



WORLD HEALTH ORGANIZATION



Executive Summary of a scientific review

Consultation on Nutrition and HIV/AIDS in Africa:
Evidence, lessons and recommendations for action

Durban, South Africa
10–13 April 2005



Interim version

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World Health Organization
Department of Nutrition for Health and Development

NUTRITION AND HIV/AIDS

Executive Summary

1. Introduction

More than 40 million people are living with HIV/AIDS worldwide and their number is rising. Between 2002 and 2010, an estimated additional 45 million people may become infected with HIV in 126 low- and middle-income countries if adequate prevention efforts are not implemented. Sub-Saharan Africa is hardest hit; nearly 30 million adults and children had HIV/AIDS in 2004. The world's highest HIV infection rates are found in southern Africa, where adult prevalence in most countries exceeds 25% and food shortages and malnutrition have combined with HIV/AIDS to bring some countries to the brink of crisis.

Malnutrition rates are increasing in the African region. Furthermore, food is often identified as the most immediate and critical need by people living with HIV/AIDS and others affected by the pandemic. African governments are currently grappling with a range of programme and policy challenges related to food, nutrition and HIV/AIDS.

It is against this backdrop of rising infection rates, unabated malnutrition and the need to formulate evidence-based recommendations that the World Health Organization (WHO) undertook the current review of nutrition and HIV/AIDS. The review was conducted under the direction of the WHO Technical Advisory Group on Nutrition and HIV/AIDS (TAG).

The purpose of the six review papers is to summarize the existing knowledge base and identify gaps in available evidence related to the complexities of the relationship between nutrition and HIV infection.

This executive summary provides a synopsis of the content of the larger review. In preparing this summary, we have attempted to summarize the key findings and knowledge gaps identified in the six scientific review papers and, where appropriate, the relevant WHO recommendations. The summary emphasizes those issues that are relevant to programme and policy actions in resource-limited settings. The key findings will be discussed at the Consultation on Nutrition and HIV/AIDS in Africa, in Durban, South Africa, 10-13 April 2005. WHO will finalize a consensus statement and recommendations for immediate action and implementation by countries.

2. Conceptual Framework

There are complex interactions between nutrition and HIV/AIDS. HIV progressively weakens the immune system and malnutrition itself may also increase the susceptibility to infections. Those who are ill from HIV infection, from poor nutrition or both are less able to find work or food to sustain themselves. In many areas of the developing world, HIV infection co-

exists with malnutrition (both in terms of macronutrient malnutrition (i.e. protein-energy malnutrition) and the hidden hunger of micronutrient deficiencies).

A fundamental goal in unraveling the interactions between nutrition and HIV infection is to determine the points of distinction among the effects of malnutrition, the unique complications of HIV infection, its treatment, and the potential areas of overlap and interaction. Of particular interest is whether nutritional supplementation (food or micronutrient supplementation) can delay or defer the point at which ARV treatment is required. In order to unravel these complex interactions WHO commissioned a series of reviews to examine six key areas related to HIV and nutrition. Core questions addressed in the review are:

- What is the impact of HIV/AIDS on the nutritional status of infected and affected adults and children?
- What is the potential impact of poor nutritional status on susceptibility to, progression of and treatment of HIV/AIDS?
- What is the impact of poor nutritional status on prevention, care and treatment of HIV-associated opportunistic infections (OI), e.g. TB, diarrhoeal diseases?
- What are the nutritional needs of people infected with HIV over and above those required by uninfected people?

The reviews were underpinned by the principle that nutritional support is an integral part of a comprehensive response to HIV/AIDS, but nutritional support of any kind cannot serve as a substitute for antiretroviral therapy. The focus on nutrition derives from the concern to determine what additional nutritional elements are required to be considered in the rapid scale up ART in high burden countries.

The technical report is divided into three major sections:

Section I covers knowledge about macronutrients and micronutrients.

Section II covers knowledge about nutritional needs and includes issues on infant feeding and HIV transmission, growth failure in HIV-infected children and nutrition of pregnant and lactating women.

Section III includes a review of current knowledge about the effect of ART on nutrition, metabolism, growth and development.

Section I

3. Macronutrients

Key Findings:

- Weight loss in adults and growth failure in children are common in HIV/AIDS infected children and adults.
- Resting energy expenditure is increased by around 10% in asymptomatic HIV-infected adults and children.
- An additional 20–50% increase in energy needs occurs during the convalescent catch-up period after a severe infection in both adults and children.
- These targets should be achieved through food-based approaches whenever possible.
- There is no evidence for increased protein requirement over and above that required in a balanced diet to satisfy the total energy requirements (12 to 15% of the total energy intake).

Evidence Base:

The energy deficit in patients with HIV/AIDS results from the direct effect of HIV, other opportunistic infections and reduced dietary intake; malabsorption; increased energy expenditure; and abnormal use of substrates, including protein. Aside from the impact of food insecurity, reduction in nutrient intake due to anorexia is one cause of weight loss in HIV-infected patients. In addition, malabsorption of high-energy substances, including fat, especially in adults may also be a contributing factor. Anorexia decreases once effective ART is started and established, thus adequate dietary intake is needed to support patient recovery and weight maintenance. Overall health, weight maintenance and nutritional status may be improved by the use of a balanced diet, regular exercise.

Knowledge Gaps:

- Identification of locally appropriate, sustainable ways of increasing dietary intake to meet the additional energy needs of HIV-infected adults and children.
- An urgent need to develop and evaluate macronutrient supplementation for the improvement of the nutritional status for infected HIV people and the potential impact of nutritional supplementation on delaying the initiation of ART.
- Evaluation of the impact of specific nutritional interventions for management of HIV-infected patients experiencing severe infectious complications.

- Identification of simple practical ways to assess nutritional status and related outcomes in patients with HIV/AIDS before and during treatment with particular reference to resource-limited settings.
- Understanding whether or how to modify established protocols for moderately and severely malnourished adults and children who are HIV-infected.

4. Micronutrients (MN)

Key Findings:

- Screening for nutritional status and assessment of dietary intake should be included routinely in HIV treatment and care for adults and children.
- Consistent limitations in study design have limited our understanding on the exact nature of the HIV–MN relationship; any policy recommendations should be based on consensus statements derived from several trials.
- Current evidence is inconclusive about the effects of micronutrient supplementation on transmission and progression of HIV infection and as for all populations, the access to and intake of a diet that provides the full range of essential MN is a critical component of health for people infected and affected by HIV/AIDS.
- Evidence from randomized-clinical trials in HIV-infected children concur with studies in non-HIV-infected subjects that large-dose of vitamin A (a single large dose of 50 000 UI before 6 months; a single dose of 100,000 UI between 6 and 11 months; a single dose of 200 000 UI every six months from 12 months onward) supplementation reduces diarrhoeal morbidity and mortality and all-cause mortality in severely vitamin A–deficient children younger than five years of age.
- Efforts to maintain adequate intakes (1 Recommended Nutrient Intake (RNI)) of all essential vitamins and minerals must remain a major emphasis of the public health programmes irrespective of HIV status and particularly in areas where both malnutrition and HIV infection are endemic.
- In areas where specific MN deficiencies are endemic, efforts should be directed to make those nutrients available for all people irrespective of the HIV status by ensuring access to a diversified diet, fortified foods and micronutrient supplements as appropriate.

Evidence Base:

The review confirmed the potential role of MN in HIV infection and vice versa. In addition to reviewing data on interactions between HIV infection and MN status, key methodological requirements of conducting such studies and a critical review of published intervention trials within that context were discussed. Examples of limitations in study design that have presented obstacles to understanding the role of MN in HIV infection included lack of baseline assessments of the nutritional status in intervention trials; lack of attention to confounding conditions, including active infections and the consequent acute phase response affecting measurement and interpretation of biochemical assessments; lack of appropriate control groups (e.g. HIV-negative samples in areas of endemic malnutrition); and reliance on non-specific outcomes (e.g. weight gain, global measures of immune function). The combination of the latter two issues limits our ability to generalize research results or to ascribe findings to an HIV-specific effect rather than a generalized amelioration of a nutritional deficiency. Consequently, it becomes difficult to advocate for an equitable intervention in settings where HIV and chronic widespread malnutrition coexist.

With regard to the impact of MN on HIV transmission, results from one randomized clinical trial indicated that supplementation with preformed vitamin A and β -carotene increased mother-to-child HIV transmission, but two other vitamin A trials found no evidence of adverse effects. Another study showed that supplementing pregnant and lactating women with high doses of a range of B vitamins, vitamin C and vitamin E reduced postnatal mother-to-child HIV transmission in the subgroup of women who were most nutritionally and immunologically compromised. Because vitamin A is an essential nutrient and vitamin A deficiency is widespread in resource-limited settings where HIV is most prevalent, there is a need to evaluate the safety of vitamin A supplementation for HIV infected adults and children. This information is essential to ensure that the global commitment to combat vitamin A deficiency may be continued without the risk of increasing mother-to-child HIV transmission.

Few studies showed that a daily supplementation may reduce HIV disease progression and mortality among adults. However, studies had methodological flaws and were subject to different interpretations. Furthermore, the protocol was different between the studies. Much of the evidence for the potential effect of multivitamin and individual mineral supplements came from a series of studies in Tanzania. Data indicated that a daily high-dose multivitamin supplement may not only reduce adverse pregnancy outcomes and mother-to-child transmission but also reduces the progression of HIV but not time to death. It is not clear whether the findings can be generalized to other populations such as HIV-infected women who are not pregnant, men and children with HIV, patients with concomitant tuberculosis and patients receiving ART.

Paramount among the concerns about this trial is that the regimen used consisted of an array of vitamins given at doses well beyond standard recommendations for pregnant women. Baseline data on the status of these women for many of the nutrients evaluated were lacking. The lack of an HIV-negative control group did not allow for the determination of an HIV-specific effect because the outcomes—CD4+ and CD8+ counts, morbidity and mortality—are all similarly affected by MN status in HIV-uninfected populations.

Specific suggestions regarding micronutrient supplementation for HIV-infected adults and children in addition to those advocated for the HIV-negative population are outlined in WHO document (Nutrient requirements for PLWHA - report of a technical consultation, May, 2003).

Knowledge Gaps:

- The safety and efficacy of specific micronutrient (MN) supplementation in HIV-infected adults and children need to be determined.
- Nutritional assessment methodologies are needed that can be effectively utilized and adapted to the various programme and service delivery models found in resource limited settings in order to tailor micronutrient interventions related to the prevention, care, and treatment of HIV/AIDS.

SECTION II

5. Infant Feeding and HIV Transmission

Key Findings:

- The overall risk of mother-to-child HIV transmission by a nonbreastfeeding mother is 15–25% (without interventions to reduce transmission) and of a breastfeeding mother is 20–45%.
- The most effective intervention for reducing HIV transmission is through the use of ARV prophylaxis in a PMTCT programme which should include access to ART when indicated.
- Because human milk can transmit HIV at any time during lactation, the rate of HIV-infection in breastfed infants is cumulative and increases with duration of breastfeeding.
- Clinical or sub-clinical mastitis is associated with HIV transmission risk.
- To reduce the risk of HIV transmission, HIV-positive mothers are advised to avoid all breastfeeding and use replacement feeding when it is acceptable, feasible, affordable, sustainable and safe to do so. Otherwise, exclusive breastfeeding is recommended during the first months of life and should then be discontinued as soon as it is feasible and replacement feeding can be provided safely.
- Early breastfeeding cessation is recommended for HIV-infected mothers as soon as replacement feeding becomes acceptable, accessible, feasible, affordable, sustainable and safe.

- Support is needed to ensure adequate nutrition and care during and after early breastfeeding cessation. When suitable replacement foods are hard to obtain, early cessation may increase malnutrition in infants and young children; malnutrition significantly increases the risk of child mortality from infectious diseases.
- New guidelines for feeding the non-breastfed child after six months are now available from WHO. The Global Strategy for Infant and Young Child Feeding, adopted by WHO and the United Nations Children's Fund, contains specific recommendations for children in exceptionally difficult circumstances, including those born to HIV-positive women, and continues to be the best source of advice.
- In making the right choice women should receive counselling, including general information about the risks and benefits of the various infant-feeding options and specific guidance in selecting the option most likely to suit their circumstances. The mother's choice should always be respected and supported.
- The guidance also recommends that women have access to follow-up care and support, including family planning and nutritional support.

Evidence Base:

An individual patient meta-analysis, conducted as part of the Breastfeeding and HIV International Transmission Study (BHITS), estimated that the cumulative probability of late postnatal transmission between four weeks and 18 months of age was 9.3%, or about 8.9% of HIV infections per 100 child-years of breastfeeding, and that the risk of transmission was constant throughout breastfeeding. In this meta-analysis, approximately 42% of all HIV infections were attributable to breastfeeding beyond four weeks of age.

A strong association was observed in BHITS between the risk of postnatal infection after four weeks of age and maternal CD4⁺ cell count: the transmission risk was eight times greater at counts less than 200 x 10⁶ cells/L and 3.5 times greater at counts between 200 and 500 x 10⁶ cells/L compared with the reference group of mothers with CD4⁺ cell count greater than 500 x 10⁶ cells/L. Low plasma CD4⁺ counts have been associated with detection of HIV DNA in breast milk.

Clinical or sub-clinical mastitis is associated with HIV transmission risk. Sub-clinical mastitis, probably commoner than clinical mastitis, is not necessarily an infection and may occur with milk stasis and breast engorgement. It may be associated with increased milk RNA load and cytokines. Mastitis is more likely to occur when the milk first arrives after birth, with inadequate milk drainage as well as mixed feeding, with poor attachment or weak suckling by an ill infant and with rapid weaning.

Maternal nutritional status may influence the risk of transmission overall and during breastfeeding. Early observational studies reported that mothers with low serum retinol levels were more likely to transmit HIV to their infants. This observation led to the implementation of several clinical trials in Africa on the effect of vitamin A supplementation with or without other micronutrients on mother-to-child HIV transmission.

The results of these studies have varied and are reported in greater detail in the micronutrient paper. In a recent study from Zimbabwe, single, high-dose postpartum vitamin A supplementation had no effect on postnatal HIV transmission risk. Maternal mid-upper-arm circumference (MUAC), however, was associated with a significantly reduced risk of HIV transmission during breastfeeding, after maternal immune status and other feeding and health variables were taken into account. Furthermore, severe maternal anaemia (hemoglobin < 70 g/L), although uncommon, was associated with a nearly 7-fold increased adjusted risk of postnatal HIV transmission from six weeks to six months of age.

The same study in Zimbabwe confirmed earlier reports indicating that risk of breastfeeding-associated HIV transmission increased with early mixed breastfeeding compared with early exclusive breastfeeding. The protective effects of early exclusive breastfeeding were greatest in the first six months yet continued throughout the 18-month follow-up period. Studies are under way to confirm these findings.

Studies are also underway to examine the safety and efficacy of different prophylactic ART regimens given to HIV-exposed infants or their HIV-positive breastfeeding mothers. No data have been published yet. Finding effective means for preventing HIV transmission during breastfeeding with appropriate interventions is an urgent priority in resource-limited settings.

Any infant feeding recommendation made needs to balance the risks of transmission of HIV infection through breastfeeding with the benefits of exclusive breastfeeding and the risks of not breastfeeding. Feeding options include breastfeeding cessation, wet nursing, use of milk banks and the potential treatment of human milk.

Knowledge Gaps:

- Whether treatment of mastitis reduces the rate of transmission at the population level is still a subject of research.
- The specific role of maternal malnutrition in HIV transmission via human milk remains to be determined.
- Data are limited on the effect of early breastfeeding cessation on infant nutrition, health and HIV-free survival.
- Finding effective means of preventing HIV transmission during breastfeeding with appropriate interventions is an urgent priority in resource-limited settings.

6. Growth Abnormalities in HIV-infected Children

Key Findings:

- Poor growth, including intrauterine growth retardation, is common in children born to HIV-positive mothers.
- Although some evidence suggests that fetal HIV infection affects fetal growth, few data show differences in birth size between HIV-infected and uninfected newborns of infected mothers.
- Although estimates of growth failure vary by study population and according to the criteria used, it is apparent that poor growth, particularly impaired statural (height) growth, has a significant adverse effect on survival independent of the degree of immune deficiency in HIV-infected children.
- Disturbances in growth are detectable well before the onset of opportunistic infections or other manifestations of HIV disease progression.
- Studies conducted in Europe and the United States show that compromised statural growth is a better indicator of disease progression in HIV-infected children than weight-based criteria.
- Traditional risk factors in non-HIV-infected children such as insufficient food intake and diarrhoea also are major contributors to poor growth in HIV-infected children and may be especially important in resource-limited settings.
- Based on the currently available evidence in children not receiving ART, energy supplementation alone improves weight gain but does not reverse deficits in height.
- Prevention, early detection and treatment of diarrhoeal and other common illnesses may be effective approaches for enhancing growth and survival in HIV-infected children together with ART when clinically indicated.
- ART when clinically indicated improves weight, growth and development, but may not totally reverse abnormalities.
- Assessments of dietary intake, anthropometry (weight, height, regional adiposity) and biochemistry where available and feasible, need to be incorporated into care and management programmes for children infected and affected by HIV.

Knowledge Base:

Whether maternal HIV per se has an independent effect on intrauterine growth apart from established obstetrical and nutritional factors is not certain. Many but not all studies report that infants born to HIV-positive mothers have significantly lower mean birth weight and length than do infants of HIV-negative mothers regardless of whether HIV transmission has occurred.

The cause of abnormal growth is multifactorial and in a given individual may involve most if not all the processes of nutrition. Growth faltering by age three to four months has been documented in studies performed in the United States of America, Europe and Africa. Height and weight impairment increases with age. High levels of stunting among children under five years are common in many countries irrespective of HIV status or exposure. Thus, in such settings it is not clear whether the documented growth deficits are due to HIV-specific effects; the more generalized effects of maternal, infant and child undernutrition; or both. Other factors associated with impaired growth in children include level of HIV replication and chronic diarrhoea.

Knowledge Gaps:

- Although studies conducted in the developed world show that compromised statural growth is a better indicator of disease progression in HIV-infected children than weight-based criteria, research is needed to determine whether this is the case for children living in resource limited settings where food insecurity and malnutrition is highly prevalent.
- The relative contribution of food and/or MN supplementation to address growth problems in HIV-infected children needs to be determined.
- Developmentally sensitive indices of nutritional assessment (both dietary intake and biochemical indices) need to be developed for resource-limited settings.

7. HIV and Nutrition: Pregnant and Lactating Women

Key Findings:

- Anthropometric measures were reported to decline with increasing viral load and decreasing CD4+ cell count in HIV-infected pregnant women.
- The rates of weight gain reported in HIV-positive mothers, however, are consistent with the weight gains in undernourished pregnant women in developing countries.
- Change in weight is appropriate for identifying women at nutritional risk and in need of intervention irrespective of HIV status.

- The few studies comparing HIV-positive and -negative breastfeeding women observed no difference in body composition changes between groups.
- Although some evidence indicates a high proportion of HIV-infected pregnant women have low or deficient levels of folic acid, albumin and vitamin A and that these are associated with increased viral load and decreased CD4+ cell count, it is not clear whether these findings were the result of generalized malnutrition endemic to the areas where these women live or HIV-specific findings is not clear.
- The standard recommendations for giving nutrition support to pregnant and lactating women needs to be followed, irrespective of HIV status.

Evidence Base:

In terms of body compositional changes and related aspects of macronutrient status, little difference has been reported between HIV-positive and -negative women in terms of weight, body mass index, MUAC and triceps skinfold thickness measurements. However, in most studies reviewed, most of the women were at early stages of HIV infection. One study reported that HIV-positive pregnant women gained less weight in each trimester than did HIV-negative women and generally less than the average weight gain reported in presumed HIV-negative women in developed countries. No studies were identified that provided data on dietary intake.

Though the observed weight loss of HIV-infected women during lactation appears to be more than that observed in HIV-uninfected women, the loss of weight is similar to that seen in breastfeeding women throughout the world. Breastfeeding did not appear to increase maternal mortality, but increased rate of weight loss (> 1.0 kg/month) and advanced maternal disease were associated with increased risk in one study.

Estimating body composition of all HIV-positive individuals is important for determining appropriate nutrition interventions. Although advanced and sophisticated methods of measuring body composition are available and useful for research purposes, simple anthropometric measurements of height, weight, body mass index, MUAC and skinfold thicknesses at four sites (triceps, biceps and sub-scapular and suprailiac sites) are generally useful for monitoring adiposity during pregnancy and lactation. Anthropometry is inexpensive, reliable if the measurer is well-trained and feasible for both health facilities and fieldwork. Assessment of lean body mass is more complex and will require other types of measurements.

With regard to MN status, the literature review revealed a high proportion of women with low or deficient status of several nutrients including folic acid, vitamin A and iron. The reported poor status may be due to inadequate dietary intake resulting from a lack of access to a varied diet rich in micronutrients, lack of access to prenatal vitamin and mineral supplements or an HIV-specific anomaly that affects the processes of nutrition.

Maternal survival is of obvious importance to the mother but also for the survival of her children. Preliminary evidence, though scanty, suggests that an HIV-positive mother who is well nourished in both macronutrients and micronutrients is likely to have improved health and immune function as determined by CD4+ cell count and viral load. Therefore, determining the best way to optimize the nutritional status of HIV-positive women is essential.

Knowledge Gaps:

- The relative contribution of inadequate dietary intake (either from food insecurity or a metabolic complication of HIV infection and/or OI), lack of access to prenatal vitamin and mineral supplements, or an HIV-specific anomaly that affects the processes of nutrition, to the short- and long-term health of pregnant and lactating HIV-infected women remains to be determined.
- The impact of HIV infection on metabolism including endocrine response during pregnancy and lactation and potential impact on body composition, nutrition and health needs to be further defined.
- Operational research is needed on the delivery of comprehensive nutrition and health services to HIV-positive women to support maintenance and improvement of body composition and MN status.
- Dietary intake, body composition assessment need to be investigated and validated in HIV-infected pregnant and lactating women in resource limited settings.

SECTION III

8. Nutritional Considerations in the Use of ART in Resource-limited Settings

Key Findings:

- HIV-infected adults and children being considered for ART and while on ART need to be screened and assessed for nutritional problems: basic anthropometry and dietary assessment are appropriate.
- Documentation is needed of dietary supplement use including use of herbal and botanical therapies (that can potentially cause drug/supplement interactions which in turn affect the efficacy, safety and/or compliance with ART) and participation in government-sponsored food and/or micronutrient supplementation programmes.
- ART can reverse but not rectify the loss of body mass (including muscle mass) that results from HIV infection.

- Metabolic complications of long-term ART are documented in HIV-infected adults, infants and children include lipodystrophy, dyslipidaemia, insulin resistance, derangements in glucose tolerance, lacticacidaemia and mitochondrial toxicity, and problems with bone mineral metabolism.
- Risk estimates vary for lipodystrophy and the ART metabolic syndrome but there is a consensus that although nucleoside reverse-transcriptase inhibitors drugs (NRTIs) such as stavudine have also been implicated, protease inhibitors (PI) are the class of drugs most commonly associated with these effects.
- These effects appear in men, women, and children, and present risks in terms of adherence with ART protocols, long-term health and quality-of-life issues and increased risk of chronic diseases including cardiovascular disease and diabetes.
- Bone problems have been associated with ART in HIV-infected adults and children. However the implication and importance of this is yet unknown and at present this does not effect the current recommendation for selection of first and second level therapies in resource-limited settings.

Evidence Base:

ART has made a significant reduction in the prevalence of wasting, largely through the reduction in viral replication. The exact mechanisms of wasting are complex (e.g. reduced intake, increased resting energy expenditure mediated by factors such as cytokine or androgenic hormones, opportunistic infections) and remain to be fully understood, weight loss remains a problem even among people on ART and continues to be an important predictor in resource-constrained areas, of poor or failing response to therapy and mortality.

Resting energy expenditure is increased in HIV-infected patients but data on changes with highly active antiretroviral therapies (HAART) are mixed, with reports of decreased, increased and neutral effects of HAART on resting energy expenditure. Differences among studies may be secondary to differences in study populations e.g. stage of HIV infection, nutritional status, anorexia, or specific drugs used.

Although the use of ART has greatly improved the long-term outlook for HIV-infected adults and children, there are well documented long term complications in some patients. Metabolic complications documented in adults, infants and children include lipodystrophy, dyslipidaemia, insulin resistance, derangements in glucose tolerance, lacticacidaemia and mitochondrial toxicity, and problems with bone mineral metabolism. Much of the data is derived from studies in nutritionally replete HIV infected individuals, and it is not yet clear whether background malnutrition will increase the likelihood of these complications.

The prevalence of poor status of calcium and vitamin D and nutritional rickets associated with calcium and/or vitamin D deficiency is high in many areas where HIV has become endemic, including Africa. Vitamin D requirements independent of HIV status may be significantly higher in highly pigmented populations. There is some limited evidence indicating problems with calcium and vitamin D homeostasis in HIV-positive people before and during ART in industrialized countries. It is unclear whether these problems interact in any significant way and what sort of assessment and interventions may potentially be required.

Data addressing the potential interaction of ART with nutritional status during pregnancy and lactation are limited. However, the body of evidence about the metabolic consequences of ART—whether used for prophylaxis against prenatal and postnatal mother-to-child-transmission or for the long-term care of the HIV-positive mother—is sufficient justification for attention to nutritional status for both HIV-infected women and their children. Data on the effect of HIV on a mother's nutritional status or the status of her infant are limited. Furthermore, data are limited for evaluating the potential effect of ART on the nutritional needs of lactating women particularly in resource-limited settings where breastfeeding is the predominant mode of infant feeding.

Data are limited regarding the effect of ART on growth in infants and children and very little experience has been gained with ART in resource-limited settings to date. Because non-standard measurements have been used in large multicentre studies, pretreatment growth rates have not been routinely measured in clinical studies, studies have not had sufficient statistical power to detect changes in growth outcome, most studies excluded or had inadequate assessment of nutritional status including lack of biochemical and/or dietary intake data, and results of analyses of viral load (e.g. among responders versus nonresponders) have been inconsistent.

ART in children contributes to anomalies in lipid and carbohydrate metabolism, including lipodystrophy, dyslipidaemia, glucose intolerance and insulin insensitivity, similar to those seen in adults, although glucose intolerance and insulin insensitivity appear to be less of a problem in younger children. It has been suggested that although long-term monitoring of the HIV-infected children receiving ART would be necessary, no intervention—dietary or other—is warranted in the short term.

Knowledge Gaps:

- Only limited data exist about the prevalence of metabolic complications on long term use of ART in resource-limited settings and how best to manage them clinically; the impact of nutritional status upon these complications especially in those that are chronically undernourished needs to be established.
- Data are needed about the potential effect of ART on the nutritional needs of lactating women particularly in resource-limited settings where breastfeeding is the predominant mode of infant feeding.

- Evaluation of the potential impact of ART on growth and nutritional status of infected and uninfected infants born of HIV-infected mothers in areas where malnutrition is common is a high priority..
- Data are needed on the interaction between poor nutritional status of bone-related nutrients (calcium and vitamin D) and ART in resource-limited settings.
- Because of the potential long-term health consequences of the metabolic complications of ART, appropriate research is needed on potential management for lipodystrophy and related conditions (e.g. diet or lifestyle changes) in adults and children, particularly those in resource-limited settings.
- It is not yet clear whether nutritional supplementation can prevent or reduce the occurrence of long-term complication due to ART in adults or children.
- Evaluation of the impact of acute or chronic severe malnutrition in children on CD4 levels, response to ART or likelihood of ART side effects.