

Nutrient requirements for people living with HIV/AIDS

Report of a technical consultation



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Abbreviations and acronyms

AEE	Activity-related energy expenditure
AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral treatment
CD4	Main target cells for HIV, the number of which decreases during HIV infection
FAO	Food and Agriculture Organization of the United Nations
HIV	Human immunodeficiency virus
IAEA	International Atomic Energy Agency
IU	International units
PLWHA	People living with HIV/AIDS
RDA	Recommended daily allowance
REE	Resting energy expenditure
TAG	WHO Technical Advisory Group on Nutrition and HIV/AIDS
TEE	Total energy expenditure
UNAIDS	The Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Fund
WFP	World Food Programme
WHO	World Health Organization

Introduction

The objectives of WHO's first technical consultation on Nutrient Requirements for People Living with HIV/AIDS (PLWHA) (Geneva, 13–15 May 2003) were:

- to review the relationship between nutrition and HIV/AIDS infection;
- to review the scientific evidence on the role of nutrition in HIV transmission, disease progression and morbidity;
- to review recommendations related to nutritional requirements for PLWHA;
- to identify research priorities to support improved policies and programmes.

The consultation included members of the WHO Technical Advisory Group on Nutrition and HIV/AIDS¹ and 20 experts from a variety of disciplines and agencies, including universities, governmental and nongovernmental organizations, training institutions in countries highly affected by the HIV epidemic, and organizations of the United Nations system with food, nutrition and HIV programmes (see Annex A for list of participants).

To facilitate the discussions at the meeting, five background papers were prepared:

- the effects of HIV/AIDS on energy metabolism;

¹ WHO has established the Technical Advisory Group on Nutrition and HIV/AIDS as the principal international technical body responsible for making recommendations to the Director-General of WHO for appropriate action in national and international settings.

- micronutrients and HIV infection, current knowledge, methodological issues and research priorities;
- micronutrients and HIV-1 disease progression among adults and children;
- nutrition considerations in the use of antiretroviral drugs in resource-limited settings;
- the role of nutrition interventions in the prevention of HIV infection and progression of HIV/AIDS.

Key issues relating to nutrition and HIV/AIDS were presented and discussed in plenary (see Annex B for agenda of the meeting) based on three technical themes:

- nutrition, infection and HIV/AIDS;
- nutritional disorders in HIV infection and their implications for establishing dietary guidelines and recommendations;
- nutrition interventions and HIV.

On this basis, working groups sought to achieve consensus on macro-nutrient and micronutrient requirements for both asymptomatic and symptomatic PLWHA in the light of the following questions:

- What is the scientific evidence to support nutrition's role in disease prevention, and in the care and treatment of PLWHA, and is the evidence sufficient to formulate recommendations?
- What approaches can be effective in improving the health, nutrition and related outcomes in PLWHA?
- What are the critical gaps in knowledge?
- What additional research is needed?

Within this perspective, the needs of four target groups were considered:

- pregnant and lactating HIV-infected women;
- adolescents and other adults living with HIV;
- HIV-infected infants and children;
- HIV-exposed infants and children born to HIV-positive mothers.

Participants formulated conclusions and recommendations, which were further reviewed, consolidated and refined by the members of the WHO Technical Advisory Group (TAG).

Conclusions and recommendations

■ Adequate nutrition, which is best achieved through consumption of a balanced healthy diet, is vital for health and survival for all individuals regardless of HIV status.

The HIV/AIDS epidemic has had a devastating impact on health, nutrition, food security and overall socioeconomic development in countries that have been greatly affected by the disease. There is an urgent need for renewed focus on and use of resources for nutrition as a fundamental part of the comprehensive package of care at the country level.

Action and investment to improve the nutrition of PLWHA should be based on sound scientific evidence, local resources, and programmatic and clinical experience with the prevention, treatment, and management of the disease and related infections. Although there are gaps in scientific knowledge, much can and should be done to improve the health, nutrition and quality of care for PLWHA and their families and communities.

The HIV/AIDS epidemic is occurring in populations where malnutrition is already endemic. As an urgent priority, greater political, financial and technical support should be provided for improving dietary quality and increasing dietary intake to recommended levels. In addition, focused evidence-based nutrition interventions should be part of all national AIDS control and treatment programmes.

Nutrition counselling, care and support interventions for PLWHA will vary according to nutritional status and the extent of disease

progression (recommendations for specific nutrient requirements are given below). HIV-related infections, such as tuberculosis and diarrhoea, not only have nutritional status as a significant determinant of their incidence and severity, but they also have severe nutritional consequences that commonly precipitate appetite loss, weight loss and wasting. Prompt diagnosis and treatment of these conditions, including use of anti-retroviral treatment (ART) when indicated, can contribute to improved nutrition and health. Improved understanding of nutrition/drug interactions is needed to inform HIV/AIDS treatment programmes.

Macronutrients

Energy

- Energy requirements are likely to increase by 10% to maintain body weight and physical activity in asymptomatic HIV-infected adults, and growth in asymptomatic children.
- During symptomatic HIV, and subsequently during AIDS, energy requirements increase by approximately 20% to 30% to maintain adult body weight.
- Energy intakes need to be increased by 50% to 100% over normal requirements in children experiencing weight loss.

Adults

Studies point to low energy intake combined with increased energy demands due to HIV infection and related infections as the major driving forces behind HIV-related weight loss and wasting. Based on increased resting energy expenditure (REE) observed in studies of HIV-infected adults, it is recommended that energy be increased by 10% over accepted levels for otherwise healthy people. The goal is to maintain body weight in asymptomatic HIV-infected adults. Although studies of energy expenditure have not shown an increase in total energy expenditure (TEE), this may have been the result of individuals compensating by reducing activity-related energy expenditure (AEE). Since maintaining physical activity is highly desirable for preserving quality of life and maintaining muscle tissue, it is undesirable that energy intake should only match a reduced level of AEE. The estimated energy requirement

therefore allows for normal AEE levels on top of an increased level of REE.

Increased energy intake of about 20% to 30% is recommended for adults during periods of symptomatic disease or opportunistic infection to maintain body weight. This takes into account the increase in REE with HIV-related infections. However, such intakes may not be achievable during periods of acute infection or illness, and it has not been proven that such high intake levels can be safely achieved during such periods. Moreover, it is recognized that physical activity may be reduced during HIV-related infections and the recommended increased intake is based on the energy needed to support weight recovery during and after HIV-related illnesses. Intakes should therefore be increased to the extent possible during the recovery phase, aiming for the maximum achievable up to 30% above normal intake during the acute phase.

Children

There are few studies on energy expenditure in HIV-infected children. Energy requirements in children can vary according to the type and duration of HIV-related infections, and whether there is weight loss along with acute infection. Although the finding of increased resting energy expenditure in asymptomatic disease has not been replicated in children, similar to asymptomatic HIV-infected adults an average increase of 10% of energy intake is recommended to maintain growth. Based on clinical experience and existing guidelines to achieve catch-up growth in children irrespective of HIV status, energy intakes for HIV-infected children experiencing weight loss need to be increased by 50% to 100% over established requirements for otherwise healthy uninfected children.

Evidence to support specific recommendations for managing severe malnutrition in HIV-infected children is not yet available. In the absence of specific data with regard to HIV infection, existing WHO guidelines¹ should be followed. Research is needed on the specific energy requirements of HIV-infected children.

¹ *Management of severe malnutrition: a manual for physicians and other senior health workers*. Geneva, WHO, 1999.

Pregnant and lactating women

At present, there are no specific data on the impact of HIV/AIDS and related conditions on energy needs during pregnancy and lactation over and above those requirements already identified for non-infected women. For now, the recommended energy intake for HIV-infected adults should also apply to pregnant and lactating HIV-infected women.

Protein

- Data are insufficient to support an increase in protein requirements due to HIV infection.

There are insufficient data at present to support an increase in protein intake for PLWHA above normal requirements for health i.e. 12% to 15% of total energy intake. Participants were aware of the published nutritional guidance suggesting increased protein intake during HIV infection, but they concluded that these recommendations were not based on rigorously conducted studies.

Fat

- There is no evidence that fat requirements are different because of HIV infection.

There is no evidence that total fat needs are increased beyond normal requirements as a consequence of HIV infection. However, special advice regarding fat intake might be required for individuals undergoing anti-retroviral therapy or experiencing persistent diarrhoea.

Micronutrients

- To ensure micronutrient intakes at RDA levels, HIV-infected adults and children are encouraged to consume healthy diets.
- Nevertheless, dietary intake of micronutrients at RDA levels may not be sufficient to correct nutritional deficiencies in HIV-infected individuals.
- There is evidence that some micronutrient supplements, e.g. vitamin A, zinc and iron, can produce adverse outcomes in HIV-infected populations.

The role of micronutrients in immune function and infectious disease is well established. However, the specific role of individual and multiple micronutrients in the prevention, care and treatment of HIV infection and related conditions merits further attention. Several studies on micronutrients and HIV are under way, and new findings should be available soon.

Observational studies indicate that low blood levels and decreased dietary intakes of some micronutrients are associated with faster HIV disease progression and mortality, and increased risk of HIV transmission. However, these studies' methodological limitations preclude definitive conclusions about the relationship between micronutrient intake and blood levels, and HIV infection.

Some studies show that there is evidence that supplements of, for example, B-complex vitamins, and vitamins C and E, can improve immune status, prevent childhood diarrhoea and enhance pregnancy outcomes, including better maternal prenatal weight gain and a reduction of fetal death, preterm birth and low birth weight. The effect of these micronutrients on HIV disease progression and mortality is under study.

Micronutrients that have produced positive health outcomes in HIV-uninfected populations include zinc supplementation for reducing diarrhoea and pneumonia morbidity in children. The safety and effectiveness of zinc supplements in HIV-infected adults and children are now being studied.

Adults

HIV-infected adults and children should consume diets that ensure micronutrient intakes at RDA levels. However, this may not be sufficient

to correct nutritional deficiencies in HIV-infected individuals. Results from several studies raise concerns that some micronutrient supplements, e.g. vitamin A, zinc and iron, can produce adverse outcomes in HIV-infected populations. Safe upper limits for daily micronutrient intakes for PLWHA still need to be established.

Children

■ HIV-infected 6-59-month-old children living in resource-limited settings should receive periodic (every 4-6 months) vitamin A supplements (100 000 IU for infants 6 to 12 months and 200 000 IU for children >12 months). This level is consistent with current WHO recommendations for the prevention of vitamin A deficiency in children.

Periodic vitamin A supplementation has been shown to reduce all-cause mortality and diarrhoea morbidity in vitamin A-deficient children, including HIV-infected children. In keeping with WHO recommendations, 6 to 59-month-old children born to HIV-infected mothers living in resource-limited settings should receive periodic (every 4–6 months) vitamin A supplements (100 000 IU for infants 6 to 12 months and 200 000 IU for children >12 months). There is insufficient evidence at present to recommend an increased dose or frequency of vitamin A in HIV-infected children.

No data are available on the efficacy of other micronutrient supplements for HIV-infected children.

Pregnant and lactating women

Iron-folate supplementation

■ To prevent anaemia, WHO recommends daily iron-folate supplementation (400 µg of folate and 60 mg of iron) during six months of pregnancy, and to treat severe anaemia twice-daily supplements. Available data do not support a change in this recommendation for women living with HIV.

Iron-folate supplementation is a standard component of antenatal care for preventing anaemia and improving fetal iron stores. WHO recom-

mends daily iron-folate supplementation (400 µg of folate and 60 mg of iron) during six months of pregnancy to prevent anaemia, and twice-daily supplements to treat severe anaemia.

As with other chronic infections, HIV causes disturbances of iron metabolism and anaemia. In view of iron's potential adverse effects, for example due to its pro-oxidant activity, which might accelerate disease progression, research on the safety of iron supplementation in adults and children with HIV infection is recommended. Based on available evidence, however, the approach to caring for HIV-infected women is the same as that for uninfected women.

Vitamin A

- Daily vitamin A intake by HIV-infected women during pregnancy and lactation should not exceed the RDA.

According to published reports, daily antenatal and postnatal vitamin A supplementation for HIV-infected women in well-designed randomized controlled trials not only did not reduce mother-to-child HIV transmission; in some settings it actually increased the risk. Thus, daily vitamin A intake by HIV-infected women during pregnancy and lactation should not exceed the RDA.

In areas of endemic vitamin A deficiency, WHO recommends that a single high-dose of vitamin A (200 000 IU) be given to women as soon as possible after delivery, but no later than six weeks after delivery. Research is under way to assess further the effect of single-dose, post-partum vitamin A supplementation among HIV-infected women.

Multiple micronutrient supplements

- Adequate micronutrient intake is best achieved through an adequate diet. However, in settings where these intakes and status cannot be achieved, multiple micronutrient supplements may be needed in pregnancy and lactation. Pending additional information, micronutrient intakes at the RDA level are recommended for HIV-infected women during pregnancy and lactation.

Micronutrient deficiencies are common in resource-limited settings where HIV infection is prevalent. Some studies show that different multiple micronutrient supplements may have produced a broad range of beneficial outcomes. During pregnancy, daily multivitamin supplementation with multiple RDA levels of B-complex vitamins, and vitamins C and E, improved birth outcomes in infants born to HIV-infected women, and increased maternal weight gain during pregnancy, haemoglobin concentration and CD4 cell counts. Daily use of this multivitamin supplement during lactation reduced postnatal HIV transmission and mortality in infants born to nutritionally vulnerable women and to women with immune deficiency. The supplements also reduced the risk of diarrhoea and improved infants' immune status.

Another micronutrient supplement formulation, with single RDA nutrient levels, improved birth weights among infants born to HIV-infected women. The impact of single RDA multivitamin supplements on HIV disease progression and transmission, which was not assessed, requires further study.

Adequate micronutrient intake is best achieved through an adequate diet. However, in settings where these intakes and status cannot be achieved, multiple micronutrient supplements may be needed in pregnancy and lactation. Pending additional information, micronutrient intakes at the RDA level are recommended for HIV-infected women during pregnancy and lactation.

The optimal micronutrient supplement composition that will be safe, ensure nutritional adequacy, and potentially produce the greatest benefits in HIV-infected pregnant and lactating women in different settings has not yet been defined. Additional research is required to determine the safety of nutrient supplements such as zinc, iron and vitamin A, and to determine whether different multiple micronutrient supplements are needed for HIV-infected women compared with uninfected women.

Nutrition and antiretroviral therapy

- Improved attention to diet and nutrition may enhance ART acceptability, adherence and effectiveness.
- National health authorities should prepare for ART access by training relevant personnel on counselling and managing ART's long-term nutritional aspects.

The consultation addressed a number of metabolic complications associated with the use of certain types of ART, including derangement in glucose and lipid metabolism, bone metabolism and lactic acidemia documented in industrialized countries. The consultation emphasized the need for evidence to improve management of these metabolic abnormalities in patients receiving ART. Particular consideration was given to gaps in knowledge relating to ART use in populations where malnutrition is endemic.

ART is an essential component of care for PLWHA. Nutritional interventions should be an integral part of all HIV treatment programmes. Improved attention to diet and nutrition may enhance ART acceptability, adherence and effectiveness. Countries should prepare for ART access through training on how to manage ART's nutritional dimension. More research is needed on appropriate strategies for such counselling and management in resource-limited settings.

Knowledge gaps and research needs

- New knowledge is urgently needed to provide the scientific evidence base required for making nutrition recommendations for rapid implementation.

Considerable progress has been made in building an evidence base on nutrition's importance in improving prevention of the disease, and treatment and care among PLWHA. The recommendations made here underscore the urgent need to fill knowledge gaps and to refine further related conclusions and recommendations. While not exhaustive, the research questions that follow (not in order of priority) are considered crucial for improving understanding of the interaction of nutrition and HIV infection, and the impact of nutrition interventions on preventing

and managing HIV infection. The term “nutrition intervention” includes both food-based approaches and micronutrient supplementation.

Impact of HIV infection on nutrition

- What is the effect of HIV infection on macronutrient requirements, particularly protein and fat? Do energy requirements for PLWHA vary at different stages of the disease, or for subjects with opportunistic infections? Are energy requirements higher for HIV- infected children and pregnant and lactating women?
- What effect does HIV infection have on micronutrient requirements for children and adults? Does maternal HIV infection affect fetal endowment of nutrients and breast-milk composition?

Role of nutrition in HIV infection

- What are optimal energy and protein intake levels during metabolic stress? Is substrate use impaired and can an excess of energy and protein be harmful?
- What are optimal nutrient guidelines for patients with chronic diarrhoea or gastrointestinal infection?
- What are safe upper limits for nutrient intakes – especially zinc, iron, selenium and vitamin A – in PLWHA?
- What effect does nutritional status have on HIV? Does nutrition affect its virulence, resistance patterns and replication?
- What is the impact of poor nutritional status on susceptibility to and transmission of HIV-1 between adults, and from mother to child?
- What effect do different infant-feeding modes have on mother-to-child HIV transmission, and child growth, nutrition and development?
- What effect does nutritional intervention have on preventing opportunistic infections and slowing disease progression?

Nutrition and ART

- What is the impact of ART in malnourished populations? Does nutritional status affect the efficacy of therapy and the risk or severity of adverse events associated with it? Would nutrition

interventions – particularly in undernourished populations and lactating mothers – provided concurrently with ART result in better health outcomes?

- Are lifestyle changes, including dietary intake and physical activity, important for managing metabolic complications of ART? Should there be a different mix of such strategies in resource-limited settings where undernutrition is prevalent?

Operational research questions

- What are the effects of improved household food technology, dietary advice, and provision of food given during hospital and/or community care on nutritional recovery, disease progression and quality of life?
- Do rehabilitation protocols and approaches for managing severely malnourished children need to be modified in the light of HIV/AIDS?
- What should food and nutrition support programmes do differently because of HIV/AIDS? For example, should they change ration size or composition for HIV-affected populations? What are the criteria for targeting food to mitigate the effects of HIV/AIDS?
- What are effective nutrition interventions for food security to mitigate the nutritional impact of HIV caused by reduced agricultural productivity and/or earning capacity?

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Annex A

Expert consultation on nutrient requirements for people living with HIV/AIDS

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Annex B

Expert consultation on nutrient requirements for people living with HIV/AIDS

Geneva, 13–15 May 2003

Agenda

TUESDAY 13 MAY 2003

09.00–09.15	Welcome address	Dr D. Nabarro
09.15–09.30	Objectives of the meeting, introduction of the agenda and participants. Selection of Chair and Rapporteur.	Dr G. Clugston
09.30–09.45	Overview of the Global HIV/AIDS epidemic	Dr G. Loth
09.45–10.00	An update on current treatment and care programmes	Dr V. Habiyambere
10.00–10.30	Overview of Nutrition and HIV/AIDS Summary of HIV/AIDS-nutrition interactions	Prof. A. Tomkins
10.30–10.35	Administrative information	
10.35–11.00	<i>Coffee/Tea break</i>	
	Session I: Nutrition, infection and HIV/AIDS	
11.00–11.30	HIV/AIDS and immunity: The specific role of nutrition	Dr P. Chevalier
11.30–12.00	Effects of HIV infection on micronutrient status	Dr H. Friis
12.00–13.30	<i>Lunch</i>	
13.30–14.00	Session II: Nutritional disorders in HIV infection and their implications for establishing dietary guidelines/recommendations	

14.00–14.15	HIV/AIDS, opportunistic infections and wasting: The role of nutrition	Dr D. Macallan
14.15–15.00	Considerations for the establishment of dietary guidance	Professor. C. Geissler
15.00–15.30	Panel discussion (presenters) <i>Coffee/Tea break</i>	
15.30–16.00	Session III: Nutrition interventions and HIV	
16.00–16.30	The role of nutrition interventions in the prevention of HIV and HIV-related disease progression	Dr S. Raghavan
16.30–17.00	Multivitamin supplementation of HIV-infected women during pregnancy and lactation: A summary of the evidence	Dr W. Fawzi
17.00–17.45	Nutritional management of HIV-infected children: A review of the issues and evidence	Dr N. Rollins
18.00	Introduction to group work, break into groups, establish formalities, identify chair and rapporteur <i>Reception – WHO French restaurant</i>	Professor A. Tomkins

WEDNESDAY 14 MAY

	Session III: Nutrition interventions and HIV (continued)	
09.00–09.30	Nutritional issues in the design and interpretation of intervention studies	Dr H. Friis
09.30–10.00	Nutritional considerations with the use of HAART in resource-constrained settings	Dr D. Raiten
10.00–10.30	Nutritional Care and Support Guidelines in the WHO Technical Reference Guide for HIV-infected women and children	Dr E. Piwoz
10.30–11.00	<i>Coffee/Tea break</i>	
11.00–11.30	Effects of HIV infection on protein and energy status, metabolism, and requirements	Dr S. Grinspoon
11.30–12.00	Panel discussion (presenters)	

- 12.00–12.30 **Group work** phase 1
 Group I – Nutrition requirements
 Group II – Nutrition and HIV transmission
- 12.30–13.30 *Lunch*
- 13.30–15.00 **Group work** continued
- 15.00–15.30 *Coffee/Tea break*
- 15.30–17.30 **Group work** phase 2 (same groups with new tasks)
 Group I – Nutrition and ARV therapy
 Group II – Nutrition and HIV progression

Note: Groups will discuss knowledge (micronutrients, macronutrients), gaps (research needs and priorities), and recommendations for target groups (infants and young children, adolescents, and adults, including pregnant and lactating women).

THURSDAY 15 MAY

- 08.30–09.30 **Presentation of group work**
- 09.30–10.45 Plenary discussions of all recommendations from Working Groups
- 10.45–11.00 *Coffee/Tea break*
- 11.00–12.30 **Discussion: Next steps**
- How to prioritise and bring other bodies on board? (research institutions and groups, NGOs, donors...)
 - Funding and resource mobilization
 - Timetable for next steps
- 12.30 Close of meeting