, 1998].

Prevalence of low serum retinol in Malawi is high, consistent with the high rates of xerophthalmia. In adolescent girls living in the lower Shire valley, 26.6% had serum retinol levels <0.70 umol/L, with the lowest levels found in the youngest girls and those that were pregnant [Fazio-Tirrozzo et al., 1998]. VAD was high in HIV-negative pregnant women (55.9% with serum retinol levels <1.05 umol/L, 31.5% <0.35 umol/L) [Semba et al., 1998a], and HIV-positive pregnant women (63.3% <1.05 umol/L) [Semba et al., 1995]. In both studies, maternal VAD was associated with increased rates of infant mortality.

Vitamin A deficiency is a major cause of visual impairment and blindness in Malawi. Corneal pathology, attributed to vitamin A deficiency and measles infection in the majority of cases, was responsible for proportionally more impairment and blindness in students in Malawi than in Uganda or Kenya [Gilbert et al., 1995].

3.2.2 Iron

WHO recommends that public health interventions should be implemented for all infants and children in situations where there is a 30% or greater prevalence of anemia (Hb < 110 g/L) in pregnant women, and that there should be supporting evidence from dietary assessment that bioavailable iron intakes are low [WHO/UNICEF/UNU, 1995]. WHO is currently setting up a data bank to record estimates of the prevalence of iron deficiency in Africa, but reliable country-level anemia data are still scarce. Current estimates of anemia in pregnant women are between 40% and 70% in most countries with an average of about 50% [MI/UNICEF, 1998]. For the countries of Eastern and Southern Africa that have gathered national-level data on recent surveys, the estimates range from about 10% for Lesotho to about 60% for Malawi [UNICEF, 1997]. Prevalence of anemia will vary according to seasonal patterns of malaria and food availability, and so the differing times of year when surveys are conducted will account for some variability.

Most of what is known regarding prevalence of anemia in Malawi concerns antenatal women, as it is for this group that the Ministry of Health and Population (MOHP) has in place a policy for iron supplementation. The MOHP carried out three prevalence surveys during the past decade. These report anemia prevalence in antenatal women in 1997, in a national sample of 814 women, to be 62.3%, compared to 56.2% in 1993, and 70% in 1991. The average haemoglobin concentration during this last survey in 1997 was 105 g/L [T. Banda, MOHP - personal communication].

In Ekwendeni in mid-1997, anemia prevalence (Hb < 110 g/L) was 62% in a group of 411 women attending the local antenatal care clinic; 34% were below 100 g/L and would be considered moderately anemic [Young et al., 2000a]. Other regional surveys of antenatal women have had similar results: 83% in a sample of antenatal women from all three regions of the country (59% with Hb < 100 g/L) [Zamaere, 1997]; 54-65% among antenatal women in Mangochi District [Huddle, 1996]; 67% in the Thyolo area [Williams 1997]; 85-92% in Chikwawa (depending on season of testing) with average haemoglobin concentration of 9.1 g/dl [Chimsuku, 1996].

Anemia is also a public health problem in Malawian children. In a 1996 nationally representative survey, anemia prevalence was 71.3%, with a mean haemoglobin concentration of 98 g/L, and moderate anemia (Hb < 100 g/L) was 50.2% [Zamaere, 1997]. In the Ekwendeni area, in 1997, the prevalence of anaemia was 83% among 577 children aged 1-5 years; 64% had Hb concentrations below 100g/L [Young et al., 2000b]. A survey in the Chikwawa area in 1994-95 found 69% of infants from 0-6 weeks of age to be anemic (19% with Hb < 8g/dl), rising to over 90% for those aged 6-12 months (30% with Hb < 8 g/dl [Chimsuku, 1996]. Very little data on anemia are available for school age children. In early 1991, in Ntcheu District, 18% of 424 school children aged 6-8 years were anemic [Shrestha, 1994].

Anemia accounts for, and is an associated factor in, a large proportion of hospital admissions, morbidity and mortality, especially among pregnant women and young children. A hospital-based study at Kamuzu Central Hospital in Lilongwe found that 23% of admissions in April and May were anemic (Hb < 90 g/L) [Nelson et al.,1992]. An earlier study, at the same institution, found anemia to be the primary discharge diagnosis in 16% of children, higher than that for any other disorder [Nelson & von Alvensleben, 1991]. The Basic Health Statistics for Malawi consistently regard anemia as a major reason for health seeking behaviour [CHSU, 1995]. In 1992, the last year that the MOHP "Basic Health Statistics" contained information regarding causes of hospital admission, anemia was the third leading cause, behind malaria and pneumonia, and the second most common among children under 5 years (see Tables 2 and 3). The leading cause of mortality among in-patients that year was "Anemia" followed by "Malaria". In the under-5 population, the leading cause of in-patient mortality was "Avitaminosis & Other Nutritional Deficiency" followed by "Anemia".

3.2.3 Zinc

Suboptimal zinc nutriture has been widely reported, among children even in North America [Gibson et al., 1989, Walravens et al., 1983] but especially in developing countries such as Malawi [Ferguson et al., 1989, 1993a]. Rural African children who consume cereal- or tuber-based diets, which are low in animal products and high in phytic acid, are likely to be particularly vulnerable to zinc deficiency [Wise, 1995; Hambidge, 1997]. Children appear to be most vulnerable to low zinc status, presumably due to their high zinc requirements for growth and development and their bodies' inability to absorb dietary zinc from their predominantly vegetarian diet [Gibson, 1994].

The best indicators to identify areas at risk of zinc deficiency include dietary deficiencies, stunting rates, anaemia rates and the prevalence of diarrhea and malaria infection in children [UNICEF/USAID, 1993]. There is no single reliable indicator to assess zinc status, although both hair zinc levels and plasma zinc levels have been used in the past [Golden, 1989], and hair zinc concentration in young children is the preferred confirmatory indicator of zinc status [UNICEF/USAID, 1993]. An increase in growth rates in zinc supplemented children, compared to controls, in areas where dietary zinc deficiency can be shown, should be considered diagnostic of zinc deficiency.

Malawi has perhaps the most reliable information on the prevalence of zinc deficiency in Africa, as evinced by the number of studies that have been carried out over the last decade [Ferguson, 1989; Ferguson, 1993b; Huddle 1996], in which low zinc intake, and low plasma (43% - 47% of pregnant women) and hair zinc (94% of children) levels were observed. About 50% of children under the age of five are stunted (25% severely stunted) [National Statistical Office, 1994]. Combined with the high incidence of malaria infection and diarrheal disease, in conjunction with the known dietary deficiencies of micronutrients, deficiency of zinc is likely to be a widespread problem in Malawi, although no intervention studies have been completed at this time.

4 Evidence for biological synergy between vitamin A/micronutrients and malaria:

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 [A. Shankar - personal communication]. This has been particularly well documented over the past decade with regard to the effects of vitamin A on childhood mortality and morbidity from measles, respiratory and gastrointestinal infection. A meta-analysis of eight studies concluded that vitamin A supplementation resulted in an average 23% reduction in all-cause childhood mortality [Beaton et al., 1993].

Some earlier studies have suggested that malnourished (low weight-for-age) children were actually less susceptible to malaria, although these studies tended to be subjective in scope and suffered from the lack of control populations [Edirisinghe, 1986; Latham, 1982; McGregor, 1988]. Other, better-controlled studies have found that malnourished subjects are at greater risk of infection, illness and splenomegaly, and are more likely to die from malaria than well nourished controls [El Samani et al., 1987; Tanner et al., 1987; Renaudin and Lombart, 1994; Tshikuka et al., 1997; Williams et al., 1997], including studies in Malawi [Burgess et al., 1975] and Zambia [Wenlock, 1979].

4.1 Vitamin A and Malaria

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 (NK) 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 has been known for some time. However, the more specific effects of vitamin A on malaria morbidity and mortality are less well documented. A number of relevant studies are reviewed here.

Some early animal studies in vitamin A deficient rats and mice did indeed indicate an increased susceptibility to malaria that was reversed by vitamin A supplementation [Krishnan et al., 1976; Stoltzfus et al., 1989]. In humans, the results have not been so clearly documented. A number of cross-sectional studies found an inverse relationship between malaria parasitemia and vitamin A levels, suggesting a possible increased utilisation 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; Sturchler et al., 1987; 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.

In a novel consideration of the relationship between vitamin A and malaria, the whitening of the retina that had been previously described in children with cerebral malaria was found to be associated with serum retinol levels of 0.29 +/- 0.1 µmol/L (mean +/- SD), compared with a mean vitamin A level of 0.41 +/- 0.2 µmol/L in children without retinal whitening. Children with retinal whitening were three times more likely to have abnormal conjunctival impression cytology results than those without whitening. The retinal whitening in children with cerebral malaria, associated with low serum vitamin A levels and with abnormal conjunctival impression cytology, may be due to acute vitamin A deficiency at the tissue level [Lewallen et al., 1998].

Some investigators now recommend the use of vitamin A supplementation in cases of malaria, however few intervention trials have been conducted to date. In the VAST Study in northern Kenya (including a Survival Study on 21,906 children 6-90 months and a Health Study on 1455 children 6-59 months), 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 a randomised, placebo-controlled trial of vitamin A supplementation among children aged 6-60 months in Papua New Guinea, supplementation resulted in a 30% reduction in *Plasmodium falciparum* (Pf) 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., 1999a].

There is, therefore, an association between vitamin A and malaria infection. Clearly, more information is needed to identify the immune mechanisms that may explain a reduction in malaria morbidity in children receiving vitamin A supplements.

4.2 Zinc and Malaria

The interaction between zinc and malaria is even less well documented. Zinc is known to be an immune modulating agent and is essential for normal immune function. It is known that zinc is important for cell-mediated immunity through neutrophils, macrophages and NK cells, and that it affects the development of acquired immunity and antibody production, particularly immunoglobulin G [Shankar and Prasad, 1998]. Some recent studies in primates have clearly demonstrated immunological effects of zinc deficiency [Vruwink et al., 1991; Golub et al., 1996]. Zinc affects multiple aspects of the immune system and is crucial for the normal development of acquired immunity. This in turn provides a biologic basis for the altered host resistance to infections, such as malaria, that has been observed during zinc deficiency.

Zinc supplementation reduces the incidence and severity of diarrhea and pneumonia [Black, 1998; Behrens et al., 1990; Sachdev et al., 1988; Sazawal et al., 1996; Simmer et al., 1988; Rosado et al., 1997]. There have been only two studies, however, on the effects of zinc supplementation in malaria. Malaria episodes were reduced among zinc supplemented pre-school children in The Gambia [Bates et al., 1993]. In PNG, among children 6-60 months, zinc supplemented children had a 29% decrease in overall health centre attendance, a 38% reduction in fever associated with Pf malaria parasitemia, and a 69% reduction in episodes of parasitemia with densities greater than 100,000/uL (severe disease) [A. Shankar - personal communication].

As with vitamin A, although there is evidence of a role for zinc in the host's immune response to malaria, and a relationship between zinc supplementation and malaria infection, much more information on the specific mechanism(s) involved is needed.

4.3 Iron and Malaria

The issue of infection and iron supplementation is more controversial, and there are few data that suggest a role for iron in the immune response. There is evidence that iron deficiency reduces T cell counts and that iron supplementation can assist with the bacteriocidal activity of neutrophils through the development of neutrophils in the bone marrow [Zimmer, 1998; Walter, 1986].

With regard to malaria infection in particular, malaria seriously worsens iron status and satisfactory improvement cannot be achieved by iron supplementation unless underlying malaria is treated [ACC/SCN, 1997]. Also, low serum iron levels inhibit replication of the malaria parasite and some studies have shown an increase in malaria episodes after iron deficiency has been treated [Masawe et al., 1974]. In a recent Malawi-based study, although oral iron therapy enhanced the haematological recovery of patients with falciparum malaria treated with sulphadoxine-pyrimethamine (SP), it also tended to prolong their parasitemia. Study children who received malaria treatment with SP had rapid and significant gains in haemoglobin concentration levels, regardless of initial Hb level, indicating that most of the anaemia in these particular patients was related to malaria [Nwanyanwu et al., 1996]. This is in contrast to a recent study, also in Malawi, which found that iron status of young children did not affect parasitological recovery from malaria. Significant increases in haemoglobin concentration were found after treatment for malaria with SP and although the Hb increase (2.2-2.7 g/dl) was dependent on initial Hb values, it was not limited by iron deficiency [Verhoeff et al., 1997]. Hemoglobin increases were even greater in northern Malawi (4.5-5 g/dl), in severely anaemic children who were given SP treatment for malaria [Bloland, 1993). A recent double-blind placebo-controlled trial of malaria chemoprophylaxis and iron supplementation in Tanzanian infants found that iron supplementation was effective in preventing severe anaemia without increasing susceptibility to malaria. The protective efficacy of malaria prophylaxis against severe anaemia was found to be 57.3% while the protective efficacy of iron supplements was 28.8% [Menendez et al., 1997].

Most recently, INACG has released a Consensus Statement on the Safety of Iron Supplementation Programs in Malaria-Endemic Regions. Review of the available evidence found that prophylactic iron supplementation was associated with relatively small, and often non-significant, increases in certain malariometric indices and that improvements in hematological status following iron supplementation were substantial and have clear public health benefit. They conclude that "*concurrent implementation of iron supplementation and malaria control activities is the ideal*" [INACG, 1999].

4.4 Interactions between micronutrients: Zn-Vit A, Vit A-Fe, Zn-Fe

In addition to the potential interactions between malaria and the various micronutrients, the micronutrients also have interactions among themselves which can result in potentiation of their effects. Zinc status influences vitamin A metabolism, absorption, transport and utilization. Zinc (or zinc & iron) supplementation is associated with

significantly higher plasma retinol than placebo [Munoz et al., 2000], although earlier studies did not show zinc supplementation having a consistent effect on vitamin A status [Christian and West, 1998].

Vitamin A supplementation, combined with iron supplementation, is more effective in reducing anaemia than iron supplementation alone [Angeles-Agdeppa, 1997; Young et al., 2000b], and periodic high doses of vitamin A alone can improve the iron status of a population [Bloem et al., 1989; Bloem et al., 1990; Suharno et al., 1993].

There is the concern that high iron intakes inhibit zinc absorption when these elements are given together in a supplement [Solomons and Jacob, 1981; Solomons et al., 1983; Meadows et al., 1983; Valberg et al., 1984; Sandstrom et al., 1985], but this effect is minimized by keeping a relatively low Fe-Zn ratio (e.g. no higher than 2:1) [Whittaker, 1998]. Zinc absorption is not inhibited when iron and zinc are given together in a meal [Solomons, 1986] or when lower amounts of iron are used in a food fortification program [Davidsson et al., 1995].

4.5 Summary of Micronutrient – Malaria relationship

Micronutrients, particularly vitamin A and zinc, have a role in immune mechanisms and malaria control. Specific immunity to malaria develops over several years of exposure to repeated infection [Baird, 1998; Reeder & Brown, 1996].The immune response to malaria is characterised by antibody-mediated immunity, cell-mediated responses and non-specific immunity, all areas that are potentially affected by vitamin A and zinc deficiency.

ITNs prevent malaria infection by reducing human contact with the malaria vector. Vitamin A and zinc work to improve the "defensive" reaction of the human host (cell-mediated immunity) and both have actions on multiple aspects of the immune system. Also, lessening the incidence of malaria infection with the regular use of ITNs will improve overall health status of the individual and likely improve micronutrient status through less systemic illness, the lowered utilisation of micronutrients like vitamin A by the infective agent, and improved diet (less anorexia, improved absorption).

The proposed integration of VACs and ITNs combines one strategy that reduces contact with the parasite and improves overall health, with another strategy that improves the defensive reaction and the development of immunity once contact is made. Therefore, the potential for actual synergism in the effects of the two strategies is apparent and should be further explored.

5 Programming experience in ITNs and Micronutrient Supplementation:

5.1 Malaria Control and ITNs:

In 1955 the Eighth World Health Assembly adopted a Global Malaria Eradication Campaign based on the widespread use of DDT against mosquitoes and of antimalarial drugs to treat malaria and to eliminate the parasite in humans. As a result of the Campaign, malaria was eradicated by 1967 from all developed countries where the disease was endemic and large areas of tropical Asia and Latin America were freed from the risk of infection [Trigg and Kondrachine, 1998]. The Malaria Eradication Campaign was only launched in three countries of tropical Africa since it was not considered feasible in the others. Despite these achievements, improvements in the malaria situation could not be maintained indefinitely by time-limited, highly centralized programmes [Bradley, 1998]. Also, mosquito resistance to DDT and of malaria parasites to chloroquine, a safe and affordable drug, began to affect program activities.

In response to the failures to control malaria, a global Malaria Control Strategy was developed by a Ministerial Conference on Malaria Control in 1992 and confirmed by the World Health Assembly in 1993 [WHO, 1993]. The basic elements of the Strategy are:

- to provide early diagnosis and prompt treatment;
- to plan and implement selective and sustainable preventative measures;
- to detect early, contain or prevent epidemics; and
- to strengthen local capacities in basic and applied research to permit and promote the regular assessment of a country's malaria situation.

The lessons from some of the areas that have adopted this strategy of control, such as Brazil, China, Philippines, and Thailand, are clear: malaria can be controlled using the tools that are currently available. The challenge is now to apply these tools among vulnerable individuals and groups experiencing high levels of morbidity and mortality, particularly in sub-Saharan Africa.

Insecticide Treated Nets (ITNs) have been proven to significantly reduce malaria related morbidity and all cause mortality in multiple field trials in Africa [Fraser-Hurt et al., 1999; Lengeler, 1998; Smith et al., 1999]. The current challenge is to promote the widescale use of ITNs through cost-effective programs, something that is unlikely to be affordable in very-low-income countries [Mills, 1998; Goodman et al., 1999]. Few large-scale operational projects have been implemented and even fewer have been adequately evaluated. The long-term surveillance of ITN interventions is imperative, particularly in light of the questions surrounding the potential impact of rebound mortality [Coleman et al 1999].

ITNs are strongly recommended by the Roll Back Malaria (RBM) initiative of the World Health Organization (WHO) as one of the main strategies to be used in the goal of a reduction by one-half of the global malaria burden. As a result, health ministries in

countries where malaria is endemic are beginning to implement the ITN strategy as integral parts of their National Malaria Control Programs (NMCP). In sub-Saharan Africa, however, implementing ITN programs on a large scale is difficult owing to the logistics and costs involved. Some of the operational constraints that have been experienced in the implementation of ITN programs in general, as well as those specifically related to Malawi, are discussed here.

Promotion and distribution of ITNs can be accomplished through four major channels, either individually or in combination:

1) Government Agencies (e.g. Ministry of Health)
2) Non-Governmental Organizations (NGOs)
3) Private Sector (existing commercial channels)
4) "Assisted" Private Sector (social marketing)

This can include distribution points that are situated centrally (district or facility-based) or locally (community or household-based) and done on a continuous or fixed-date process. Retreatment can be done on an individual or community-wide basis and be provided either through fixed, mobile or home-based services, or through community-wide retreatment campaigns, each having advantages and disadvantages.

The National Malaria Control Programme (NMCP) of the Malawi Ministry of Health & Population (MOHP) has included the promotion of ITNs as an important strategy for the control of malaria in the country [GOM, 1998]. They are relying much on the efforts of NGOs in Malawi to assist with this process. As a result, there are a number of mosquito net distribution programs underway and nets are readily available in the marketplace. As yet, however, there is no efficient national system in place for the regular retreatment of nets. The experiences of three NGO ITN programs (PSI, CCAP, CPAR) are reviewed below.

The Blantyre Insecticide Treated Net (BITNET) project, operated by Population Services International (PSI) is the largest ITN program in Malawi. BITNET aims to reduce malaria disease and death in the Blantyre District of Malawi by maximizing ownership and appropriate use of ITNs through creating demand and improving access to affordable nets and insecticide [D. Chavasse - personal comm.]. It is based on a social marketing approach to health behavior change [Schellenberg et al., 1999].

The wider objectives of BITNET are:

- to make affordable ITNs widely available
- to focus on promotion of retreatment
- to promote year round use of ITNs
- to develop specific strategies to target the rural population
- to develop specific strategies to target poorer sections of the community
- to promote preferential use of ITNs among young children and pregnant women.

The PSI social marketing initiative has a focus on promotion and education for behaviour change, relying on radio messages as well as drama shows, video shows, newspapers, billboards, painted walls, stickers in public transport and painted PSI delivery vans. Two different nets are sold. A conical net is promoted mainly for the richer urban population at a higher price (US$ 6.80) and then a rectangular net, mainly for the poorer rural population (US$ 4.50). Procurement cost of the nets is the same, so PSI has maximised cost recovery from richer urban people while subsidising the net most appropriate for poorer rural people (rectangular). As a result of the emphasis on promotion and affordability, great progress has been made after only one year of implementation with net sales of 76,370 and a retreatment rate of about 25%, based on the number of retreatment kits sold.

The ITN Program of the Church of Central Africa, Presbyterian (CCAP) Synod of Livingstonia Health Department, is integrated into the primary health care delivery system at three hospitals in the northern region. It promotes the strategies of early recognition and management of malaria infection and the promotion of ITNs for prevention [Ekwendeni, 1998]. The program trains community health volunteers in malaria prevention and control, including the recognition and management of malaria infection, malaria prevention and the proper use of mosquito nets and insecticide. These volunteers then educate their communities, promote and sell treated nets and assist in their proper use and retreatment. Initially treated nets are sold at US$4.50 for double rectangular nets and US$6.00 for large conical nets (approximately 20% subsidy), while a second net for a household is sold at half price. This provided protection to all family members, and not just the head of the household who would normally use the net if only one was available.

After one year, 50% of households had one net in use and 25% had more than one net in use. Forty-six percent of children under the age of five, living in the sampled housholds, were sleeping under a net on a regular basis. Slightly more than half of these were sleeping under a net that had been treated within the past year. Of those households currently without nets, 86% stated that the reason was that they "can't afford one" [Young, 1999]. It is encouraging that almost half of the children under five are currently using a net, however many of these nets have not been retreated in the past year even though the insecticide is subsidised.

One of key aspects in the success of the Synod ITN program was community education (IEC) and promotion before the implementation stage. As well, the close relationship between the community and the implementing partner, as the major health providers in the area for the past 100 years, assisted in the ready acceptance of many villagers to a relatively new approach. The main constraints encountered in the implementation of the program are:

- inability to reach those who are unable to afford nets and insecticide;
- maintaining effective monitoring of the program given economic and staff capacity constraints; and
- the need to subsidise (20-30%) nets and insecticide.

These constraints are very similar to that which have been found in other ITN programs and in other countries [e.g. Plourde, 1999].

The Malaria ITN Sub-project operated by CPAR-Malawi has been operational for less than 6 months [CPAR, 2000]. This programme is focused around IEC and promotion at the community level and utilises trained, community-based volunteers to promote and sell the ITNs, much along the lines of the CCAP program. Some of the problems experienced so far include the fact that the program was launched at a time of year when money was not readily available at the household level and although the demand is high, few people are able to pay for the nets. Most rural Malawian households have access to cash at the time of harvest, from the sale of maize, and this usually takes place in the months of June to August. However, the prime time for sale and promotion of ITNs occurs just prior to the peak malaria season in Malawi which corresponds to the months of December to February. Unfortunately these are the relatively "lean" months in the country, just prior to the harvest, when little food and money are available.

As found in all the present ITN programs in Malawi, cost of ITNs and the priority placed upon them by the decision-makers in the household, generally men and elders, place an important constraint on effective implementation. In Ekwendeni, men control the majority of resources within the household. At times, the use of cash or resources by male household or kin members in Malawi conflicts with household food requirements and expenditures for necessary health care [Bezner Kerr, 1998; Scherr, 1993]. Men often use limited cash resources for the purchase of alcohol, which was found to have a direct result on gender relations within the household and on the high levels of spousal violence that were reported [Bezner-Kerr, 1998]. Gender relations, both within and beyond the household, have a critical influence on food security and household expenditure [UNICEF, 1987; Malindi, 1995; Sigman, 1995) and need to be taken into account for effective program planning in Malawi.

The ITN trials completed this decade in SSA achieved high coverage and high re-treatment rates under artificial experimental conditions. While necessary to understand protective efficacy, the approaches used to deliver the intervention provide few indications of what coverage of net re-treatment would be under operational conditions [Some et al., 1997; Kachur et al., 1999]. Varied delivery and financing strategies have been proposed for the sustainable delivery of ITNs and re-treatment programs. One recent study found that ITN were most effectively delivered through existing MCH channels and that specific promotion and innovation was necessary to achieve substantial net retreatment levels [Fraser-Hurt and Lyimo, 1998].

In Kenya, a series of suitable delivery strategies were used to continue net re-treatment in an area of a previous ITN effectiveness trial [Snow et al., 1999b]. The trial adopted a bi-annual, house-to-house re-treatment schedule free of charge using research project staff and resulted in over 95% coverage of nets issued to children. During the year following the trial, sentinel dipping stations were situated throughout the community and household members informed of their position and opening times. This free re-treatment service

achieved between 61-67% coverage of nets used by children for three years. In 1997 a social marketing approach, that introduced cost-retrieval, was used to deliver the net re-treatment services. The immediate result of this transition was that significantly fewer of the mothers who had used the previous re-treatment services adopted this revised approach and coverage declined to 7%. In another case, very few nets were found to have been retreated in the intervening years when a study site was visited three years after completion [Kachur et al., 1999]. Understanding why optimal ITN use declines, particularly in regard to retreatment, is important for the improvement and sustainability of future ITN efforts.

In summary, the constraints encountered and important lessons learned in the implementation of ITN programs in Malawi and sub-Saharan Africa include:

1) Marketing and promotion of ITNs requires further development, with particular reference to strategies for promoting retreatment. (Acceptability)
2) Scaling up from subsidy to full cost-recovery poses significant challenges to ensure a viable and sustainable programme. (Sustainability)
3) Cost of nets and insecticide. The present cost continues to be high, often due to import taxes and custom duty. (Affordability)
4) How to reach the most needy and vulnerable of the population which consists primarily of rural subsistence farming households and female-headed households, particularly those with small children. (This includes aspects both of Accessibility and Affordability in order to increase Coverage)
5) Monitoring and evaluation of programmes, as they increase in size, presents problems for staff with limited information management training and capacity.
6) Identifying the most effective distribution system. Ensuring that community members are full partners in the process and that essential human and financial resources at the community level are harnessed.

With particular reference to retreatment, the constraints are:

1) Poor awareness of the role of insecticide (people think that the net alone provides enough protection)
2) Availability of insecticide at community level
3) Cost of retreatment

Other key issues are:

- Decision making and division of labour at the household level (both related to gender relations)
- Seasonality of disposable income
- Attitudes & behaviours related to health

The WHO Roll Back Malaria program, at the recent partnership meeting in Geneva (Feb. 2000), identified ITNs as one of four recognised priority technical areas. Malaria control

experts at the conference listed a number of operational research areas that require further investigation and coincide with the constraints identified above:

- new mechanisms for service delivery;
- availability, affordability, promotion and dissemination;
- increasing local production and demand;
- using public/private partnerships to bring down the cost of bednets, and improve the market for them;
- encouraging private and public donors to subsidise the provision of bednets for those who cannot afford them;
- promoting the need to regularly retreat bednets with safe insecticides;
- long-lasting treatment of nets;
- consequences of long-term use of ITNs; and
- promotion of appropriate ITN use during pregnancy.

5.2 Micronutrient Supplementation:

5.2.1 Vitamin A

The ideal biological vitamin A supplementation protocol would have frequent, low-dose supplements, so that the risk of toxicity can be minimized. In reality, contact opportunities with the vulnerable populations in developing countries are infrequent. Therefore most countries have prophylactic distribution of high dose oral supplements to women and children, based on the following IVACG guidelines [WHO, 1997]: Infants < 6 mo. (not breastfed) – 50,000 IU, infants 6-12 mo. – 100,000 IU (every 4-6 mo.), children > 1yr. – 100,000 IU (every 4-6 mo.), women – 200,000 IU (within 8 wk. of delivery).

Low dose vitamin A does not need to be administered under supervision of the health system, and therefore can make use of community-based institutions, volunteers and commercial outlets. Daily (5,000 to 10,000 IU) or weekly (25,000 IU) doses for supplementation are being explored.

National vitamin A supplementation programs make use of various distribution channels. These include:

1) During routine contact at hospital or health centre level
2) During provision of the routine immunization schedule
3) During National Immunization Days (NIDs)
4) During other national campaigns (National "Health Days")
5) Through other routine Primary Health Care channels such as MCH
6) Door-to-door delivery at the household level (rarely used)

In many countries, VA supplementation has been linked to National Immunization Days (NIDs) [WHO, 1998], and this has often been responsible for improving VAC coverage. A four country study found that giving vitamin A during immunisation contacts is highly

cost-effective, however coverage of children over one year of age is low [Sanghvi et al., 1999]. A review of 25 programs reported found supplementation with VA to be low-cost, acceptable and clinically effective within the relatively short-term, *providing* that coverage of the population is good (at least 65%) [West & Sommer, 1987]. A major constraint in VAC distribution programs is maintaining high coverage of the target population on a sustainable basis. Linking VAC distribution with NIDs has resulted in a high proportion of children receiving at least one vitamin A supplement per year. A major challenge now is for national programs to find alternative strategies as NIDs are phased out. Some countries are experimenting with social marketing strategies such as "health weeks" or "national micronutrient days" in order to try and sustain the coverage. In some programs, poor coverage is reported to be due to many factors including lack of personnel, lack of health worker motivation, inadequate supply of VAC, transport and distribution problems, lack of administrative and political support, program fatigue and lack of IEC [ACC/SCN, 1993].

There is concern that VA interferes with the immune response to vaccines, but this does not appear to be the case, as evinced from a number of presentations at last years IVACG meeting [Bahl et al., 1999; Rahman et al., 1999; Shankar et al., 1999b]. However, there is contradictory evidence from recent studies of supplementation linked to immunisation in early infancy, in Ghana, India and Peru, in that there was no sustained impact either on vitamin A status beyond the age of 6 months, or on infant morbidity [WHO/CHD, 1998]. If there is immune response interference, or no sustained impact on vitamin A status, the widely advocated coupling of VAC administration and routine immunization may need to be re-examined. This emphasizes the need for exploring other sustainable approaches; linking VAC distribution with ITN retreatment may be a viable alternative.

In Malawi, the Ministry of Health and Population (MOHP), with UNICEF support, has implemented a program of vitamin A supplementation for children from 6 months to 6 years, and postnatal women, following the WHO protocol [GOM, 1996]. In order to increase coverage, this has been combined with an immunization campaign, such as a polio or measles campaign (NID), although not on a regular basis. A nationally representative survey in Malawi indicated that only 16% of children 0-59 months had received at least one dose of vitamin A in their lifetime (28% had received at least one dose by 48-59 months). Only 23% of women reported receiving vitamin A within 8 weeks of their last birth [NSO, 1997]. As a result, in the past few years, the MOHP has concentrated on NIDs for VAC distribution.

A study by the International Eye Foundation found that only 13% of children more than 11 months of age had documented proof of receiving vitamin A supplements in the previous 6 months and recent coverage declined with increasing age. Vitamin A coverage of children was not associated with the gender of the child, maternal literacy, distance to health facility, or the presence of village health volunteers. However, post-natal coverage was significantly higher (55%) in villages that had health volunteers compared to villages that did not (23%). VAC coverage for both women and children varied widely by sub-district, ranging from 2.4% to 24.5% for children and from 0% to 38.7% for mothers [Berger et al., 1995]. This illustrates clearly that there are missed opportunities for both

mothers and children to receive VAC. This may in part rest with the health workers themselves if the value of the supplement is not appreciated, community members are not encouraged to consume them, and sufficient stocks do not exist to cover demand.

Community-based distribution of micronutrients may offer the best strategy for reaching a wider proportion of the target population, particularly those children over one year of age who may not attend a health facility for immunization. There is a long history of use of village-based health volunteers in Malawi, and although motivation for sustaining participation is sometimes a concern, this method of distribution may need to be further explored.

It was reported, *"There is a need to think in terms of integration within existing delivery systems including health and nutrition services. Supplementation possibilities have tended to be bounded by the traditionally-used delivery systems, which has limited opportunities. A full assessment of all available options, including novel delivery systems, needs to be explored."* [ACC/SCN, 1993].

The possibility of linking vitamin A distribution with retreatment of nets, such as presented here, is one such "novel delivery system" that requires exploration. Some important “cross-cutting” constraints that seem to be present in all vitamin A programs reviewed was the lack of knowledge or awareness of VAC benefits at both the community and health-worker level; the need for development of more, culturally-appropriate IEC materials; regular and reliable supply of appropriate supplements; and coverage of an increased proportion of the most vulnerable population groups.

5.2.2 Iron

The following guidelines are recommended for iron supplementation programs in developing countries:

Table 5 - WHO/UNICEF Guidelines for Iron Supplementation [INACG, 1998]

Population Group	Dosage (elemental iron)
Pregnancy	60 mg daily during pregnancy and for 3 mo. postpartum
Children 6-24 months	12.5 mg daily (begin at 3 mo. for low birth weight infants)
Children 2-5 years	20 - 30 mg daily
Children 6-11 years	30 - 60 mg daily
Adolescents and adults	60 mg daily

More recently, with respect to iron supplementation in malaria endemic areas, INACG has published a consensus statement which recommends that:

1) iron supplementation should continue to be recommended in malarious areas where IDA is prevalent. The subgroups that should be targeted are pregnant women and young children, especially infants of low birth weight;

2) implementation of oral iron supplementation programs in malarious areas should be actively promoted; and

4) countries should develop specific national guidelines for implementing and monitoring iron supplementation *in coordination with malaria interventions to control anemia* [INACG, 1999].

Routine iron supplementation is the primary approach to reducing iron deficiency anemia during pregnancy, and as a result, many countries have adopted the INACG guidelines. In Malawi, it is the recommendation of the MOHP that every pregnant woman be provided with iron/folate tablets during pregnancy, although this is often limited by problems in procurement, supply and distribution, as well as potential problems on the side of the receiver related to compliance/adherence. In fact, the recommendations of the MOHP to supplement during lactation were cancelled, due to problems with adequate supply [T. Banda - personal communication]. Current recommendations are to provide one or two iron tablets (60 mg elemental iron/tablet) plus folic acid (250 ug), each day to pregnant women from mid pregnancy until term [GOM, 1999].

Coverage of pregnant women in Malawi with iron/folate supplements is low, with estimates of regular intake ranging from 30% to 56% [NSO, 1997; Williams, 1996; Zamaele 1997]. Many of the women surveyed took the supplements for only one to two months, due to inadequate supply and adverse effects. Part of the problem rests with health workers themselves in not appreciating the degree of the problem and the health benefits from the provision of adequate supplements [Williams, 1996].

According to a national survey, 40% of pregnant women had visited an antenatal care (ANC) clinic at least once during the current pregnancy. Knowing that iron/folate supplements are generally only provided to pregnant women through these clinics, and taking a liberal estimate of 75% coverage of supplementation for women attending ANC, this translates into an overall coverage rate of 30% for all pregnant women in Malawi. Given present estimates of about 475,000 births/year in this country [UNICEF, 1998], approximately 332,500 pregnant women/year would not be covered with supplements. As with vitamin A, the constraints in the iron supplementation program in Malawi, and likely in other countries, are: lack of knowledge or awareness of health benefits, the need for IEC materials, regular and reliable supply of appropriate supplements, and lack of coverage among the most vulnerable population groups.

Research is ongoing to determine the most cost-effective regimen for iron supplementation in various age groups and contexts. Several studies have indicated the

effectiveness of providing weekly iron/folate supplementation [Ridwan et al., 1996 Schultink et al., 1995; Tee et al., 1999], and this was supported in Malawi among pregnant women [Young et al., 2000a], children [Young et al., 2000b], and adolescent girls [Young et al., 1998]. These studies, conducted within the Malawi context, concluded that weekly iron/folate supplements had similar hematologic effects in comparison to a daily supplement in subjects with mild to moderate anemia, with the advantages over a daily supplement of improved adherence and fewer adverse effects. As a result, the Malawi MOHP developed guidelines for supplementation that were felt to be feasible and sustainable. This involves daily supplementation for pregnant and lactating women, and low birthweight infants, and weekly supplementation for children and adolescents [GOM, 1999]. A multi-project analysis of intermittent iron supplementation concluded that daily or weekly dosing with iron are both effective, although daily iron is more effective than weekly iron in improving hemoglobin concentration and ferritin levels, particularly during pregnancy [Beaton and McCabe, 1999].

5.2.3 Zinc

At the present time there are no known national public health programs in existence for the provision of zinc supplements to population groups at risk, although some small-scale programs exist on an experimental basis. As a result, there are many unanswered operational questions with regard to the effective provision of these supplements. It is expected that many of the operational issues and constraints would likely be similar to those experienced for iron and vitamin A.

5.2.4 Weekly "Multiple Micronutrient" Supplementation

In recent years, weekly supplementation with lower doses of vitamin A has been advocated. WHO/UNICEF/IVACG Guidelines on vitamin A supplements endorse the use of a weekly supplement as an alternative to the high-dose vitamin A supplements currently provided, if it is felt that this would result in higher coverage or a more sustainable, cost-effective programme [WHO, 1997].

There is also interest by WHO, UNICEF and others regarding the effectiveness of a weekly *multiple micronutrient* supplement [UNICEF/WHO, 1997], and recent studies have been conducted using this approach [Angeles-Agdeppa et al., 1997; Thu et al., 1999]. As a follow-up to an effectiveness trial of weekly micronutrient supplemention (iron, folate, vit A, vit C, vit B complex) to preschool children [Young et al., 2000b], a weekly community supplementation program has been implemented in the Ekwendeni area of Malawi involving community health volunteers in an attempt to improve availability, access and compliance [Ekwendeni, 1998]. A combined, weekly micronutrient supplement that is shown to be effective could be attractive to government health ministries and donors, as the potential of combating two (or more) major childhood nutritional disorders would be more cost effective than single nutrient interventions.

A weekly supplement of vitamin A, in addition to iron, would be effective in combating the effects of vitamin A deficiency as well as improving hemoglobin status [Young et al., 2000b; Thu et al., 1999]. Weekly supplements may provide a more efficient and effective method to reach the target groups at a community level. The recent informal technical consultation on vitamin A supplementation, convened by UNICEF, endorsed the use of a weekly supplement as an alternative to the high-dose vitamin A supplements currently provided [GVAI report]. This confirms the recommendations on the use of weekly supplements from the WHO/UNICEF/IVACG Task Force, particularly if this would result in a higher coverage or a more sustainable program [WHO, 1997].

The Malawi MOHP is examining the feasibility of providing universal, multiple micronutrient (iron, zinc, folate & vitamin A) supplementation to children and women of childbearing age. The 1999 Malawi MOHP 5-year plan to control anaemia includes recommendations to provide an "appropriate weekly multi-micronutrient supplement" to all women and children by the end of five years [GOM, 1999].

6 Lessons for Future Implementation of an Integrated Program:

Operational aspects of both ITN and micronutrient supplementation programs involve: IEC and promotion, community mobilisation, supervision and training, procurement and distribution, monitoring and evaluation, administration, and technical support. A critical analysis of the links between ITNs and micronutrient supplements, at each of these levels, is needed. That is, “At each level of the operational framework, how can the important aspects of the ‘separate’ programs be combined in order to improve overall administration, efficiency and effectiveness”? Emphasis in this discussion will be placed on vitamin A, as this is the area where most programming experience exists and will be the focal point for beginning integration of the programs.

Tables 6 and 7, below, summarize the similarities in programming and epidemiology between vitamin A and ITNs.

Table 6 - Similarities in Programming between Vitamin A Supplementation and ITNs

	Vitamin A Supplementation	ITN Distribution & Retreatment
Periodicity	Every 6 months	Every 6 months
Target Group	Children under 5 Pregnant/Lactating Women	Children under 5 Pregnant Women
Promotion/IEC	Focus on "Positive Health" (VAD - causes, effects, prevention)	Focus on "Positive Health" (Malaria- causes, effects, prevention)
Distribution Channels	Health Centres Health Workers Community Volunteers (Commercial Outlets)	Commercial Outlets Health Centres Health Workers Community Volunteers
Monitoring & Evaluation	Coverage Morbidity Mortality (coverage = % receiving VAC)	Coverage Morbidity Mortality (coverage = % sleeping under ITN)

Table 7 - Similarities in Epidemiology between vitamin A deficiency and malaria

Risk Factor	VAD	Malaria
Age	Pre-school children School-age children Adolescents	Pre-school children (endemic areas) School children and adults (epidemic areas)
Physiologic Status	Pregnancy Lactation	Pregnancy
Diet	Diet low in vitamin A, or caretenoids and fats	Diet low in vitamin A and zinc
Immune status	Underlying infection	Underlying infection
Cultural factors	Dietary related, feeding patterns	Sleeping arrangements Health seeking behaviour
Seasonality	All year but with peak period pre-harvest (i.e. December to March in Malawi)	All year but with peak period during/after rains (i.e. January to April in Malawi)
Socio-Economic Status	"Disease of Poverty" related to lack of available income for purchase of food	"Disease of Poverty" related to lack of financial resources for purchase of prevention and treatment
Location	Poor growing areas, landless (urban, peri-urban)	Low-lying, wet areas, anywhere with mosquitos
Knowledge	Lack of awareness of VAD (causes, prevention, effects)	Lack of awareness of malaria (causes, prevention, effects)

6.1 Linking of Mobilisation and IEC (Information, Education and Communication):

Mobilisation is generally carried out through the same channels for both ITNs and VAC. This begins with coordination and communication with national, district and community leaders in order to increase awareness of the public health problem. Next, community-level sensitization and awareness-raising must occur. Community health volunteers and committees that are already trained in one or both interventions should be utilized.

The target groups for IEC initiatives are similar and ITN/VAC integration can take advantage of existing fora and media for transferring messages on the benefits of VAC and ITNs in illness prevention and control. It is important that not only the traditional recipients of health education (women of reproductive age) be addressed but that also the decision-makers in the household, (usually men and elders), be included. This is critically important for ITNs as the action of expending financial resources for this disease prevention commodity must be understood to be a priority health issue for those involved. The timing for community mobilization and education can also be done simultaneously as the priority months for prevention of malaria infection and nutritional deficiencies coincide. In Malawi, this occurs during the months of December to March, at the beginning of the rains and just prior to the harvest period. This is also offset by roughly six months from the time during the harvest when financial resources are at a peak. This would allow for ease of programming campaigns, such that nets and retreatment can be offered at a time when people are most likely to pay (July and August) and again, six months later, when food (nutrition) is at a minimum and malaria is about to reach its peak incidence (January and February). It may also allow for some flexibility in payment schedules, as households can be given the opportunity to pay for a whole year of "service" at one point in the year, when money is available, and then have the service provided again when it is most needed in the "lean" months.

Intensive, combined IEC will be key. The content of IEC messages must communicate the importance of both ITNs and Vitamin A in the protection from illness and disease, but at the same time try to avoid possible confusion in multiple messages. There must be a focus on the role of the <u>insecticide</u> in addition to the ITNs and VACs themselves. Care must be taken to avoid a choice being made between either ITNs or vitamin A, <u>both</u> must be promoted and provided, and <u>both</u> malaria and VAD must be prevented. It will be important to point out that VAC is not a "malaria vaccine", and although improved vitamin A status appears to have a role to play in disease prevention and mitigation, it should be combined with the most effective malaria prevention strategy available. The lessons learned from previous programs points to the importance of including traditional communication channels for education such as <u>drama</u>, <u>songs</u> and <u>stories</u>.

Some potential IEC messages are:

"Two-Handed Control for the Malaria and Malnutrition Killers" - Net/Insecticide in one hand (treatment kit?) and VAC/Mangoe in the other.

"Eating a Mango under an ITN" - Importance of getting adequate dietary vitamin A and prevention of malaria, in order to remain healthy.

"Mutu umodzi susenza denga"

"Chala chimodzi sichiswa nswabwe"

These local Malawian sayings or proverbs are roughly translated as "You can't build a house on one pole", and correspond to the notion of "Two hands are better than one". These can be used in an attempt to get across the message that both strategies together will be most effective for prevention and control of malaria and VAD.

6.2 Procurement and Distribution:

It is important that the "time-link" be kept in mind for all levels in the procurement of supplies (nets, insecticide and supplements) so that all are available for distribution at the appropriate time. At the present time, supplies are procured from different channels. ITNs are generally procured directly either from a supplier in-country or internationally. Vitamin A supplements are generally supplied by the Ministry of Health or UNICEF. This may change as the National Malaria Control Programme of the Ministry of Health & Population in Malawi becomes more involved with the procurement and distribution of ITNs. This would streamline the procedure for ITN and VAC supplies even further. However, the distribution level of both, once procured, is generally the same, involving working through health workers and volunteers at the district and community level. Workload can be reduced by providing the distribution of ITNs, retreatment and VAC together as it is usually the same health workers involved, even when the programs have been traditionally operated separately (or "complementary"). The most effective strategy for distribution at the community level would involve using front-line workers (such as Health Surveillance Assistants in Malawi) and community health volunteers as "agents". These agents would promote the health benefits of ITNs and VAC, identify beneficiaries and assist with the distribution. Sale and distribution could be combined with community Drug Revolving Funds (DRFs), often coordinated by these same community-level health workers and volunteers.

ITNs/retreatment and micronutrient supplementation can be combined for community-level distribution on a house-to-house basis, during local "market days", or through periodic "Health Days". A combination of these approaches may be most effective. A community "Health Day", where education is provided through drama, songs and stories, ITNs and net retreatment kits are sold, mass dipping of nets is performed and VACs are distributed, can take place on set days throughout the year. In Malawi, sales would best take place, for reasons stated previously, during the June/July harvest time and again six

months later during the December/January rainy season. Alternatively, sales and distribution can take place during the regular market day in the community, which is usually held once a week (daily in larger centres). This provides a central gathering point for the local community and sales of essential household items, clothes and food. These approaches can be complemented with house-to-house visits by health volunteers to identify those who did not, or were unable to, take part in the "Health Day" or market day activities. These strategies should ensure coverage of an increased proportion of the target population. It may be easier to mobilize the community, and especially the vulnerable population, when a "free" service is being provided, namely the provision of free vitamin supplements, particularly if adequate and appropriate promotional activities are carried out beforehand. This may provide an added incentive to participate for some who would not otherwise attend.

With successful implementation of the integrated approach, alternative distribution strategies such as those described for weekly supplementation of micronutrients can be explored. A daily micronutrient supplement could not likely be efficiently linked to a once or twice yearly net retreatment program due to the large quantities of supplements required. However, there is potential for linking a weekly supplementation regime with the retreatment (e.g. 25 tablets every 6 months or 50 tablets once yearly).

6.3 Supervision and Training:

As it is generally the same health workers who are involved in health programming, whether it is for ITNs or micronutrients, integration presents a more efficient process of supervision. Integration would allow for the development of a training program directed at the various cadres of health personnel that addresses the combined strategies. Supervisory visits, at the central, district or community level can take advantage of this linkage with the result likely being a more efficient and cost-effective health service. A supervisory tool that can be applied at various levels, such as a checklist for managers, should be developed which would allow the easy collection of necessary information for both ITNs and VAC.

An appropriate, country-specific training manual should be developed that combines some of the existing information for ITN and vitamin A programs, streamlined into one document. By conducting the training in one program, efficiency of both programs will be improved. Resources and time for training in the setting of a developing country like Malawi is an often cited constraint to effective programming.

6.4 Monitoring and Evaluation:

Baseline data can be collected on both interventions (ITNs and vitamin A) at the same time through the application of a combined survey tool. This can be adapted to include the collection of data related to other micronutrients like zinc and iron if needed and applied at specified points throughout the life of the project (mid-term, end of project). A monthly monitoring form which combines the necessary process indicators for ITNs and vitamin A will be developed from existing forms presently in use. If morbidity data are

needed for illness related to malaria and vitamin A deficiency, this can be collected together through various means, including the household level through regularly administered "morbidity recall" surveys, village level through collection of statistics by a village health committee or volunteer, or at the health centre level by the health care worker. Corroborating blood/serum evidence such as parasitemia rates or vitamin A levels can be collected at the same time.

Mortality data is often difficult to collect as many deaths occur at the village level and there is no system presently in place for the village-level collection of vital statistics. The Malawi MOHP is currently conducting pilot testing of a vital statistics registration form by village headmen in Nkhata Bay District.

6.5 Administration:

From an administration standpoint, combination of two existing separate programs should streamline activities. This should result in fewer staff positions required, for the same coverage, or the ability to provide more "service" with the existing staff. Combining IEC, Promotion, Mobilisation, Procurement, Distribution, Monitoring, Supervision and Training should result in one staff member being able to perform duties in one or more of these key areas for both ITNs and micronutrients at the same time. For example, one person should be able to look after procurement and distribution of ITNs, insecticide and micronutrient supplements at the same time rather than requiring someone to distribute ITNs on one day and another person to distribute VACs on another. With IEC being combined, one person can cover both areas during the same session to the same target group, rather than having "malaria messages" on one day, in one location and "micronutrient messages" on another. If the same monitoring form is being used for the collection of process indicators and supervision for both ITNs and VAC then this will obviously result in fewer "person-hours" being required. Altogether, this should result in a more efficient and cost-effective system.

Transportation is often a limiting factor in the successful implementation of community health programs in the developing world. In Malawi, resources devoted to the operating, maintenance and hiring of vehicles are often disproportionate to other aspects of a program. Combining activities for ITNs and micronutrients should relieve a portion of the transportation resources for other purposes.

6.6 Addressing the Affordability of ITNs:

ITNs are usually more available to the "middle class", those more "well-to-do" as opposed to the "really needy", due to the cost-recovery component (this does not apply to VACs which are generally free). One Malawi ITN survey found that, in the impact area, approximately half of the households owned a bike and/or a radio (“upper class”) and half did not (“lower class”). Seventy-five percent of net sales had gone to the "upper class" and 25% to the "lower class” [CPAR, 2000]. Innovative methods need to be devised in order to make the ITNs and retreatment more affordable to those that are the most needy, and this has been a constant constraint across programs as evinced by the

presentation in Chapter 5. A workshop to discuss plans for ITN/VAC integration was held in Malawi during February, 2000 [CPAR, 2000]. Some ideas with regard to targeting and coverage among the poorer households included:

1. Subsidy - either from source (donor) or at the community level through price differential and market segregation (like PSI program).

2. Credit basis - establish a committee at the community level to administer a credit scheme.

3. "Net-for-Work" - CPAR has experience with a Food-for-Work program in Malawi. It is usually the "poorest of the poor" who participate in this type of program. Perhaps the "work" involved, which will lead to the acquisition of the ITN, could in some way be linked to malaria control (environmental strategies) or nutrition (community gardens, planting of seedlings).

4. Community IGAs - Micro-enterprise and Savings schemes, once again linked to malaria control or (more likely) nutrition, such as community gardens through women's farmers groups. Communities could carry out a wealth ranking exercise, using Participatory Rapid Appraisal (PRA), with appropriate assistance, to ensure community input into the choosing of needy households.

5. Church Groups - Churches and local prayer houses have a history of working with the poor and helping the poor in their community. Communities could take advantage of this and have churches identify and then assist the poor in their congregation to procure ITNs.

7 Opportunities for VAC/ITN Integration:

The most obvious opportunities for VAC and ITN program integration exist in regions where there is co-occurrence of VAD and malaria (discussed in detail below). However, while co-occurrence would be an initial and necessary criterion, there are other criteria to consider in programming decisions. Ideally, the initiation of VAC/ITN integration would take place where separate programs are already successfully operating, and the integration would add to the efficiency of the programs. In practice, programmers will more often be working to strengthen existing VAC (or ITN) programs, and adding on an ITN (or VAC) component. At least initially (in the coming few years while the best practices for VAC/ITN integration are being field tested), it probably is not advisable to launch an integrated VAC/ITN program when there is no experience with either program areas. Other issues to consider:

- Is VAC distribution consistent with the current national health policy?
- Is ITN distribution and retreatment consistent with the current national health policy?
- What are the current means of VAC distribution? Is VAC distribution currently an add on to NIDs (which may soon be phased out, and thus a complete replacement distribution mechanism is required), a stand alone "micronutrient day" or "child health day" which may be complemented by ITN integration, through some other form of massive campaign, or through special community level outreach?
- Seasonality: Are there annual fluctuations in VAD (often peaks pre-harvest)? malaria (peak in rainy season)? income (peak post-harvest)?, time available for attending retreatment clinics or health campaigns (greater availability in the off season)? accessibility to children (related to school year)?

7.1 Geographical Co-occurrence of VAD and Malaria.

7.1.1 Global

Malaria and vitamin A deficiency are public health problems in much of Africa, Asia and Latin America and the Caribbean. Prevalence data for malaria are incomplete. The highest malaria prevalence, measured in attack rates per month of exposure on no prophylaxis, is found in regions of Irian Jaya (20%). Solomon Islands and Vanuatu (~ 8%) are also very high. Sub-Saharan and West Africa (~2.4%), and East Africa (~1.5%) also have significant health problems, while the rates are lower in the Indian subcontinent (~1/1000) and South and Central America (~1/10,000) [Kain and Keystone, 1998; Fryauff et al., 1998; dos Santos et al., 1999; Steffen, 1991; K. Kain, pers comm, March 2000]. More detailed (i.e., geographically specific) estimates of numbers and proportion of population *at risk* of malaria in Africa have recently been provided by MARA (Mapping malaria risk in Africa - http://www.mrc.ac.za/mara/), detailed at about the scale of 5km by 5km. These estimates are developed from models incorporating climatic (temperature, rainfall) and geographic (latitude, altitude, topography, forest cover) data to predict the suitability of the habitat for malaria transmission. While the underlying algorithm was developed using malaria prevalence data, and the model is thought to be

fairly accurate, it has not been validated for all of Africa. For making public health programming decisions, it is sufficiently accurate. Similar models are not available for outside of Africa.

Estimates of the prevalence of VAD in children (less than 5 years of age) have been generated for most countries in the world in 1995, using either national surveys, extrapolating from sub-national surveys, or using a predictive equation based on prevalence of underweight, and infant mortality rate (see footnote 1). The prevalence of VAD is high throughout Africa and South Asia (clinical ~1%, subclinical ~20%). In the Middle East and North Africa, East Asia and the Pacific, and Latin America and the Caribbean, the prevalence of VAD is lower (clinical ~0.25%, subclinical ~9%). There is marked variation within the countries within these regions, with a high in Afghanistan of 5.2% (clinical), and a low of 0.1% in numerous countries [MI/Tulane/UNICEF, 1998].

The relationship between malaria risk and VAD in children of sub-Saharan Africa is depicted in Figures 1 and 2. Each point on the graph represents an African country. Figure 1 presents the *proportion* of children; Figure 2 presents the *absolute number* of children, reflecting the total country-level burden of illness (Nigeria, an outlier with more than twice as many children at risk as any other country, is left off of Figure 2). Note that in Africa, at a national level, almost every country has such a high risk of malaria and high VAD that public health interventions are called for. At a subnational level, though, there are specific areas where VAD and malaria deviate from the national average. The regions are estimated with accuracy for malaria risk, but not as well documented for VAD, with only a handful of countries providing subnational VAD data. In general, the prevalence of subclinical VAD varies no more than two-fold from the highest to the lowest region within a country [John Mason, personal communication, March 2000]. Even without existing subnational data, a nutritionist knowledgeable of a country's general health and food security disparity would be able to identify regions within the country that would have VAD prevalence higher or lower than the national estimate. One could even use the algorithm for predicted VAD based on prevalence of underweight and IMR. This has not been tested, but it is reasonable to expect the relationship to hold – at least approximately – at a subnational level. In most cases, the accuracy of the

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1 $\ln(1/p - 1) = 7.23 - (0.0216 * IMR) - (0.0131 * \%\ underweight)$, where p = prevalence of VAD. Micronutrient Initiative/Tulane/UNICEF, 1998, progress in Controlling Vitamin A Deficiency. MI:Ottawa

2 All malaria data from http://www.mrc.ac.za/mara/ and all VAD data from MI/Tulane/UNICEF, 1998.

prediction would not be limited by the strength of the algorithm, but the existence of reliable subnational data [John Mason, personal communication, March 2000].

7.1.2 Malawi

At the present time, good data on malaria prevalence and vitamin A deficiency do not exist on a District level, although there have been surveys carried out in various areas of the country. However, taking the prediction of populations at risk of malaria from the MARA data bank and using estimates of VAD by regional breakdown, rough mapping of the co-occurrence of the two in Malawi can be done (see figure 3). As can be seen, there are very few parts of the country not considered at high risk for malaria, mainly the areas of highest elevation. Among areas where VAD surveys have been done, Dedza lies in the lowest risk malaria area.

There are plans for a full Demographic and Health Survey (DHS) to be carried out in Malawi later this year. This DHS is being organised in such a way that reliable and valid data will be collected which will allow for analysis to be done at a District level. The Ministry of Health & Population in Malawi is in the process of decentralizing much of the health service in the country and most decisions with regard to health delivery will be made by the District Health Officer (DHO) at the District level. Once the District level data are available, we will be able to apply the VAD algorithm and get a better idea of the sub-national distribution of the co-occurrence of VAD and malaria prevalence in the country. In the meantime, public health needs are obvious with regard to addressing the problem of malaria and micronutrient deficiency in Malawi and action will be taken toward the integration of programmes as described in this review.

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Figure 1. Magnitude of VAD and Malaria Risk in African Children (under 5 years), by Country

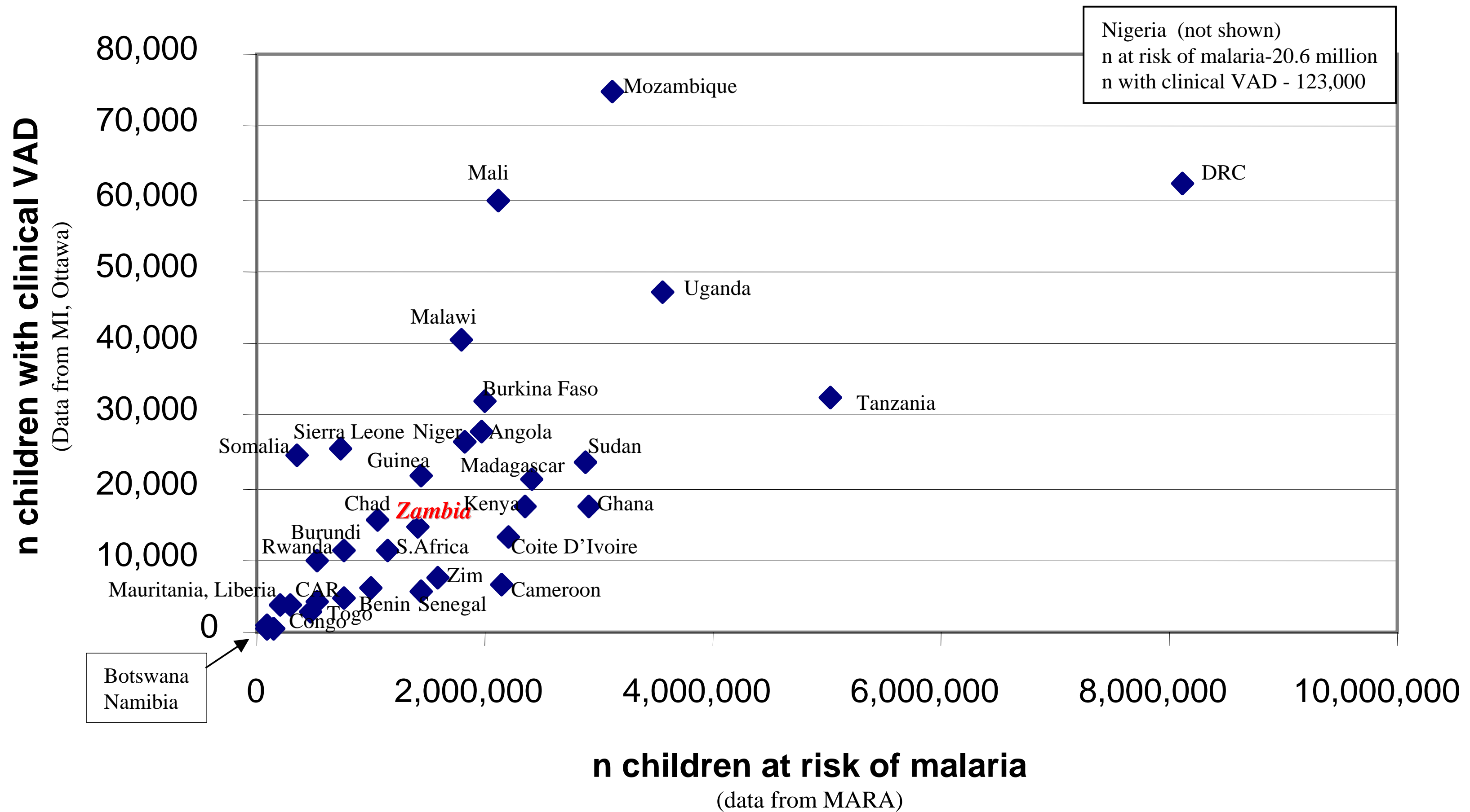

Figure 2. Proportion of VAD and Malaria Risk in African Children (under five years), by Country

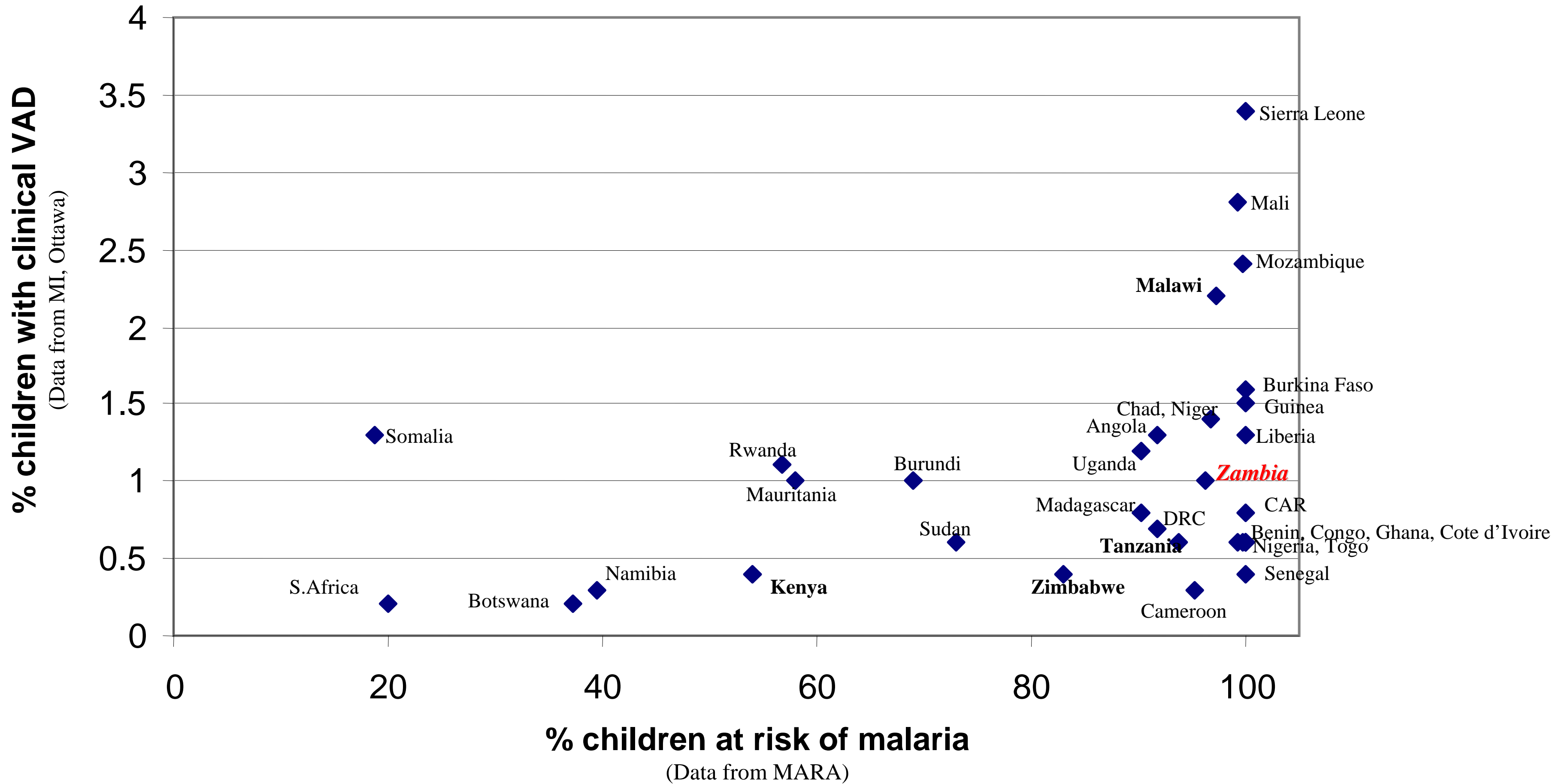

Figure 3. VAD and risk of malaria in children in Malawi.
Shaded areas represent areas of Malawi where risk of malaria is low, other areas all high risk (www..mrc.ac.za/maramap). Percentages represent total VAD (X1B+NB) =1% (references in text)