

Nutrition and HIV

? Questions

- Do people living with symptomatic HIV infection or AIDS require a therapeutic diet?

🔑 Key Take-Home Messages

- Nutrition is an important component of care for people living with HIV (1–5).
- Nutritional needs for people living with HIV can vary; therefore, dietary recommendations should be individualized to meet specific needs (1–3, 6).
- In general, asymptomatic people living with HIV appear to have greater energy requirements compared to the general population (2, 3, 7–10).
- After symptomatic periods, it is critical that people living with HIV recover lost weight (6); it is suggested that energy requirements during recovery may be increased by 20–30% (11).
- Treatment for dyslipidemia, a metabolic complication independently associated with HIV and antiretroviral therapy (12–14), includes dietary management (6, 15–21).
- Some systematic reviews (22–25) and preliminary studies (13, 26–28) have identified probiotics as a dietary supplement that may have a positive impact on the health of people living with HIV.

! The Issue and Why It's Important

Good nutrition plays an important role in the maintenance of overall health, regardless of HIV status (29, 30). However, for people living with HIV, nutritional status plays a crucial role in maintaining the immune system and preventing progression to AIDS (1). Managing nutrition is essential to managing HIV and AIDS (2); evidence suggests that taking a proactive approach to nutrition can improve health outcomes related to the adverse metabolic, cardiovascular, and psychological complications that result from

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HIV and antiretroviral therapy (ART) (31). By receiving appropriate nutrition, people living with HIV will experience less sickness, become stronger, and improve their quality of life (15).

Various conditions associated with HIV pathogenesis can influence nutritional status through reduced caloric intake, increased requirements, and malabsorption, which contribute to malnutrition (2). Furthermore, although ART has increased the life expectancy of people living with HIV (32, 33), these medications are associated with a variety of nutritional complications (1) and can have an adverse impact on overall health (34).

This review presents nutritional information for people living with HIV, includes guidelines from various international organizations, and synthesizes research evidence from reviews and studies. Additionally, a variety of health challenges associated with HIV and ART are explored in the context of nutritional intervention. Notwithstanding the inter-environmental differences, there are significant disparities between high- and low-resource settings concerning undernutrition (35) and receipt of ART (36). Consequently, this synthesis focuses on people living with HIV in high-resource settings; however, some systematic reviews included heterogeneous data, and some nutritional recommendations did not specify the target population. Where possible, these details are noted.

What We Found

Nutritional needs among people living with HIV

Overall, there appears to be a paucity of research on specific nutritional requirements of individuals living with HIV in high-resource settings who are taking ART.

Recommendations from various national and international organizations

The Academy of Nutrition and Dietetics (U.S.) and the Dietitians of Canada have stated that optimal nutrition is an essential part of care at all stages of the HIV care continuum (37, 38). While the Dietitians of Canada do not have a current official statement on nutrition or nutritional interventions and HIV (39), the Academy of Nutrition and Dietetics recommend that all people living with HIV routinely receive medical nutrition therapy provided by a registered dietitian nutritionist (3). Furthermore, the Academy recommends an individualized diet (3), a suggestion supported in the literature (1, 2, 6).

In 2003, the World Health Organization (WHO) published a technical document (30) outlining nutrient requirements for people living with HIV. Thereafter, a working group sponsored by the National Institutes of Health (U.S.) was formed to review existing evidence

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13. Ceccarelli G, Fratino M, Selvaggi C, Giustini N, Serafino S, Schietroma I, et al. A pilot study on the effects of probiotic supplementation on neuropsychological performance and microRNA-29a-c levels in antiretroviral-treated HIV-1-infected patients. *Brain and Behavior*. 2017;7(8):e00756.

and support development of new WHO guidelines and a workshop executive summary (10) was published in 2011. The summary outlines the following set of recommendations for asymptomatic adults living with HIV, which encompasses males and females of various age ranges, regardless of ART status:

- Target energy (i.e. caloric intake) for asymptomatic adults is 10% more than that which is recommended for the general population;
- Macronutrients (i.e. carbohydrates, proteins, and fats) provided at recommended amounts for the general population;
- Micronutrient (i.e. vitamins and minerals) intake should be at one Recommended Dietary Allowance or a routine multivitamin (10).

Supporting evidence for recommendations

Energy expenditure

Energy requirements refer to the dietary energy intake (i.e. calories from carbohydrates, proteins, fats, and alcohol) the body requires for growth and maintenance (40). Energy expended to sustain normal body functions and homeostasis at rest is known as resting energy expenditure (REE) (8, 40) and is a component of total energy expenditure (41).

An increase in REE can lead to nutritional imbalance and wasting (8). People living with HIV may have a higher REE and REE adjusted for fat-free mass compared to those who are HIV-negative (3), even among individuals who are clinically stable (8). One meta-analysis of studies found that overall REE per kilogram of fat-free mass was higher in people living with HIV by approximately 9% compared to HIV-negative individuals (7). Furthermore, in the subsample of people living with HIV, symptomatic individuals had a significantly higher REE per kilogram of fat-free mass compared to asymptomatic individuals, though the author suggests further studies are needed to confirm this (7). Another review found that REE among adults with untreated asymptomatic HIV is about 10% higher compared to healthy controls, an increase which may be similar to asymptomatic adults receiving ART (9).

Finally, a prospective, cross-sectional study in an HIV outpatient clinic in Ohio among asymptomatic women with no secondary infections (n=87) found that REE was elevated regardless of ART status or viral load (41). The authors conclude that differences in REE are a result of HIV infection, not ART, and should be included in the nutritional assessment of adult women living with HIV (41).

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Macronutrients

While providing adequate amounts of macronutrients for people living with HIV is beneficial, the optimal amount of nutrients is unclear (42). The Academy of Nutrition and Dietetics suggests that more research regarding macronutrient intake among people living with HIV is warranted (3). A Cochrane systematic review published in 2013 evaluated the effectiveness of macronutrient interventions in reducing morbidity and mortality among adults and children living with HIV (43). Included trials were small, and conducted in a variety of resource settings. Participants were at different stages of HIV infection and had varied treatment statuses. Due to the heterogeneity of the studies, the Cochrane systematic review authors were not able to conclude whether supplementing with macronutrients had an effect on morbidity and mortality (43).

The workshop executive summary notes that while increases in protein intake have previously been recommended for people living with HIV, the evidence is insufficient to support such a recommendation (10). Guidelines and other advice for people living with HIV regarding macronutrients generally encourage consuming a diet that is balanced and nutritious (15, 29, 44).

Micronutrients

It is common for people living with HIV to have micronutrient deficiencies due to malabsorption, drug interaction, disrupted metabolism, and changes in gut-barrier function (1).

Three systematic reviews that explored the impact of micronutrient supplementation in people living with HIV were identified, though none were solely among individuals on ART in high-income settings:

- One meta-analysis published in 2015 examined the effect of micronutrient supplementation on mortality and rate of HIV disease progression (45). Micronutrient supplementation significantly slowed disease progression to AIDS among adults not on ART in three trials; however, only one trial was from a high-income economy, and it was conducted in the pre-HAART era. Authors also found evidence across seven trials in low-income settings that micronutrient supplementation may possibly reduce mortality; however, a definite assertion could not be made based on the data set.
- A Cochrane review from 2017 assessed micronutrient supplementation in adults for reducing mortality and HIV-related morbidity (46). Studies investigating the role of micronutrients in metabolic morbidity related to ART were excluded. The synthesis included 33 trials with over 10,000 participants. Ten (30%) of these trials were conducted in

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25. Ray S, Vaidya L. Role of functional probiotic food groups in enhancing CD4 cell profile of HIV infected population — A short systematic review. *International Journal of Engineering Science Invention*. 2014;3(12):14–20.

high-income economies (Denmark, Italy, Singapore, and US) and included 1,706 (17%) participants receiving HAART. From the total number of included trials, authors were not able to consistently demonstrate that micronutrient supplementation had clinically important benefits, but note that this should not be interpreted as a reason to deny individuals micronutrients if a deficiency has been identified. Furthermore, authors suggest that trials with larger sample sizes are needed in order to further explore the impact of micronutrients on individuals on ART.

- Another meta-analysis of six randomized controlled trials found that supplementing with multiple micronutrients reduced the mortality and morbidity of adults living with HIV, but all six included studies were conducted in low-resource settings (47).

Antiretroviral therapy

While there seems to be no significant dietary accommodations needed for asymptomatic people living with HIV other than those needed to address an increase in REE, there are some nutritional implications associated with taking ART. Appropriate diet can help manage the side effects caused by ART (29) and assist in medicine absorption (48, 49).

It should also be noted that some medications for HIV need to be taken with a snack, meal, or on an empty stomach (1, 50), and some should not be mixed with certain foods or particular supplements (1, 50, 51). While a full exposition of food-drug interactions is beyond the scope of this review, it is important that people living with HIV communicate with their health care providers to avoid potential interactions between medication, food, and supplements (52).

Symptomatic conditions associated with HIV and ART and nutritional recommendations

There are specific symptomatic conditions experienced by people living with HIV that are associated with the virus itself, ART, or both. The following section explores a variety of conditions associated with HIV and nutritional interventions that may positively impact disease symptoms and medication side effects.

Weight loss/undernutrition

In addition to the aforementioned increase in REE, other common symptoms among people living with HIV associated with weight loss include difficulty swallowing, wasting, vomiting, and diarrhea (1, 2).

People living with HIV may experience compromised nutrition due to dysphagia (i.e. difficulty swallowing), a symptom of esophageal candidiasis (53, 54). This is despite the fact that ART has

26. Ceccarelli G, Brenchley JM, Cavalari EN, Scheri GC, Fratino M, Pinacchio C, et al. Impact of high-dose multi-strain probiotic supplementation on neurocognitive performance and central nervous system immune activation of HIV-1 infected individuals. *Nutrients*. 2017;9(11):1269.

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significantly reduced the prevalence of this opportunistic infection (53). One study among sixteen cohorts of the North American AIDS Cohort Collaboration on Research and Design between the years of 2000 and 2010 found that esophageal candidiasis has remained prominent in the era of ART (55). Esophageal candidiasis can contribute to decreased oral intake, resulting in weight loss (53).

Another reason for weight loss may be due to wasting, an HIV-associated condition despite antiretroviral therapy (1). Cachexia, or wasting, is characterized by a loss of muscle and/or fat mass which is related to an underlying illness (56). HIV-associated weight loss has been identified as an independent predictor of mortality (57), and can be caused by a host of factors including insufficient dietary intake and metabolic alterations (1, 58). One retrospective observational study among an American managed care population (n=22,535) found that 1 in 10 individuals experienced HIV-associated weight loss; this tendency was associated with more comorbidities, greater use of health care resources, and higher cost (59). Another study across six U.S. cities (n=1,428) found that women who were underweight prior to continuous ART were more than twice as likely to die from AIDS compared to women of normal weight (60). Additionally, another study done among a cohort of military service veterans (n=4,184) in the U.S. found that weight gain in the first year after starting ART was associated with lower mortality rates among those who were not initially overweight (61).

In addition to the above conditions, some people living with HIV may experience nausea, vomiting, and diarrhea as a side effect of some antiretroviral drugs (1, 62, 63). In particular, the incidence of noninfectious diarrhea related to ART (as opposed to infectious diarrhea related to opportunistic infections) has increased among people living with HIV (64, 65). Diarrhea can change energy requirements (3), contribute to nutritional losses (2), impede adherence to ART (65), and reduce quality of life (65). Treatment for noninfectious diarrhea associated with ART includes prescription antidiarrheal medication (64) and may include dietary changes (65). However, one review on noninfectious diarrhea from 2014 notes that there is little evidence supporting diet modification for managing noninfectious diarrhea (66). This review cites one small randomized trial from 2008 in New York City that found dietary intervention reduced stool frequency and improved stool consistency (67). Though evidence in the literature appears to be sparse, some sources maintain that dietary intervention can help to manage diarrhea (15, 63, 68).

Generally, nutritional therapy targeting weight loss is difficult unless the underlying cause is discovered (8). Nonetheless, some guidelines have been established for wasting among people living with HIV. In 2006, the European Society for Clinical Nutrition and Metabolism (ESPEN) published a set of enteral (i.e. oral nutritional supplements and tube feeding) nutrition guidelines pertaining to

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wasting in HIV (11). The authors note that while undernutrition has decreased in people living with HIV, it is still common. These guidelines are for people living with HIV and do not make distinctions among gender, sex, or ART status. Some of these recommendations include:

- Indication of nutritional therapy when there is significant weight loss (>5% in 3 months) or a significant loss of body cell mass (>5% in 3 months) has occurred;
- Consideration of nutritional therapy when the body mass index is <18.5 kg/m²;
- Indication of tube feeding when normal food intake and optimal use of oral nutrition supplements do not achieve appropriate energy supply (e.g. if an individual has difficulty swallowing);
- Indication of enteral nutrition in patients with diarrhea and/or malnutrition;
- Target protein intake of 1.2g/kg of body weight per day in stable phases, potentially increasing to 1.5g/kg of body weight per day during acute illness.

During symptomatic periods, increased energy needs are typical (6). Guidelines from ESPEN state that during the recovery phase of opportunistic infections hypermetabolism (i.e. increased metabolic activity) is common and that energy requirements may need to be increased by 20–30% (11). Furthermore, it is important that weight lost during a symptomatic period be recovered during an asymptomatic period to maintain lean body mass (6).

Metabolism of glucose and lipids

As discussed previously, increased REE and wasting are two conditions people living with HIV may encounter. Though these two conditions may contribute to weight loss, REE (8) and wasting (1) may be a result of underlying changes in metabolism.

The HIV virus itself, independent of ART, is associated with metabolic dysfunction (12). However, metabolic complications are also associated with ART use, despite the fact that antiretroviral regimens prescribed today have safer metabolic profiles (12, 69, 70). Two of the most common metabolic complications among people living with HIV are insulin resistance and dyslipidemia (69). Insulin resistance in particular is closely related to ART (70), while dyslipidemia is related to the virus itself and ART (14). Insulin resistance and dyslipidemia are risk factors for type 2 diabetes and cardiovascular disease, respectively (1). Both of these conditions are increasing among people living with HIV (12).

38. Fields-Gardner C, Fergusson P, American Dietetic Association, Dietitians of Canada. Position of the American Dietetic Association and Dietitians of Canada: Nutrition intervention in the care of persons with human immunodeficiency virus infection. *Journal of the American Dietetic Association*. 2004;104(9):1425–41.

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Insulin resistance

Hyperglycemia, or high blood glucose (i.e. high blood sugar), is a risk factor for diabetes (20). Diabetes occurs when the body is not producing or using insulin properly; as a result, glucose accumulates in the blood stream and can cause damage to the heart, kidneys, nerves, and eyes (20, 71). Though some first generation antiretroviral medications were strongly associated with the development of diabetes, current ART regimens do not appear to impact glucose metabolism to the same degree (72). Nevertheless, some current antiretroviral drugs are associated with the development of type 2 diabetes (70, 73) by increasing insulin resistance or impairing insulin secretion, thereby promoting hyperglycemia (73).

Changes in diet can have a significant impact on glucose control (72). A healthy diet can manage type 2 diabetes. Consuming foods like vegetables, fruits, whole grains, beans, and lean meats, and avoiding processed foods that are high in sugar and salt are recommended for people who have type 2 diabetes (71). One review recommends that simple carbohydrates should be less than 30% of total carbohydrate intake (6). Spreading out carbohydrate intake throughout the day can also be helpful in managing blood sugar levels (15, 20).

Dyslipidemia

Dyslipidemia occurs when there are abnormal amounts of lipids (i.e. fats) in the bloodstream (14, 15) and is a risk factor for cardiovascular disease (14, 19-21). For people living with HIV, the virus itself, in addition to antiretroviral drugs, can impact blood lipid levels and is associated with dyslipidemia (14, 21, 74). Lifestyle changes, such as dietary intervention, are recommended as treatment for HIV dyslipidemia in Canada (15), the U.S. (16), the U.K. (17), and in Europe (18). Generally, dietary recommendations for managing dyslipidemia among people living with HIV include limiting the intake of saturated fat (6, 15, 17, 18, 20, 21) and including more fruits, vegetables, and grains into a diet (6, 15, 17, 18, 20, 21). One meta-analysis from 2012, primarily focused on North Americans on ART, found that omega-3 supplements and dietary intervention effectively lowered triglycerides (a type of fat found in the blood) (19).

Dietary supplements: Probiotics

The search of the literature identified numerous publications about the mechanisms through which probiotic supplementation may impact health outcomes among people living with HIV. Probiotics are a dietary supplement and can be defined as “live microorganisms that, when administered in adequate amount, confer a health benefit on the host” (75) and naturally occur in fermented foods such as yogurt, kefir, sauerkraut, and tempeh (76).

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Three systematic reviews investigated the impact of adding probiotics to the diets of people living with HIV:

- One systematic review evaluated the use of probiotics across a range of outcomes in adults and children living with HIV, regardless of ART status or active infection (22). Authors reported that probiotics appear to positively impact clinical symptoms and moderately improve CD4 count; additionally, no or mild adverse effects were reported in the reviewed studies;
- A meta-analysis of randomized clinical trials in adults living with HIV across high- and low-income settings found that taking probiotics and prebiotics at the same time significantly increased CD4 count in females (23). Probiotic supplementation alone (without prebiotics) increased CD4 count in females, while in males, it decreased. Authors suggest that sex may influence outcomes in probiotic supplementation;
- A systematic review suggested that consuming probiotics over an extended period may improve the CD4 count of people living with HIV (24).

A few preliminary studies from Italy continue to investigate the potential positive impacts of probiotics in the health of people living with HIV:

- A longitudinal pilot study explored the safety and effectiveness of a probiotic supplement for treating inflammatory bowel diseases (27). Participants (n=10) were men virally suppressed and on ART. Authors found that probiotic supplementation was associated with restoration of the physical and immunological integrity of the mucosal intestinal barrier;
- Another study evaluated the impact of probiotic supplementation on neuroinflammation and cognitive performance (26). Participants (n=35) were men and women, all on an effective ART regimen. At the end of the intervention, the group receiving the probiotic supplement had reduced central nervous system immune activation levels and improved cognitive performance;
- A nonrandomized, longitudinal pilot study among people living with HIV on ART who were virally suppressed (n=10) explored the impact of probiotic supplements on brain function and behaviour (13). In this before-and-after study, participants treated with probiotic supplements showed significant improvements on some neuropsychological and behavioural tests after taking probiotics;

52. U.S. Department of Health and Human Services. What is a drug interaction? Available from <https://aidsinfo.nih.gov/understanding-hiv-aids/factsheets/21/95/what-is-a-drug-interaction-> Accessed April 25, 2017. 2018.

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- Another preliminary study among thirty males on ART studied the effect of certain probiotic strains on inflammation (28). Participants consumed a bottle of fermented milk containing a specific probiotic twice a day for four weeks. Supplementation appeared to be a safe and affordable strategy to support immune response among the participants.

Factors That May Impact Local Applicability

The evidence presented in this synthesis primarily focuses on adults living with HIV on ART in high-income country settings. Guidelines for pregnant women, infants, adolescents, and the elderly may be different. This review also does not account for social factors that may affect nutrition, such as the cost associated with nutrition. Furthermore, most of the guidelines and recommendations presented here do not consider the implications cultural practice may have on nutrition and HIV (e.g. fasting). Finally, the evidence presented on nutrition and HIV is not intended to replace the advice of medical professionals.

What We Did

We searched Medline using a combination of [HIV or antiretroviral (text terms) or Acquired Immunodeficiency Syndrome or Antiretroviral Therapy, Highly Active or Anti-Retroviral Agents (MeSH terms)] and (diet* or nutri* or malnutri* or micronutri* or supplement*) as title terms. Reference lists of identified review articles were also searched. Additionally, we conducted searches on Google and Google Scholar using different combinations of the terms: nutrition, antiretroviral therapy, HIV, supplements, metabolism, dyslipidemia, diabetes, and probiotics. For official statements and related literature we also contacted the following organizations: the Dietitians of Canada, the Academy of Nutrition and Dietetics (U.S.) and the American Society for Parenteral and Enteral Nutrition. Searches were conducted on February 16-28, 2018 and results were limited to English language articles published from 2008 to present in high-income countries. The search yielded 824 references from which 76 studies were included. Sample sizes of primary studies ranged from ten to 22,535.

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Rapid Response: Evidence into Action

The OHTN Rapid Response Service offers quick access to research evidence to help inform decision making, service delivery and advocacy. In response to a question from the field, the Rapid Response Team reviews the scientific and grey literature, consults with experts, and prepares a brief fact sheet summarizing the current evidence and its implications for policy and practice.

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