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ORIGINAL PAPER

A Review of the Role of Food Insecurity in Adherence to Care and Treatment Among Adult and Pediatric Populations Living with HIV and AIDS

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Abstract Adherence to antiretroviral therapy (ART) is critical for reducing HIV/AIDS morbidity and mortality. Food insecurity (FI) is emerging as an important barrier to adherence to care and treatment recommendations for people living with HIV (PLHIV), but this relationship has not been comprehensively examined. Therefore, we reviewed the literature to explore how FI may impact ART adherence, retention in medical care, and adherence to health care recommendations among PLHIV. We found data to support FI as a critical barrier to adherence to ART and to other health care recommendations among HIV-infected adults, HIV-infected pregnant women and their HIV-exposed infants, and child and adolescent populations of PLHIV. Associations between FI and ART non-adherence were seen in qualitative and quantitative studies. We identified a number of mechanisms to explain how food insecurity and ART non-adherence may be causally linked, including the exacerbation of hunger or ART side effects in the absence of adequate food and competing resource demands. Interventions that address FI may improve adherence to care and treatment recommendations for PLHIV.

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Introduction

Adherence to antiretroviral therapy (ART) is critical for reducing HIV/AIDS morbidity and mortality. Indeed, ART non-adherence is the most consistent predictor of incomplete viral load suppression, development of drug resistance, and progression to AIDS and death [1–5]. Although ART has significant individual clinical benefits [6, 7] and substantially reduces sexual [8] and vertical transmission of HIV [9], these benefits hinge upon the timely detection of infection, rapid linkage to care, and high levels of adherence. Thus, identifying the many barriers to initiating and sustaining ART is critical to ensure its individual and public health benefits.

Food insecurity, when people do not have physical, social, and economic access to sufficient safe and nutritious foods that meet their dietary needs and food preferences for an active and healthy life [10], is emerging as an important barrier to adherence to care and treatment recommendations for people living with HIV and AIDS (PLHIV). To date, most research has examined associations between food insecurity and adherence to ART among the general adult HIV-infected population. However, burgeoning data also suggest that food insecurity may negatively impact adherence to care and treatment recommendations among specific sub-populations, such as HIV-infected pregnant women and their HIV-exposed infants as well as children and adolescents living with HIV infection.

Thus, the purpose of this paper is to provide an overview of the relationship between food insecurity and adherence

to HIV care and treatment recommendations for PLHIV, and to review the evidence on potential pathways by which food insecurity may adversely impact adherence to HIV care recommendations among three distinct populations: (1) general adult populations of PLHIV, (2) HIV-infected pregnant women and their HIV-exposed infants, and (3) child and adolescent populations of PLHIV.

Methods

We conducted a narrative review of the state of the evidence on food insecurity and ART adherence. We identified key articles in the qualitative and quantitative literature that illustrate current findings on this relationship. We searched PubMed and Google Scholar using key words such as "food security," "food insecurity," "adherence," "compliance," "HIV," "AIDS," and "nutrition" to identify relevant literature. Relevant English language articles were reviewed for possible inclusion. We also identified sources from the bibliographies of included papers and conference presentations related to food insecurity and adherence to treatment and care.

Results

Overview of Barriers to Adherence Among PLHIV

"Adherence" encompasses the entire spectrum of activities required to preserve the health of PLHIV, including early testing, retention in care, and initiation and continuation of ART [11, 12]. There are a number of comprehensive models for understanding healthcare utilization and adherence, described elsewhere [11, 13–15]. These models often describe barriers to adherence to HIV care and treatment recommendations as operating at the individual, household, institutional, or structural levels (summarized in Table 1, stratified by dimension within each level) [11, 16, 17]. Food insecurity, while usually assessed at the household level, has negative health impacts at the individual level and is strongly linked with structural factors at the community level (such as food availability and prices).

Individual-level barriers include patient-related characteristics, such as fear of disclosure [18–20, 53] concurrent mental illness and addiction [24, 54, 55], denial of HIV diagnosis or other health beliefs [28–30], level of trust in providers [28, 30, 56], and distance and transportation costs to and from clinics [18, 20, 31, 34]. In addition, regimen-related factors influence adherence at the individual level including medication side effects, regimen characteristics, and dosing schedule [27, 35–37, 53, 57].

At the household level, besides food insecurity, interpersonal relationships with partners or family members can also influence the decisions to seek HIV testing, engage in care, and stay in care. Lack of support from family or friends has been found to be a significant risk factor for non-adherence to ART [19, 26, 28, 53]. Unstable housing [25, 43] and other financial constraints [35, 24, 19, 26, 44] are other important household-level barriers. There is strong evidence that women in poorer households access health services, such as antenatal care, less frequently than women in households that are better off [58, 59]. This is critical given that a large proportion of women do not know their HIV status when they become pregnant, and accessing health care is requisite for being tested. Pressure to share medications is another household factor known to negatively impact adherence to ART [38].

At the institutional level, distance to the facility [18, 35], heavy staff workloads [18, 46], long waiting times [18, 20, 29], and high user fees [18] have been identified as challenges to adherence to ART and retention in HIV care. At the community level, structural barriers to adherence to ART include HIV-related stigma and discrimination [18, 24, 35], gender inequalities [48, 60], weak food or agricultural systems [49], political or economic crises [50–52] and poverty and poor living conditions [19, 61, 62].

Many of these barriers and facilitators to adherence to ART are universally important and relevant in both resource-rich and resource-poor countries. However, they often manifest differently in different settings. For example, in resource-poor countries, poverty itself may inhibit the ability to obtain treatment through prohibitive healthcare-associated costs, while in resource-rich countries it may be the correlates of poverty such as addiction or depression that prevent PLHIV from obtaining adequate care or adhering to medications [4].

Adherence to ART among pediatric populations has additional challenges across all these levels, as it is the product of the combined influences of child, caregiver, and household characteristics, medication regimen (e.g. pill size, availability of pediatric dosing), and features of the community and culture [63–65]. Pediatric adherence is also often complicated by the fact that many HIV-infected children have not been told of their diagnosis and do not understand why they must take medications [66]. Disclosure of HIV status to the child and to others may have both positive and negative implications for adherence to ART, as disclosure to the child influences the child's own motivation and willingness to take medications, whereas disclosure to others has the potential to affect social support, stigma, and/or discrimination at school or in the community, which could potentially negatively affect adherence [64, 66, 67].

Table 1 Factors influencing ART adherence among HIV-infected adults

Level	Factors	Examples, by Country
Individual	Fear of disclosure	Botswana, Tanzania [18]; Kenya [19]; Uganda [18, 20]
	Mental health	United States [21, 22]; Zambia [23]
	Alcohol or drug use	Cameroon [24]; Canada [25]; South Africa [26]; United States [27]
	Health beliefs	Botswana [28]; South Africa [29]; Tanzania [30]; Zambia [23]
	Level of trust in providers	Botswana [28]; Nigeria, Uganda [31]; Tanzania [30, 31]; United States [32]
	Distance to clinic/transportation costs	Botswana [18]; Nigeria [31]; South Africa [17]; Tanzania [18, 31, 33]; Uganda [18, 20, 31, 34]
	Side effects	Botswana [35]; Italy [36]; South Africa [29]; United States [32]
	Regimen factors (e.g. complexity of dosing)	United States [27, 37]
	Incorporating treatment into daily schedules	Tanzania [30]; United States [32]; Zambia [38]
Household	Food insecurity	Canada [39]; France [40]; Kenya [81]; Peru [41]; Rwanda [85]; South Africa [17, 48]; Uganda [80]; United States [42]
	Family and partner relationships	Cameroon [24]; South Africa [26]; United States [32]; Zambia [23]
	Social support	Botswana [28]; Nigeria, Tanzania, Uganda [31]; United States [21]
	Unstable housing	Canada [25]; United States [43]
	Financial difficulties	Botswana [35]; Cameroon [24]; Kenya [19]; South Africa [26]; Uganda [44], United States [45]
	Pressure to share medications	Zambia [38]
Institutional	Long waiting times	Botswana, Tanzania [18]; Uganda [18, 20]; South Africa [29]
	High user fees	Botswana, Tanzania, Uganda [18]
	Heavy workloads of healthcare staff	Mozambique [46]; Tanzania, Uganda [18]
	Poor counseling	Cameroon [24]
	Medication stock-outs	Cameroon [24]
Community	Stigma and discrimination	Botswana [35]; Lesotho, Malawi, Swaziland, Tanzania [47]; South Africa [17, 26, 47]; Uganda [20]; Zambia [23]
	Gender inequalities	South Africa [48]
	Weak food or agricultural systems	Kenya [49]
	Political crises	Kenya [50–52]

Vicious Cycle of Food Insecurity and HIV

Food insecurity and HIV are "syndemic": there is a positive biological and social interaction in which one exacerbates the negative health effects of the other [68]. It is increasingly recognized that food insecurity both heightens vulnerability to HIV infection and at the same time exacerbates poor clinical outcomes among PLHIV [69–72]. Among PLHIV, food insecurity has been associated with incomplete HIV RNA suppression [73, 74], CD4 decline over time [75], lower body mass index [76], reduced quality of life, increased opportunistic infections, increased hospitalizations [77], and HIV-related mortality [71], often even after controlling for other markers of socio-economic status (SES). Advanced HIV-related illness further undermines income generation and food access, perpetuating a devastating cycle in which food insecurity is both a cause and consequence of deleterious health outcomes [78]. It is important to recognize that although food insecurity is highly correlated with poverty, the two are not synonymous, e.g. a household may have few assets but ample food. Indeed, studies have shown that food insecurity is associated with worse HIV health outcomes and ART non-adherence even after adjustment for SES [77, 79, 40, 42].

Food Insecurity and Adherence to ART Among Three Populations

HIV-Infected Adults

The possibility that food insecurity could negatively impact adherence among PLHIV was initially described in qualitative studies from low-resource settings in South America and sub-Saharan Africa. For example, a study among Ugandan individuals initiating ART found that lack of

access to food was a key contributor to ART non-adherence and treatment interruptions among individuals on ART, and a barrier to ART initiation among those who had not yet initiated therapy [80]. South African health care providers [17] and PLHIV in South Africa [48] and Kenya [81] also reported food insecurity as one of the most important barriers to ART adherence. In Peru, respondents noted difficulties posed by nutritional requirements and being able to find enough food as barriers to ART adherence [82]. Studies have also shown that food insecurity negatively impacts adherence to treatment for other chronic diseases, such as tuberculosis [83].

Qualitative studies have highlighted four primary mechanisms by which food insecurity impedes adherence to ART in the general adult population of PLHIV (Table 2): (1) Fears or actual experiences of increased hunger on ART when people have to take ART on an empty stomach; (2) Fears or actual experiences of exacerbated side effects of ART in the absence of adequate nutritional intake; (3) The need to make trade offs between getting food or getting medicines leading people to sell or trade medicines for food or other resources; and (4) The need to make trade offs between paying for food and other medical care (including transport costs to clinic) leading to poor retention in medical care.

Intractable hunger with ART has been reported in qualitative studies from a number of African countries, where it has been perceived to be a strong contributor to ART non-adherence [18, 48, 80, 84]. For example, in a questionnaire administered to 71 HIV patients in Rwanda, 76 % participants indicated that "having too much appetite and not enough to eat" reduced adherence [85]. Similarly, in rural Uganda, HIV-infected participants described defaulting from treatment when food was scarce because they could not tolerate the increased hunger they experienced on ART. In addition, some individuals were reluctant to initiate ART in the first place, for fear of experiencing hunger without access to an adequate diet [80]. Increased hunger on ART has been hypothesized to be related to improved appetite after immunologic recovery and decreases in circulating cytokines [86–88].

Adverse side effects of ART taken without food, such as nausea, vomiting and stomach pain, are a second mechanistic link to poor adherence [4, 36]. In qualitative studies in sub-Saharan Africa, PLHIV have complained that taking pills on an empty stomach led to headaches, stomach pain, dizziness, shivers or tremors, loss of energy, fainting, sweating, and rapid heartbeat [48, 80, 84]. This mechanism of worsened ART side effects in the absence of food contributing to ART non-adherence has been reported in a variety of settings including Uganda, Mozambique, and Kenya [80, 81, 89].

A third mechanism is that in the face of limited resources, demands for food may compete with resources needed to procure medicines. Even when clinic consultations are "free," clinical care is not without costs. These include opportunity costs, such as income foregone while traveling far distances to clinics or waiting in long lines for care, as well as expenditures required to receive care, such as payment for transportation to health care facilities. In many settings PLHIV struggle to simultaneously afford food, household expenses (e.g. rent, school tuition), medications, healthcare fees, and transportation costs to the clinic [44, 80, 90]. These competing demands sometimes contribute to trading or selling ART for food or other resources, further compounding problems with adherence. While these mechanisms have not been as well characterized in resource-rich settings, HIV often affects the poorest and most marginalized populations in those settings who face similar competing demands [25, 91, 92].

Quantitative Studies

A number of quantitative studies in resource-rich and -poor settings have substantiated these qualitative findings of an association between food insecurity and non-adherence. For example, in a cross-sectional study among 2,353 HIV-

Table 2 Overview of mechanisms for how food insecurity may contribute to non-adherence

Type of non-adherence	Mechanisms
ART non-adherence	Fear or actual experience of greater hunger on ART without access to an adequate diet
	Fear or actual experience of side effects on ART that are exacerbated in absence of food
	Competing resource demands e.g. food, leads medicines to be sold or traded
Poor retention in medical care	Competing resource demands prevent individuals from travel to clinic because of time or financial constraints
Non-adherence to recommendations for breastfeeding in the context of HIV	Perceived or real problems with breast milk production while experiencing food insecurity
	Competing economic activities prevent mother from being with child to breastfeed per recommendations

infected US veterans, the proportion of those experiencing food insecurity (assessed using the validated Household Food Insecurity Access Scale) increased as adherence, measured by the proportion of time off of ART, decreased [74]. Among a cross-sectional sample of 457 HIV-infected individuals receiving highly active antiretroviral therapy (HAART) in British Columbia, Canada, 71 % were food insecure (using a modified version of the validated Radimer/Cornell Questionnaire), and in unadjusted analyses there was an association between food insecurity and self-reported sub-optimal ART adherence, lower CD4 cell counts, and higher HIV viral loads [39]. In a national cross-sectional survey of 1,809 HIV-infected patients in France, food privation in the household (defined as inability to afford at least one daily meal due to lack of money during the previous 4 weeks, indicated by a single-question response) was significantly associated with increased odds of self-reported ART non-adherence among 613 HIV-infected heterosexual men, but not among heterosexual women ($n = 408$) after adjustment for the financial situation of the household and other covariates [40]. In a cross-sectional study that measured adherence with telephone-based unannounced pill counts among a convenience sample of 268 HIV-infected men and 76 HIV-infected women in Atlanta, food-insecure respondents (per an adapted version of the US Food Security Scale) had substantially reduced odds of ART adherence (defined as taking at least either 80 or 90 % of medications) after controlling for SES-related factors such as education, unemployment, and income [42]. Food insecurity was also associated with barriers to HIV care and treatment, such as unstable housing, lack of transportation, substance abuse, and lack of social support [42].

Fewer quantitative studies have examined the relationship between food insecurity and adherence to ART in resource-poor countries. In a longitudinal study among 134 HIV-infected adults in urban Peru, food insufficiency (defined as lack of enough food in the household in the previous month, according to a single question assessment) was significantly associated with a twofold increase in the odds of suboptimal adherence to ART. Associations held after adjusting for adherence self-efficacy, social support and other confounders, and there was a positive linear relationship between increasing frequency of food insufficiency (never, sometimes, often, almost always) and suboptimal adherence [41]. Inclusion of SES indicators (i.e. low education, unemployment, lack of basic services) in the analysis did not change the effect estimate by >10 % in either direction and was therefore not included in the final multivariate model [41].

A prospective cohort study of 488 HIV patients in rural Zambia indicated that baseline food insecurity was a strong predictor of sub-optimal ART adherence in unadjusted analyses, but when adjusted for factors such as wealth, the effect disappeared [93]. Importantly, they did not use a validated measure of food insecurity, and defined food insecurity as a lower number of meals taken during the "hunger season" than during most of the year, which is likely true for many poor families, even those who are food secure.

In addition to interfering with ART adherence, some data suggests that food insecurity may negatively impact adherence to clinic visits. For example, in a cohort of 458 HIV-infected ART-treated individuals in rural Uganda, mild and moderate food insecurity (assessed by the Household Food Insecurity Access Scale) were associated with missed clinic visits after adjusting for clinical, behavioral and SES confounders. Interestingly, in models where explanatory variables were lagged by 3 months relative to outcomes, severe food insecurity was associated with fewer missed clinic visits [77]. The authors explain that accessing outpatient care is a product of both need for care and means to get care when needed; it is therefore possible that individuals who were severely food secure were less likely to miss outpatient clinic appointments over the long run because they were sicker, and had higher need for care.

Food-related interventions have the potential to interrupt the various pathways through which food insecurity reduces adherence to ART and undermines the health of HIV-infected individuals [16]. Several intervention studies have shown positive impacts of food supplementation on HIV clinical outcomes, adherence to ART, and other treatment recommendations. For example, food supplementation programs in Zambia and Haiti demonstrated that food assistance improves a range of clinical outcomes, including adherence to ART [94–97].

HIV-Infected Pregnant Women and their HIV-Exposed Infants

Pregnant women are more likely to experience greater food insecurity than non-pregnant women because they have greater nutrient demands, less physical ability to obtain and prepare food, and less ability to engage in income-generating labor [98]. Limitations on their movement or physical activity may also be culturally proscribed, further exacerbating food insecurity. Strikingly, there are very few data on how food insecurity negatively impacts adherence to ART and other care recommendations among pregnant women [99]. Yet this population warrants particular attention because non-adherence has implications not only for a woman's health, but also for the health of her children, including the risk of vertical transmission of HIV. Increased food insecurity experienced by pregnant HIV-infected women may impact maternal health and infant care behaviors, including adherence to ART as well as to other healthcare recommendations, e.g. gestational weight gain and breastfeeding practices (Table 2).

Antenatal and postnatal clinical care is critical for preserving the health of HIV-infected women and their infants [100] and antenatal clinic attendance increases the likelihood of clinic-based delivery, a recommendation for HIV-infected mothers [101]. Although care for HIV-infected pregnant women is provided free-of-charge in most parts of the world, food insecurity may impede the receipt of clinical care, as it does in the general HIV-infected adult population, by mechanisms previously discussed. Studies are needed to understand the impacts of food insecurity on access to and retention in antenatal and postnatal care, and whether the effects of food insecurity are distinct from the effects of low SES.

The 2010 WHO guidelines recommend the use of ART prophylaxis during pregnancy for all women, including those who are not eligible for ART for their own health, to reduce the risk of vertical transmission [102], and co-trimoxazole to reduce the risk of chorioamnionitis, prematurity and neonatal mortality [103, 104]. Further, the administration of ART prophylaxis during birth and in the early postpartum period has been demonstrated to reduce the risk of vertical transmission; as such, daily nevirapine or zidovudine in early life is recommended per international guidelines [105]. However, because clinics are the primary source for these medications, and most of these medications are dispensed to women in quantities sufficient for only 1 or 2 months, sporadic antenatal care due to competing resource demands for food can result in an irregular supply of medicines, which impedes sustained adherence to ART [101]. The existence of this relationship should be investigated empirically.

Adequate gestational weight gain is one of the most important modifiable predictors of birth outcomes [106]. Among pregnant HIV-infected women, wasting and low weight gain during pregnancy have been associated with increased mother-to-child transmission [107, 108] and increased risk of pre-term delivery and low birth weight [109]. It is recommended that HIV-infected women gain between 0.3 and 0.5 kg per week [110], yet pregnant women who are food insecure likely have less access to both desired quantities and quality of foods. This is particularly problematic during gestation, a time when most women become more selective about food intake because of nausea and vomiting [111], as they simultaneously need to increase their macronutrient and micronutrient intake. For these reasons, data on how food insecurity impacts gestational weight gain among HIV-infected women are needed.

In terms of safe infant feeding, the 2010 WHO recommendations encourage exclusive breastfeeding (EBF) for the first 6 months of life, even in the absence of ART, unless "environmental and social circumstances are safe for, and supportive of, replacement feeding" [112]. This is based on data showing a greatly elevated risk of vertical transmission associated with mixed feeding (breastfeeding and feeding other foods in the first 6 months of life) compared to EBF for 6 months as well as lower non-HIV morbidity and mortality rates observed among HIV-exposed, exclusively breastfed infants compared to their mixed fed counterparts [113]. However, there is some evidence that mothers experiencing food insecurity feel unable to produce enough breastmilk to exclusively breastfeed for 6 months. In Malawi, for example, women of indeterminate HIV-status experiencing food insecurity felt that their breastmilk production was inadequate and were more likely to supplement their infant with non-breastmilk foods prior to 6 months of age [114]. Similarly, Kenyan [115] and Ugandan [116] HIV-infected mothers experiencing food insecurity felt they were unable to exclusively breastfeed for 6 months. Even when mothers feel able to produce sufficient milk, food procurement activities may necessitate early separation from baby—which can also lead to early mixed feeding, or breastfeeding for shorter time than the 12 months minimally recommended in 2010 by the WHO. It is likely that food insecurity also prohibits a mother's ability to provide adequate nutrition to her children after the weaning period, further exacerbating the negative impacts of food insecurity, but this has not been explicitly evaluated in studies.

In summary, there are numerous ways that food insecurity may impact the ability of caregivers to adhere to recommendations to improve maternal health and reduce vertical transmission among HIV-exposed infants. Yet, there remains a striking dearth of actual data on the relationship of food insecurity to adherence to care and treatment recommendations among pregnant women and their infants. This area would benefit from both longitudinal observational studies as well as intervention studies to see if the mitigation of food security improves women's ability to adhere to guidelines for the care of herself and her HIV-exposed infants.

Pediatric Populations

Since HIV-infected children are reliant on caregivers for both medication and daily meals, children may be especially vulnerable to the potential for food insecurity and other resource constraints to impede adherence to ART. Indeed, food insecurity has now been cited as an important barrier to ART adherence among HIV-infected children in a number of studies in sub-Saharan Africa [63, 66, 67, 117].

Many of the mechanisms for how food insecurity negatively impacts adherence among children are similar to those described above among adults. However, an important difference is that among pediatric populations, one needs to consider both factors that affect children's adherence directly as well as factors that impede the ability of caretakers to provide care that supports adherence; this may be strongly related to the age of the child. For

example, younger children are more reliant on the capacity of caregivers to procure and administer medications, whereas older children may face difficulties in managing treatment around school schedules and concerns about confidentiality [63].

Caregivers in Western Kenya reported that lack of sufficient food posed a challenge to pediatric ART adherence because of the belief that the medicine was too strong to be taken without food or that food was required to mitigate side effects [63]. In Democratic Republic of the Congo, HIV-infected children 8–17 years old similarly reported that side effects were alleviated through food consumption and that they would refuse to take their medicine if there was no food available [67]. The fact that some caregivers are elderly poses some new barriers to adherence not seen among the general adult population of PLHIV. For example, in Zimbabwe, immobility and the inability to work threatens the ability of elderly caregivers to secure enough food and maintain adequate ART for the children in their care [117].

The benefit of food supplementation on adherence has also been observed among children. A food supplementation intervention at a pediatric HIV/AIDS clinic in eastern India improved clinic visit adherence, CD4 counts, and reduced hospitalizations and deaths [118]. Further research is needed to understand the interplay between food insecurity, adherence to ART, and adherence to general care recommendations among HIV-infected children and the extent to which addressing food insecurity among children and their caregivers may contribute to improved pediatric adherence.

Way Forward

The research reviewed provides evidence of strong associations between food insecurity and poor adherence to care and treatment recommendations, and suggests plausible causal mechanisms (Table 2). However, there is a dearth of evidence from well-conducted longitudinal studies or experimental or quasi-experimental trials of interventions to confirm these findings and proposed mechanisms and to guide the development of initiatives in this area [119]. Particularly lacking are rigorous studies on the pathways by which food insecurity may impact adherence among vulnerable sub-populations, specifically, pregnant and lactating women and children.

Qualitative studies focusing on barriers to HIV care and treatment have been instrumental for hypothesis generation and understanding the complex interplay between food insecurity and adherence. In terms of quantitative work, nearly all published epidemiologic studies of food insecurity and ART adherence have been cross-sectional, which limits conclusions about causality. In addition, variability in the definitions and measurements of food insecurity, SES and adherence in these studies has limited comparisons of findings across settings. Furthermore, there is still little evidence on whether food insecurity interferes with adherence to other health recommendations beyond ART among adult and pediatric populations. Ultimately, data from rigorous longitudinal studies are needed to guide the development of interventions for PLHIV, especially during the first 6–12 months after ART initiation [77]. Data from both rigorously evaluated programmatic settings and randomized controlled trials will help to confirm and further refine the postulated causal mechanisms behind poor adherence to ART and thus suggest the most potentially efficacious interventions.

The few studies of the effects of food supplementation on HIV outcomes, including adherence (discussed above), suggest that food supplementation may be a promising approach to improving ART adherence. Nevertheless, there are many unanswered questions surrounding the role of food supplementation both in reducing food insecurity and improving adherence. These include: (1) whether food assistance should be used as an essential emergency intervention for malnutrition or as a longer-term approach to improve response to ART; (2) whether reducing food insecurity actually increases adherence to ART and to other health recommendations; (3) what types of food packages should be used for supplementation (and this will likely differ by country and context); and (4) what the optimal duration of food supplementation is. While food supplementation provides critical nutritional support, it may not fully address all facets of food insecurity (e.g., anxiety about stability of food supplies), and can perpetuate dependency on food aid [94, 95, 120].

Livelihood interventions that aim to sustainably increase food security may be more likely to achieve long-term improvements in adherence to ART. Livelihood intervention strategies typically integrate HIV care with income-generating programs, supporting clients in small-enterprise activities, agricultural production, or animal husbandry [49, 78, 121–124]. These interventions address numerous upstream pathways through which food insecurity negatively impacts health and thus show promise for having positive impacts on HIV/AIDS prevention, care and treatment.

Conclusion

In summary, more than 15 years after the HAART era began, the clinical efficacy of HIV care has never been greater. However, obstacles to adherence continue to undermine both the individual and public health benefits of widespread access to ART. Food insecurity is emerging as one such prominent barrier to ART adherence and to care and treatment recommendations in both resource-rich and -poor settings, and among adult and pediatric populations. While this review has demonstrated that there are clear

associations between food insecurity and poor adherence to HIV care recommendations as well as plausible mechanisms that can explain these correlations, more rigorous evidence is needed from longitudinal studies to determine whether these associations are indeed causal. Additionally, intervention studies are needed to evaluate the mechanisms and extent to which improving food security may lead to improvements in adherence to treatment and care recommendations. Evaluating the effectiveness, sustainability, and cost-effectiveness of various interventions to mitigate food insecurity, thereby improving adherence, will likely maximize the enormous potential impact of ART.

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