

Executive summary—Nutritional Care of HIV-Infected Adolescents and Adults, including Pregnant and Lactating Women: What Do We Know, What Can We Do, and Where Do We Go from Here?^{1,2}

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ABSTRACT

The HIV pandemic continues to place an unbearable burden on the international community, with disease prevalence remaining highest in resource-limited settings in Africa, Asia, and the Americas. HIV is most often imposed on conditions of food insecurity and consequent malnutrition, poor sanitation, and chronic exposure to a myriad of infectious (eg, malaria, tuberculosis, and diarrheal) and noncommunicable (eg, obesity, diabetes, cancer, and cardiovascular) diseases. Women and children continue to bear the greatest burden. Two essential tenets underpin our approach to HIV: 1) antiretroviral drugs (ARVs) are essential to prolong lives and to halt the spread of HIV and AIDS and 2) food and sound nutrition are essential to human health. The challenge is to apply sound principles of clinical care and nutrition science to the safe and efficacious implementation of ARVs and for long-term care for people living with HIV and AIDS. The WHO has played a leading role in developing guidelines to support this goal with the generation of general recommendations regarding nutritional needs of people living with HIV and AIDS and specific guidelines for the nutritional care of HIV-infected infants and children (<14 y of age). These proceedings represent a summary of the work accomplished at a workshop sponsored by the NIH to review the existing evidence to support changes in the recommendations regarding nutrient requirements for people living with HIV and AIDS; to support development of new WHO guidelines for adolescents and adults, including for pregnant and lactating women; and to identify a research agenda to address outstanding knowledge gaps. *Am J Clin Nutr* 2011;94(suppl):1667S–76S.

INTRODUCTION

The HIV pandemic continues to place a great burden on the international community and creates particular hardship in areas with limited resources. Disease prevalence remains highest in resource-limited settings in Africa, Asia, and the Americas (1) and is most often imposed on conditions of food insecurity and consequent malnutrition, poor sanitation, exploding epidemics of NCDs³ (eg, obesity, diabetes, cardiovascular risk), and chronic exposure to a myriad of other infections including malaria, tuberculosis, and enteric diseases. Although the disease affects people of all age groups, women and children continue to bear the greatest burden (1). Much has been learned and much remains to be explored, but at the core of what we know are 2 essential tenets: 1) ARVs are essential to prolong lives and to halt

the spread of HIV/AIDS and 2) food and sound nutrition are essential to human health.

In light of the successful efforts to scale up prevention, care, and treatment programs, the challenge is to determine how to apply sound principles of clinical care and nutrition science to the safe and efficacious implementation of ARVs and for long-term care for people living with HIV and AIDS. Moreover, a need exists to assess a number of outstanding questions with regard to the role of food and nutrition in HIV and related comorbidities. To address these needs, a joint effort was initiated by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the Office of AIDS Research of the NIH, and the Department of Nutrition for Health and Development of the WHO. The intent was to review the state of the science and progress made and to identify outstanding issues that need to be addressed to support the revision of existing recommendations and development of new guidelines for nutritional care of HIV-infected adolescents and adults, including for pregnant and lactating women.

WHO: TECHNICAL GUIDANCE

The WHO is the lead technical agency for the development and dissemination of evidence-based public health guidance. In that role, the WHO has played a prominent role in efforts to fully integrate food and nutrition in all aspects of prevention, care, and treatment of HIV and AIDS. A chronologic overview of the processes and activities initiated by WHO in partnership with the NIH and the international health community is shown in **Table 1**.

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³ Abbreviations used: ART, antiretroviral therapy; ARV, antiretroviral drug; CVD, cardiovascular disease; MMN, multiple micronutrient; NCD, noncommunicable disease; NUGAG, Nutrition Guidelines Expert Advisory Group; RDA, Recommended Dietary Allowance; WG, working group.

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TABLE 1
Nutrition and HIV: a WHO/NIH collaboration¹

- WHO advisory group on nutrition and HIV
2003 recommendations
Three regional consultations: SSA (2005), Southeast Asian region (2007), French-speaking Africa (2008)
2009—New guidelines for nutritional care of HIV-infected infants and children
- NIH research efforts
Request for applications and expanding research portfolio
Integration of nutrition into existing research networks
- Impact
PEPFAR food and nutrition guidance
Global fund
Integration of nutrition into clinical management

¹ PEPFAR, President's Emergency Plan for AIDS Relief; SSA, sub-Saharan Africa.

The core questions that the WHO advisory group intended to address are highlighted in **Table 2**.

Since the completion of the infant and young child guidelines (2), the WHO has implemented a new process for developing guidelines that consists of several steps intended to evaluate in a systematic manner the strength of the extant evidence to support such guidance (3). The process includes the constitution of an NUGAG charged to identify key questions to be addressed in support of new guidance. The new WHO adolescent and adult guidelines will be developed by using this new process and will be based on an update of the original 2003 recommendations and technical papers with specific focus on adolescents (>14 y of age) and adults, including pregnant and lactating women. To facilitate this process and to identify existing gaps in our current knowledge, a state of the science workshop was organized and convened in July 2010 in Washington, DC. These proceedings are the culmination of that process.

THE WORKSHOP

The goal of the conference was to address core questions that emerged during the WHO NUGAG deliberations. A particular focus was on the development of the evidence to support answers to those questions and to identify critical gaps to help inform a research agenda. The workshop was organized to specifically address the issues outlined in **Table 3**.

In anticipation of the workshop and in coordination with WHO, members of the NUGAG met in June 2010 and identified additional issues to be addressed in the workshop. Members of the NUGAG were asked to chair WGs assigned to develop draft working papers on 3 target groups: adolescents (to include

TABLE 2
Core questions for the WHO advisory group

- 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 comorbidities and opportunistic infections (eg, tuberculosis, diarrheal diseases)?
- What are the nutritional needs of people infected with HIV over and above those required by uninfected people?

TABLE 3
Core issues to be addressed¹

- The state of the science to support (or to not support) changes in the 2003 recommendations
- The role of food and nutrition in the prevention, care, and treatment of HIV and related comorbidities in
Adolescents (age >14 y)
Adults
Pregnancy, lactating women
- Potential interactions between ART, diet, nutrition, and health including
Potential impact of nutritional status on efficacy of interventions, including ARVs
Potential impact of ARVs on nutritional status of HIV-infected individuals
Evaluation of evidence regarding nutritional implications of ART metabolic disorders, eg, dyslipidemias, bone problems
- Nutritional implications of interactions between HIV treatments and comorbidities
- Implications of food insecurity for prevention, care, and treatment of HIV across all 3 target groups
- Factors affecting successful implementation of new guidelines in affected communities

¹ ART, antiretroviral therapy; ARVs, antiretroviral drugs.

orphans and vulnerable children), adults (men and women), and pregnant and lactating women. WG chairs were asked to ensure that each paper addressed the topic area from the perspective outlined in **Table 4**. Draft working papers were presented at the meeting and subsequently revised on the basis of content presentations and interactions with other WGs. In addition to this Executive Summary, which includes synopses of the WG papers, these proceedings contain the articles that reflect the content-specific presentations.

MEETING SUMMARY

The opening session included a series of overviews and perspectives on food and nutrition-related activities from the WHO, the President's Emergency Plan for AIDS Relief, and the World Food Program. This was followed by the first content-specific session, which covered current knowledge with regard to energy and macro- and micronutrients.

Lisa Kosmiski reviewed the extant knowledge regarding energy needs and the strength of the evidence as pertains to the initial WHO recommendations. She concluded that the evidence supports the existing recommendations (ie, increase of 10% for asymptomatic adolescents and adults). She noted that currently

TABLE 4
Coverage of working group papers

- Identification of cross-cutting issues that affect all groups
- Research: the quality and strength of the evidence and priority research gaps to be addressed
- Clinical: how to address the target group in a clinical setting; including issues specific to available interventions, nutritional assessment, and prevention, care, and treatment of comorbidities
- Program: include perspectives from those responsible for implementation of programs intended to serve the HIV-affected community, including potential impact of changes in current recommendations in terms of cost, capacity, and implementation

no specific data are available with regard to caloric needs to support growth and development of HIV-infected adolescents (4).

Alan Jackson followed with a review of the data on macronutrient (protein, carbohydrate, fat) needs. He concluded that macronutrients should be consumed at recommended amounts (RDA), with additional adjustments made that are consistent with the energy needs (ie, if calories are increased by 10%, the macronutrient content should be increased proportionately). His primary message was that macronutrients need to be considered not only as an energy source but also as a source of essential nutrients (amino acids, essential fatty acids). He also emphasized that a synergy exists with micronutrients such that macronutrients are metabolically dependent on micronutrients (vitamins/minerals as cofactors of key enzymes).

Janet Forrester summarized the current state of science regarding micronutrients and HIV, focusing on the use of MMNs, as that was the focus of the 2003 recommendations. She concluded that the results of available randomized clinical trials are mixed with little consistency regarding dose (single compared with multiples of RDAs) or composition of MMN supplements. Therefore, there is no compelling justification to change the 2003 recommendation of ensuring one RDA of essential micronutrients preferably by food or by supplementation (5). With specific regard to pregnant women, it was worth noting that the need for MMNs at amounts of one RDA was reinforced by the recent Cochrane review regarding MMN efficacy in pregnant, uninfected women (6). These findings were complemented by the recent report in HIV-infected women of comparable beneficial effects, which were also observed at one-RDA amounts (7). On the basis of these reports and the lack of evidence indicating an additional HIV-specific need, no compelling justification was found to change the 2003 recommendations of ensuring one RDA of essential micronutrients, preferably by food or by supplementation if necessary (5).

The following session addressed a range of issues related to HIV comorbidities. Soumya Swaminathan provided an overview of tuberculosis as the major HIV-related comorbidity. She highlighted 3 overlapping crises: high rates of malnutrition, livelihood/food insecurity, and HIV/tuberculosis. She suggested that undernutrition may be the greatest population-attributable factor for tuberculosis and reported that data support a pre-eminent role for tuberculosis rather than HIV in HIV patients with wasting. She emphasized the need to focus on integration and coordination between different departments (agriculture, social protection, health, HIV/tuberculosis programs) to most effectively address these interactions and to improve service and care for HIV-affected populations. Naomi Levitt followed with a seminal talk on the concept and reality of "colliding epidemics" occurring in sub-Saharan Africa. Levitt addressed the high and rising prevalence of NCDs such as diabetes, cardiovascular risk, and cancer, in sub-Saharan Africa and globally and the fact that the HIV pandemic is superimposed on top of the NCD epidemic. She emphasized that NCDs should not only be considered as an outcome of HIV and its treatment but need to be considered in their own right in the context of HIV. She further recommended integration of NCDs into HIV care and vice versa (8).

The interaction of nutrition and ART was the focus of the next session. The opening talk in this session provided an overview of basic understanding of what is currently known about the bidirectional interaction between nutrition and pharmacology. This

was followed by an update of the specific aspects of this relation as it relates to ART. Building on the conclusions of the original WHO report (9), the presentation reinforced the notion that certain traditional therapies and nonnutrient dietary supplements and foods affect the bioavailability of ARV medications [eg, garlic (10), medicinal plants (11), African potato (12), ginkgo biloba (13)]; use of "traditional medicines" may also affect ARV use (adherence) and efficacy (14); there is an emerging body of evidence with regard to the potential impact of large doses of certain essential nutrients (eg, vitamin A, vitamin C, iron) on ART efficacy and safety; and a substantial body of evidence exists with regard to the impact of ART on the metabolism of adults and children. Many of these effects have dietary and nutritional implications (15).

The impact of nutritional status on disease progression was the focus of the presentation by Amita Gupta. Gupta reported that malnutrition is likely to play a role in disease outcomes, but several unanswered questions remain about the impact of nutritional status among persons receiving ART in these settings. Studies have reported a direct association between BMI (in kg/m²) <18 and accelerated disease progression. However, limited data exist regarding the role of macro- or micronutrients in disease progression (16).

Philippa Musoke followed with a review of the importance of food and nutrition in resource-limited settings. She emphasized the need to initiate ART early in HIV-infected children and adolescents, particularly in light of data indicating an intractability of immune response in older children, even with viral suppression. It is also imperative for nutritional interventions to improve growth and weight gain. She concluded that as metabolic complications become more evident consequent to prolonged ART exposure, adolescents exposed to HIV early in life will be a highly vulnerable group that needs monitoring and care, especially in resource-limited settings (17).

In the final presentation in this session, Steven Grinspoon provided a comprehensive overview of the extant knowledge about metabolic complications of HIV infection and its treatment and the implications for clinical care (18). He reported that compelling evidence exists for an increased risk of CVD in HIV-infected populations. The mechanism or mechanisms for this effect is unclear, but he hypothesized that it is likely multifactorial and appears to be only partly (25%) driven by traditional risk factors (eg, smoking, dyslipidemia, impaired glucose tolerance, visceral adiposity), and there are many nutritionally related components that should be targeted. He suggested that factors such as HIV-related inflammation may be playing a significant role and need to be further explored. He then highlighted the impact of HIV infection and treatment on bone health, noting that HIV-infected patients (both men and women) have reduced bone density, disturbed bone turnover, and increased fracture rates. Grinspoon highlighted the roles of nutritional, body composition, and endocrine and inflammatory factors in bone loss and emphasized that numerous treatment strategies may be appropriate. He stressed that such treatments are best targeted at specific etiologic factors such as increased turnover or androgen deficiency.

Issues pertaining to clinical management and prognostic indicators were the theme of the next session. Ruth Bland provided an overview of general principles that underpin the implementation of guidelines and used the rollout of the new WHO guidelines for nutritional care of HIV-infected infants and

children as a case study. She highlighted the need for guidelines to be simple to understand, to address health worker key decisions, to be user-friendly (used as a daily reference tool but built on other well-accepted guidelines), to be able to integrate into existing services, and to be based on a well-thought-out plan for dissemination and training.

Preeyaporn Srasuebkuul concluded the session with a review of her work to identify key prognostic indicators for HIV-related outcomes. On the basis of her analysis of data from studies in Southeast Asia, she presented several conclusions, including the following: serious non-AIDS-related complications in HIV-infected populations included diseases associated with aging in the general population (eg, CVD, diabetes); CD4 counts and older age are strongly related to both AIDS and death and to certain serious non-AIDS outcomes; anemia and low BMI were the strongest predictors for both AIDS and serious non-AIDS-related conditions; and the direct relation between nutrition, morbidity, and mortality is still unclear.

The final content session focused on emerging new paradigms to increase the visibility and importance of the role of food security in prevention, care, and treatment of HIV and AIDS. The seminal work in this area has been led by Sheri Weiser who presented some of her data on the impact of food insecurity on HIV risk and treatment. She reported the results of studies conducted in the United States and Africa. Weiser noted that, under certain circumstances (eg, limited access to treatment, care, and food), provision of food leads to improved ART adherence. However, in scenarios found in many low- and middle-income settings, food insecurity is associated with worse ART adherence as a consequence of negative feedback (eg, ART leads to improved appetite, which, in absence of food, leads to poor adherence). Food insecurity is associated with worse virologic and immunologic outcomes, worse physical and mental health status, and increased risk of mortality. She reported a strong relation between food insecurity and multiple high-risk sexual behaviors and vulnerability to sexual violence and abuse (19).

TABLE 5
Adolescent-specific issues

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- Exposure during adolescence and throughout adulthood to infection and inflammation and exposure to ART¹ that collectively may contribute to
 - Impaired longitudinal growth
 - Delayed puberty
 - Impaired accrual or actual loss of bone mass
 - Alterations in fat mass and distribution
 - Dyslipidemia
 - Insulin resistance, diabetes
 - Altered cardiac function
 - Accelerated cardiovascular disease (increased carotid intima media thickness)
 - Impairment in cognitive function or other neurologic issues
 - End-organ disease secondary to HIV or ART
 - Adherence to ART is challenging for many HIV-infected youth
 - Developmental differences in pharmacokinetics/dynamics that may affect ART and potential impact on safety and effectiveness
 - Pregnancy in HIV-infected adolescents confers additional risk
 - Adolescents' relatively robust immune systems, along with potential positive impact of nutritional support and healthy lifestyle choices, might delay HIV progression and time to ART in recently infected adolescents
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¹ ART, antiretroviral therapy.

TABLE 6
Adolescent-specific evaluation

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- Tanner staging for anyone over age 10 y
 - Documentation of height, weight, and, ideally, mid-upper arm circumference at each clinical assessment measured by using consistently applied techniques
 - Detailed social history, including the following
 - Consideration of the internal and external environment/food security assessment
 - Who is making the food choices?
 - Is there an adult in household?
 - How much or how many meals are eaten away from home?
 - What are the sources of food available?
 - Psychosocial factors including
 - Mental health: depression, etc
 - Assessment of cognitive ability/impairment
 - Peer support networks
 - Risk behavior: unprotected sex, sex for money or food, drug use, alcohol, smoking
 - Reproductive health: pregnancy prevention or planning for pregnancy, contraception
 - Body image, eating disorders
 - Assessment of functional capacity and physical activity level: work and leisure
-

In the final presentation, Louise Ivers, whose work is conducted primarily in Haiti, offered some data and insights regarding the sex-specific issues associated with food insecurity. She reinforced many issues covered by Weiser. In particular was the observation that food insecurity has special implications for women, especially with respect to economic, biological, psychological, and social factors. In the United States, food insecurity is associated with pregnancy complications and low birth weight and with depression and anxiety in mothers and behavior problems in children. She also reinforced the importance of food assistance, noting that it is associated with improved food security in Haiti (20).

WG SUMMARIES

As noted, the 3 WGs (on adolescents, adults, and pregnant/lactating women) met before, during, and after the workshop to draft their reports. These reports are thus informed by interactions within each group as well as with other WGs, presenters, and attendees at the workshop. The WGs were charged with identifying key cross-cutting issues to be considered, irrespective of the target group. Each WG reflected on the impact of the following themes: 1) nutrient recommendations and strength of evidence for change, 2) ART-specific considerations, 3) food insecurity, and 4) comorbidities. The WGs were also tasked with providing advice to workshop organizers and the NUGAG regarding key research priorities and to itemize what data can be used as basis of guidelines. These summaries were not intended to represent the views of the WHO or the NIH and should not be used as recommendations for clinical care or policy purposes as that is the purview of the WHO.

Adolescent WG summary (WG chair: Kathleen Mulligan)

Adolescents represent 25–30% of persons known to be infected with HIV worldwide (reflecting ~9–10 million adolescents/young adults with HIV infection). Of that number, 63% live in sub-

TABLE 7
Nutrient-specific recommendations for adolescents

Nutrient	Conclusion	Comment
Energy	For asymptomatic adolescents, target energy intake of 110% of that recommended for healthy adolescents	No empirical evidence that energy requirements are greater in HIV-infected adolescents compared with non-HIV-infected adolescents. However, the application of the current WHO recommendation provides continuity in bridging the recommendations for HIV-infected children and adults and a margin of safety in estimating energy requirements. Caution is needed to avoid the potential for overweight and obesity and consequent complications.
Macronutrients (carbohydrate, protein, fat)	When increasing calories per current WHO recommendations, ensure relative percentages of macronutrients	Although some studies in adults have suggested that protein requirements may be higher with HIV infection, as yet there is no consistent evidence that increasing protein intake above required amounts for uninfected populations is beneficial.
Micronutrients (vitamins, minerals)	Maintain current WHO recommendations (ie, ensure one Recommended Dietary Allowance for all essential nutrients, preferably through a well-balanced diet)	Overall, in the absence of specific evidence of differing requirements consequent to HIV infection, there is not sufficient evidence to support a general policy encouraging the use of daily oral nutrient supplements. Vigilance will be needed to ensure dietary adequacy of micronutrients, particularly in areas of high food insecurity or poor dietary diversity. Additional attention may be warranted for specific nutrients (eg, vitamin A, vitamin D, calcium, iron) either in terms of dietary intake and poor exposure or in the context of potential treatment interactions.

Saharan Africa, 76% of whom are female, and 21% live in the Asia Pacific region. Although the numbers are alarming, the ability to address this group is complicated by their diversity and the complexity of this critical stage in human development.

In an effort to address the adolescent group, the WG grappled with 2 core issues: how to define “adolescence” and whether to consider those infected early in life separately from those exposed later in life. With regard to the former issue, the WG considered data from studies that included persons aged 14–24 y. This approach was inclusive of current WHO definitions of early adolescents (21) and the wider upper age range used by ongoing trials involving adolescents [eg, the Adolescent Trials Network in the United States, the International Maternal, Pediatric, and Adolescent Clinical Trials Group (IMPACT)].

The WG recognized that children who acquired HIV infection in early life have a unique development profile that may include stunting or delayed puberty as a result of inadequate virologic suppression, malnutrition, and other factors. However, many of those same factors may be present in those acquiring HIV later in life. Although there may be a number of research questions that may be addressed about potential differences between these 2 groups (perinatally infected compared with those infected later in life), the WG concluded that adolescents face the same issues with adherence, maturation, food security, and the challenges of carrying a chronic disease regardless of the time of acquisition of HIV. Consequently, early and recently infected adolescents were considered as a single group for the purposes of these deliberations, with the understanding that the unique impact of HIV infection and its therapies on each individual would be shown during the nutritional assessment.

In terms of general overarching issues facing adolescents irrespective of HIV status, the WG referred to the concepts outlined by the WHO (21). With regard to specific issues confronting HIV-infected adolescents, the WG provided the list outlined in **Table 5**. The first step in providing optimal nutritional care and management of HIV-infected patients starts with clinical assessment. With regard to adolescents, the WG high-

lighted a number of specific issues to be addressed in this population as outlined in the **Table 6**.

The WG highlighted optimized HIV care, including appropriate ART, and treatment and prevention of comorbidities as the cornerstones of nutritional management of HIV-infected adolescents. A priority for this group is to build healthy habits to prepare for a lifetime of self-care. In terms of specific recommendations, overall dietary goals for HIV-infected adolescents are consistent with those in non-HIV-infected adolescents and include meeting the needs of normal growth; consumption of a high-quality, nutrient-dense diet; building good eating habits; avoiding obesity through limiting intake of energy-dense but nutritionally poor foods; engaging in physical activity; and avoiding cigarettes, alcohol, and drugs.

The WG emphasized that the nutritional management of HIV-infected adolescents must be integrated into not only patient-based clinical care but also family-centered care. The WG’s conclusions regarding nutrient-specific recommendations are presented in **Table 7**. Although the WG found few published studies in this age group to justify specific quantifiable recommendations for either macro- or micronutrients, they recognized

TABLE 8
Care and management of HIV-related comorbidities in adolescents

- Dyslipidemia (elevated triglycerides, total, LDL, and non-HDL cholesterol; low HDL cholesterol); insulin resistance; diabetes should be recognized and minimized in adolescents with HIV infection
- Lipid and other metabolic testing may not always be available as part of clinical care
- The major goal should be to minimize abnormalities through nonpharmacologic means and in accordance with established guidelines for non-HIV-infected adolescents and HIV-infected adults
- Low-fat diets alone are not the optimal way of minimizing lipid abnormalities; intake of simple sugars should also be minimized
- Pharmacologic management of diabetes and dyslipidemia should be performed in accordance with established guidelines for HIV-infected adults and for non-HIV-infected children and adolescents

that HIV-infected adolescents are at nutritional risk (as are uninfected adolescents). Therefore, even the achievement of current goals for non-HIV-infected adolescents would represent a major improvement in care.

HIV-infected adolescents with specific evidence of growth failure, weight loss, or other nutritional deficiencies should be managed according to the guidelines for nutritional management of non-HIV-infected adolescents. In addition, effective treatment of HIV infection and other comorbidities should be a priority. The WG suggested that dietary management of specific metabolic disorders, including dyslipidemia and diabetes, should also occur in accordance with current recommendations for HIV-infected adults and non-HIV-infected adolescents. Some additional specific suggestions are offered in **Table 8**.

The WG offered some specific thoughts with regard to 2 particular potential problems, obesity and bone/growth-related issues. With regard to obesity, the WG suggested that because it increases risk of metabolic complications and other comorbidities, care must be taken to avoid unwarranted weight gain. That said, the WG also recognized that currently no data exist on the long-term impact of voluntary weight reduction in HIV-infected patients. However, given the demonstrated difficulty of losing weight and maintaining weight loss, the WG emphasized prevention as being most likely to be successful if initiated before the age of 14 y, perhaps as early as ages 5–9 y. The WG emphasized that optimal BMI targets for adolescents is an area of research priority. The WG concluded that the major goal should be to minimize abnor-

malities through nonpharmacologic means and in accordance with established guidelines for non-HIV-infected adolescents and HIV-infected adults. With regard to bone growth, adolescence is the period in which peak bone mass is achieved, so it is particularly important to ensure adequate intake of vitamin D and calcium and to emphasize the importance of weight-bearing exercise and avoidance of alcohol and tobacco.

Maternal (pregnant and lactating women) WG summary (WG chair: Peggy Papatheakis)

After considering the evidence presented, this WG suggested that some recommendations for pregnant and lactating women be stratified on the basis of criteria such as the following: 1) condition (pregnant, breastfeeding), 2) HIV stage (stratified by CD4 T cell count), 3) age (14–20 y, >20–30 y, >30–50 y), 4) weight or BMI, 5) food security score, 6) micronutrient status including hematologic status (presence of anemia), and 7) treatment status (ART or other drugs). The WG also suggested that in assessing body composition in areas without access to scales, eg, visible wasting should be added as a criterion for management decisions. The WG noted that decreasing mid-upper arm circumference in pregnancy could be used as a sign of wasting; however, this cannot be used in lactating women due to physiologic tissue redistribution during this time (22). The WG recommendations are outlined in **Table 9**. In addition, the WG also offered a series of suggestions regarding clinical care and assessment.

TABLE 9
Nutrient-specific recommendations for pregnant and lactating women¹

Nutrient	Conclusion	Comment
Energy	Adults: the 10% increase in resting energy expenditure currently recommended is likely reasonable for asymptomatic HIV-positive pregnant and lactating women.	Although current recommendations are applicable, the WG cautioned that if the mother has had an inadequate rate of weight gain during pregnancy based on her prepregnancy BMI, excessive weight loss postpartum, or other ongoing health issues, then energy requirements may be higher. With regard to pregnant adolescents, the WG noted that the energy needs may be even greater than 10% above those of nonpregnant adult females. However, the data are insufficient to quantify what that difference would be. More studies are required in this area.
Macronutrients (carbohydrate, protein, fat)	Adults and teens: data are insufficient to support a change in 2003 recommendations of one RDA of all essential macronutrients (ie, % of energy from fat, protein, or carbohydrate) for pregnant and lactating women.	The WG noted that, although not addressed specifically in 2003, in pregnancy and lactation essential fatty acid needs are 30% higher than those of nonpregnant women, and adequate fatty acid intake should be ensured in a manner consistent with recommendations for uninfected women.
Micronutrients (vitamins, minerals)	Considering that food insecurity is likely, micronutrient needs are higher during pregnancy and lactation, and deficiencies appear to be more common in HIV-infected women (24), the working group recommends supplementation of one RDA amounts of micronutrients for all HIV-positive pregnant and lactating women. Supplements should contain the 14 core micronutrients provided in the UNICEF UNIMAP (UN multiple micronutrient preparation) supplement.	Supplementation at higher amounts is not recommended at this time and may in fact be harmful in the case of vitamin A, vitamin D (25), iron, and others (26). Iron supplementation is recommended at the RDA amount for HIV-positive pregnant women. It is not recommended in lactating HIV-positive women unless iron deficiency anemia is shown, given the potential negative consequences of iron on HIV and potential interactions with other comorbid infections (27). In the presence of anemia, nutritional iron deficiency should be confirmed before supplementation is offered.

¹ RDA, Recommended Dietary Allowance; WG, working group.

TABLE 10
Specific diet and nutrition considerations for pregnancy and lactation

- Counseling for best infant feeding practices should be conducted in a manner consistent with current WHO guidelines (eg, AFASS¹, exclusive breastfeeding, safe weaning, and complementary feeding)
- Nutritional assessments should include screening for micronutrient status: anemia/iron deficiency before and after pregnancy
- Dietary intake assessment should include
 - Usual diet, diet pattern, diet diversity, and diet constraints
 - Assessment of food security
 - Household assessment to include: Who cooks/procures food for the household? Who lives in the home? How much control does the woman have over food decisions/choices/preferences/access?
- Sanitation: assessment of and counseling about food and water safety/sanitation (important in AFASS assessment for breastfeeding)
- Social/cultural assessment: assessment of food taboos and education (eg, culturally imposed avoidance of eggs during pregnancy, thereby eliminating a potentially good accessible source of protein/essential fats)
- Supplement use (including public health interventions) and traditional therapy use

¹ AFASS, Acceptable, Feasible, Affordable, Sustainable and Safe.

Anthropometric measurements

Body composition: Total weight gain and rate of weight gain during pregnancy and postpartum weight loss must be monitored and compared with “expected” findings on the basis of prepregnancy BMI; mid-upper arm circumference can be used, but should be interpreted with caution.

Height: During pregnancy, height should be measured at first visit, and for pregnant teens, height should be measured at each visit.

BMI: BMI should be calculated if height and weight are obtained in the first trimester. Weight should be measured at each visit, ideally every month in the second half of pregnancy.

Postpartum assessment: Weight can be measured when the mother accompanies the infant to well-baby/vaccine visits. Ideally, weight should be measured at 6 wk after delivery and subsequent weights measured at 2–3-mo intervals. A weight loss of >10% in these women postpartum should trigger the start of ART as per WHO stage III criteria (23).

Specific clinical considerations

In consideration of potential comorbidities and complications of pregnancy, screening should be performed for the following:

Gestational diabetes: Insulin resistance can occur irrespective of HIV status; moreover ARV and overweight are risk factors for development of gestational diabetes. Therefore, screening for gestational diabetes should be done for all HIV-positive pregnant women who have a prepregnancy BMI ≥25 with the use of a 2-h 75-g glucose tolerance test at ~24 wk of gestation

Blood pressure: Blood pressure should be measured at each antenatal visit;

Breast health: This should be assessed at each postpartum visit to prevent, diagnose, and treat potential mastitis

Nutrition-related symptoms (eg, nausea, vomiting, diarrhea, oral lesions, etc, that might affect dietary intake/nutritional status): These should be assessed at each visit during pregnancy

TABLE 11
Nutrient-specific recommendations for adults¹

Nutrient	Conclusion	Comments
Energy	For asymptomatic adults, target energy intake of 110% of that recommended for healthy adults.	In the absence of any new data, the WG concluded that the prior recommendations to provide an extra 10% of daily caloric intake as nutritional support for asymptomatic HIV-infected adults are warranted; however, the group noted that the prior recommendations to increase energy intake by 30% for HIV-infected adults with symptoms or active opportunistic infections had limited evidentiary support.
Macronutrients (carbohydrate, protein, fat)	Continue to ensure that macronutrients are provided at recommended amounts for uninfected adults (as percentage of energy and where specified in specific amounts).	The prior recommendations note that there is no evidence to support the need for increased protein intake in HIV-infected adults, although an increase in protein is often suggested in nutritional counseling in the resource-sufficient setting. The WG concluded that this recommendation should be clarified and that it should be stressed that, although there is no evidence to support a recommendation for increased protein intake, neither is there any evidence to suggest that protein intake should not be increased. The WG emphasized that the collection of data to support quantitative recommendations for daily protein intake is a high priority research question. The WG also observed that insufficient data exist to support HIV-specific recommendations regarding the type or amount of fat for HIV-infected adults.
Micronutrients (vitamins, minerals)	Insufficient evidence to support a change from 2003 recommendations of one RDA for essential micronutrients.	The WG concluded that the studies of micronutrient supplementation have been diverse in terms of design, amount and type of micronutrient evaluated, study duration, and outcomes. Consequently, it is not possible to recommend anything other than the current one RDA or a routine multivitamin. The WG viewed the evidence sufficiently compelling to comment on the potential harm from higher doses of selected micronutrients (eg, vitamin A; MMN supplements, which may promote increased viral replication and increased shedding of virus in genital secretions, thus potentially increasing risk of transmission of HIV). These findings suggest that there may be a safe dose range beyond which there are safety concerns.

¹ MMN, multiple micronutrient; RDA, Recommended Dietary Allowance; WG, working group.

TABLE 12Nutritional interventions to ameliorate mild to moderate malnutrition in HIV-infected adults¹

Level of malnutrition	Not eligible for ART	Receiving ART ²		Complicated advanced HIV, comorbidities (eg, opportunistic infections, malignancies)
		Initiate ART	Stable ART	
No overt malnutrition (local BMI standards and weight stable)	Assess and address food insecurity, nutrition assessment and counseling (dietary quality/diversity) to encourage and maintain good nutrition			
Mild-moderate [BMI (in kg/m ²) <18.5, BMI >16]	Comprehensive assessment and counseling and outpatient targeted nutritional therapy	Comprehensive assessment and counseling and outpatient targeted nutritional therapy	Ongoing monitoring and outpatient targeted nutritional therapy	Comprehensive assessment and counseling and targeted nutritional therapy
Severe (BMI <16 or symptomatic overt malnutrition)	Intensive therapy, nutritional recovery			
Overweight (BMI >25–30) or obese (BMI >30)	Assess and address food insecurity, nutrition assessment and counseling (dietary quality/diversity, encourage physical activity when feasible) to encourage and maintain good nutrition			

¹ Data are from references 28 and 29.² ART, antiretroviral therapy.

and lactation. Issues specific to pregnant and lactating women and diet/nutritional assessment are outlined in **Table 10**.

Adult WG summary (WG chair: Christine Wanke)

As with the adolescents WG, the adult WG grappled with the issue of what defines the universe of people living with HIV and AIDS. The WG identified several obstacles to achieving a definition of what constituted an “adult.” The definition of adult solely by age range alone was complicated by various factors including regionally based social and cultural definitions, discrepancies in specific age cutoffs for relevant nutritional and clinical variables, and variability of nutritional status and related clinical variables among different age groups across the adult spectrum (eg, adolescents compared with older adults living with HIV). The WG emphasized the importance of ensuring that data on all age ranges of adults, including the growing group of older adults living with HIV, as well as on male and female adults, be included in studies of prevalence, incidence, and interventions. The WG emphasized a need to evaluate dietary/nutritional status through broad application of what they termed the *ABCD* approach to include elements of Anthropometry, Biochemistry, Clinical, and Dietary assessments. This approach, while a focus of the adult group, was recognized to have broad application across all target groups.

The adult WG concluded that there was little evidence to challenge what has been recommended previously for HIV nutrition support. The WG highlighted a set of research priorities that are critical in gathering the data necessary to make targeted and appropriate recommendations for nutrition content, to define the appropriate target groups for interventions, and to determine entry and exit criteria for nutrition interventions. The nutrient-specific recommendations for adults are outlined in **Table 11**. In addition to these specific recommendations, the WG discussed nutritional interventions for amelioration of mild-moderate malnutrition in HIV-infected adults as shown in **Table 12**. These were taken from the current WHO recommendations for treating malnutrition in the general population (28, 29). These recommendations were not considered to be based on specific scientific

evidence but were rather suggested because there were no scientific data to recommend any deviation from current standards of care.

Research priorities: cross-cutting issues

During the course of the deliberations, it became clear that there were a number of issues that affected all 3 groups. Many of

TABLE 13Cross-cutting issues across different age groups¹

- Effect of nutritional status on disease progression, time to ART, and response to treatment of HIV and related comorbidities
- Experimental design based on sound principles of nutrition science and intended to foster harmonized trials of nutrition interventions with endpoints that allow comparison across trials
- Diagnosis, prevention, care, and treatment of NCDs
 - Obesity: clinical implications, how to measure it, how to assess impact, care and treatment
 - Diabetes
 - CVD risk and treatment
- Macro-/micronutrients and dietary supplements
 - Data need to quantify HIV-specific requirements across all age/sex groups.
 - Safety of dietary supplements (nutrients and other supplements, eg, herbals/botanicals)
 - Safety of “universal” MN programs (eg, iron, vitamin A in context of HIV prevention, care, and treatment)
- Issues regarding specific MNs
 - Vitamin D/calcium
 - Iron (safety and effectiveness)
 - Vitamin A (safety and effectiveness)
- Assessment of needs to include consideration of
 - Social/cultural context
 - Food security
 - Field/clinical assessment of body composition
- Tools for nutritional assessment: exposure, status, and functional effects
- Need for effective program linkages
- Technical and resource capacity

¹ ART, antiretroviral therapy; CVD, cardiovascular disease; MN, micronutrient; NCDs, noncommunicable diseases.

TABLE 14
Proposed research agenda by target group¹

Target group	Research priorities
Adolescents	<ul style="list-style-type: none"> ● Population-specific normative data for growth and development, including bone mineralization, in adolescents ● Energy requirements in HIV-infected adolescents: is 110% the correct target? ● Macronutrient requirements: is protein requirement higher than for non-HIV-infected adolescents? ● Micronutrients: should vitamin D and calcium supplementation be routinely provided, given the high prevalence of vitamin D insufficiency and heightened vulnerability of adolescents as they approach peak bone mass? ● Are there special requirements for HIV-infected adolescents during pregnancy? Nutritional and developmental effects in persons infected in early life as they reach adolescence and early adulthood ● Novel, effective, culturally sensitive ways to incorporate optimal nutrition and physical activity into the lives of HIV-infected adolescents in the context of adherence to ART and choices for a healthy lifestyle ● Can nutritional supplementation prolong the time until initiation of antiretroviral therapy is needed in adolescents with recently acquired HIV, whose immune systems may be relatively robust and able to provide an adequate response against HIV? ● What is the optimal BMI (or BMI z score) in HIV? ● What are the nutritional implications of perinatal exposure to HIV and ART in uninfected individuals who reach adolescence?
Maternal	<ul style="list-style-type: none"> ● Specific associations between nutritional status (over-/undernutrition, macro-/micronutrients, food insecurity), HIV status (CD4/viral load), and disease progression, birth outcomes, newborn health, maternal health ● Specific associations between nutritional status (macro-/micronutrients) and maternal-to-child transmission (eg, perinatal risk) ● Impact of nutritional status on <ul style="list-style-type: none"> ● Lactation performance (initiation, duration, milk composition) in context of HIV with and without ART ● Maternal health in context of lactation ● Factors affecting transmission via human milk (eg, mastitis) ● Safety of specific micronutrients in context of preventing mother-to-child transmission (eg, vitamin A) and maternal/infant health (eg, iron) ● Impact of ART on nutritional status during pregnancy and lactation; relation to maternal and infant health outcomes ● Relation between body composition/weight and health of mothers and newborns <ul style="list-style-type: none"> ● What is the relation between body weight and maternal/infant health outcomes? ● When is it appropriate to intervene regarding maternal over-/underweight? ● Are there differences in impact of body weight and lactation performance in HIV-infected women vs uninfected women? ● Differences in all of the above in adolescents? ● Impact of differing needs for growth and demands of pregnancy/lactation in adolescents
Adults	<ul style="list-style-type: none"> ● An appreciation of the importance of nutrition to an aging/elderly HIV-infected population is a major research gap. This group should be included in all studies evaluating the nutrition and HIV relations in adults, including the items listed below. ● Data to identify best and appropriate anthropometric measures both in terms of clinical outcome and perhaps as surrogates of other biomarkers (eg, CD4) ● Data on the optimal amount of energy intake to maintain weight (“normal” weight). In all stages of infection (CD4 count and viral load), treated and untreated across the full spectrum of “adult” years, in both sexes, with and without comorbid conditions ● Further data to support quantification of optimal macronutrient (eg, protein intake to maintain lean body mass) and micronutrient intakes in all stages of infection (CD4 and viral load, treated and untreated) across the full spectrum of adults, both sexes, with and without comorbid conditions ● Specific data with regard to the role of nutrition in prevention, care, and treatment of comorbidities, including CVD, renal disease, bone-related problems, and diabetes in adults ● Data need to support clinical care <ul style="list-style-type: none"> ● Determination of the best time to initiate nutritional intervention including impact of nutrition on disease progression and time to initiation of ART ● Duration of nutritional interventions ● Data to support best methods for assessment of nutritional status (intake, status, function) ● Role of food security in short- and long-term prevention, care, and treatment of HIV-infected adults ● To determine the impact of the initiation of ART on nutritional status ● Social/cultural research on factors that affect the acceptability of specific interventions and the best means of delivering nutritional interventions

¹ ART, antiretroviral therapy; CVD, cardiovascular disease.

the issues highlighted during these deliberations are listed in **Table 13**. As noted, a major objective of the workshop was to identify research priorities that would provide insights and support to not only the WHO guideline development process but to support a targeted research agenda aimed at a future programmatic activity for funding agencies, including the NIH. Specific research agendas were identified by each WG and are presented in **Table 14**.

The authors' responsibilities were as follows—KM: drafted the adolescent WG summary; PP: drafted the maternal (pregnant and lactating women) WG

summary; CW: drafted the adult WG summary; and DJR: compiled the WG drafts and wrote the manuscript and has primary responsibility for final content. There were no conflicts of interest declared.

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