Changes in Food Insecurity, Nutritional Status, and Physical Health Status After Antiretroviral Therapy Initiation in Rural Uganda

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Objective: To investigate whether time on antiretroviral therapy (ART) is associated with improvements in food security and nutritional status, and the extent to which associations are mediated by improved physical health status.

Design: The Uganda AIDS Rural Treatment Outcomes study, a prospective cohort of HIV-infected adults newly initiating ART in Mbarara, Uganda.

Methods: Participants initiating ART underwent quarterly structured interview and blood draws. The primary explanatory variable was time on ART, constructed as a set of binary variables for each 3-month period. Outcomes were food insecurity, nutritional status, and PHS. We fit multiple regression models with cluster-correlated robust estimates of variance to account for within-person dependence of observations over time, and analyses were adjusted for clinical and sociodemographic characteristics.

Results: Two hundred twenty-eight ART-naive participants were followed for up to 3 years, and 41% were severely food insecure at baseline. The mean food insecurity score progressively declined (test for linear trend $P < 0.0001$), beginning with the second quarter ($b = -1.6$; 95% confidence interval: -2.7 to -0.45) and ending with the final quarter ($b = -6.4$; 95% confidence interval: -10.3 to -2.5). PHS and nutritional status improved in a linear fashion over study follow-up ($P < 0.001$). Inclusion of PHS in the regression model attenuated the relationship between ART duration and food security.

Conclusions: Among HIV-infected individuals in Uganda, food insecurity decreased and nutritional status and PHS improved over time after initiation of ART. Changes in food insecurity were partially explained by improvements in PHS. These data support early initiation of ART in resource-poor settings before decline in functional status to prevent worsening food insecurity and its detrimental effects on HIV treatment outcomes.

Key Words: food insecurity, antiretroviral treatment, HIV, Uganda, nutrition, physical health status

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INTRODUCTION

Food insecurity is highly prevalent in sub-Saharan Africa, especially among people living with HIV/AIDS, where it is estimated that more than half of HIV-infected individuals are food insecure.[1–3] The food insecurity and HIV/AIDS epidemics are intertwined in a vicious cycle, with each exacerbating vulnerability to and intensifying the severity of the other condition.[4,5] Food insecurity increases vulnerability to HIV infection by driving risky sexual behaviors, contributing to practices that increase mother-to-child transmission, and contributing to general undernutrition and micronutrient deficiencies that impair mucosal integrity and host defenses.[5–8] Among individuals already infected, food insecurity has been associated with worse health outcomes, including reduced adherence to antiretroviral therapy (ART),[9,10] worsened virologic and immunologic responses,[9,11–13] more frequent self-reported opportunistic infections,[1] declines in physical and mental health status,[1,13] and increased risk of mortality.[14] HIV/AIDS, in turn, worsens food insecurity because of death and illness of productive family members, leading to loss of labor, reduced economic capacity, and increased caregiver burden.[4,15–18] Additionally, stigmatized individuals may have more trouble finding work, are less able to rely on social networks for food during times of scarcity, and may have more

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difficulties obtaining loans to alleviate poverty and food insecurity.[4,19,20]

The advent of ART has resulted in large reductions in AIDS-related morbidity and mortality, which may have implications for the overlap between the food insecurity and HIV/AIDS pandemics.[21,22] Some studies from resource-rich settings have shown that physical health status improves considerably shortly after initiation of ART.[23–26] Studies from both resource-rich and resource-poor settings have shown that nutritional status often improves substantially on ART, although the results have been somewhat inconsistent.[27–30] Theoretically, improved physical health should improve functional status and economic productivity, which in turn could lead to improvements in food security and nutritional status. The negative impacts of HIV-related disruptions in social relationships, however, may still hinder food security after ART initiation. There are little data on the impact of ART initiation on food insecurity in any setting, or on possible mechanisms by which ART initiation may contribute to changes in food insecurity.

To address these gaps in the literature, we undertook a longitudinal study to understand the impact of ART initiation on food insecurity, nutritional status [operationalized by body mass index (BMI) and mid-upper arm circumference (MUAC)], and physical health status among HIV-infected individuals initiating ART in rural Uganda. We hypothesized that among ART-naive individuals in rural Uganda, food insecurity will decrease and nutritional status will improve over time after initiation of antiretroviral therapy. We further hypothesized that changes in food insecurity on ART will be mediated primarily as a result of improved physical health status and that changes in nutritional status will be mediated by improvements in physical health status and food insecurity. Understanding the impact of ART use on food insecurity and nutritional status among HIV-infected individuals in sub-Saharan Africa can inform food insecurity programs and policies for earlier initiation of ART in resource poor settings.

METHODS

Participants and Study Design

Participants were recruited from the Uganda AIDS Rural Treatment Outcomes (UARTOs) study, a prospective cohort of HIV-infected individuals initiating ART free of charge at the Mbarara Regional Referral Hospital Immune Suppression Syndrome (ISS) Clinic in Mbarara, Uganda.[31] Participants were eligible for participation if they were about to start ART for the first time, older than 18 years, and lived within 20 km of the ISS Clinic. Beginning in August 2007, measures of food insecurity were added to the UARTO survey instrument with the aim of understanding the impact of food insecurity on HIV/AIDS outcomes. Therefore, all UARTO patients initiating ART after August 2007 were included in the current analysis. Participants were followed until November 2010.

We conducted quarterly assessments using standardized interviewer-administered instruments, detailed anthropometric measurements for nutritional status, and phlebotomy for plasma HIV RNA levels and CD4+ T-cell counts. In our questionnaires, we collected information about sociodemographic and clinical characteristics, including food insecurity and physical health–related quality of life. All surveys were translated and back translated into Runyankole and administered by a native Runyankole speaker. Approval for all study procedures was obtained from ethical review boards at the University of California at San Francisco, Partners HealthCare, and Mbarara University of Science and Technology.

Measures

The primary explanatory variable was time on ART, constructed as a series of indicator variables for each 3-month period subsequent to ART initiation. Our primary outcome, household food insecurity, was measured by the Household Food Insecurity Access Scale (HFIAS), which has been validated in at least 8 countries,[32–34] including sub-Saharan African settings. Questions cover several domains of the experience of food insecurity, including insufficient food intake, insufficient food quality (variety and preferences of type of food), and anxiety and uncertainty about the household food supply. The internal consistency of this measure was high in this sample, with a Cronbach α of 0.91 at the baseline time point. We used 2 measures of nutritional status. BMI was calculated from weight and height measurements (killograms per sqaure meters). Mid-upper arm circumference (MUAC) was measured using a Gulick II tape measure with tensiometer. The study protocol required that at least 2 measures be taken and recorded. If the difference between the first and second measures exceeded a standardized cutoff according to the Anthropometric Standardization Manual at a specific body site, then a third measure was taken and the average of the 2 closest measures was used.[35] Physical health–related quality of life was measured with the Medical Outcomes Study–HIV Health Survey Physical Health Summary (PHS), validated in several sub-Saharan African settings.[26] This measure consists of 35 items grouped into 11 domains, and a higher score reflects a better health-related quality of life.[36] This measure has been correlated with AIDS-related events and has been studied among a variety of patient groups with HIV/AIDS.[37] Social support, examined as an additional possible mediator, was measured using the Social Support Scale,[38] a modified version of the Duke-University of North Carolina Functional Social Support Questionnaire.[39] The scale consists of 10 items related to perceived emotional and instrumental support. Each of the items is scored on a 4-point Likert-type scale, and higher scores reflect greater social support. The Cronbach α was 0.91 at baseline, indicating high internal consistency.

We selected baseline sociodemographic and clinical covariates for adjusted models based on prior literature and theory,[5,13,40,41] including gender, marital status (married or cohabitating vs other), employment status (employed vs unemployed), educational attainment (at least a high school education vs did not complete high school), number of persons in the participant's household, distance to the Mbarara ISS Clinic in hours of travel time, CD4 cell count measured as a continuous variable in 50-cell increments, and positive screen for heavy drinking as measured by the 3-item consumption subset of the Alcohol Use Disorders Identification Test.[42]

To measure household wealth, we used 25 variables denoting household assets and characteristics to create a continuous household asset index following the methodology proposed by Filmer and Pritchett,[43] with higher values representing greater household wealth relative to others in the sample.

Analysis

Data were analyzed with STATA statistical software, version 11.0 (Stata Corporation LP, College Station, TX). We fit multiple linear regression models pooled over observation periods with HFIAS score, BMI, mid-upper arm circumference, and PHS as the linear dependent variables and cluster-correlated robust estimates of variance to account for within-person dependence of observations over time. Estimates were adjusted for potential confounding by sociodemographic and clinical variables measured at baseline. A Wald-type F test was used to assess the joint statistical significance of the time indicator variables. A test for linear trend in the time indicator variables was performed by refitting the adjusted model with duration of ART specified as a continuous variable.

To determine whether changes in food insecurity over time were potentially explained by changes in physical health status, we also included concurrent PHS in the models as a time-dependent variable and then reassessed the estimates and statistical significance of the time indicator variables. Using similar methods, we also investigated (1) whether changes in social support potentially explain changes in food insecurity (in light of prior work showing that higher social support and social capital may be associated with decreased food insecurity)[44–46] and (2) whether changes in food insecurity and/or PHS potentially explain changes in nutritional status.

RESULTS

In total, 257 participants were ART naive at baseline and were eligible for inclusion in the analysis. Of this group, 29 participants were excluded because of having incomplete data on any of our primary outcomes of interest, with a remaining sample of 228 individuals included in the current analysis. Out of the 228 individuals included in our analysis, 8 died and 28 were lost to follow-up. Among the 29 excluded individuals, 6 died and 8 were lost to follow-up. Although there was a statistically significant difference between the included and excluded participants in terms of death and lost to follow-up ($\chi^2 = 17.2$, $P < 0.001$), the included and excluded participants had no statistically significant differences in terms of our key outcomes of interest, including HFIAS, PHS, BMI, and MUAC (*P* values ranged from 0.2–0.9). Depending on their date of enrollment, at the time of this analysis, participants had been monitored for 3 months–3 years after initiation of ART, with a median follow-up time of 1.8 years.

Most participants were women [161 (71%)]. At baseline, the mean age was 34.4 (SD 8.7), 53 participants (23%) had achieved a secondary education, and 101 participants (44%) were married (Table 1). The mean baseline CD4 count was 185.1 (SD = 122.4), and median CD4 count at ART initiation was 161. The mean HFIAS score was 8.8, with 185 participants (81%) categorized as food insecure, 74 (33%) as moderately food insecure, and 97 (43%) as severely food insecure. At baseline, 14% had a BMI < 18.5 kg/m^2, and 11% had MUAC consistent with malnutrition (<22 cm for women, <23 cm for men).

Food insecurity decreased steadily over time after ART initiation (Table 2, Fig. 1). In adjusted analyses, the mean HFIAS score at nearly every time point was lower than the preceding time point, beginning with the second quarter [$b = -1.7$; 95% confidence interval (CI): -2.8 to -0.6] and ending with the final quarter ($b = -6.5$; 95% CI: -10.4 to -2.7). F tests for the joint statistical significance of the time indicator variables and for a linear trend in them were also statistically significant ($P < 0.001$). Of the 86 individuals who were severely food insecure at baseline and provided at least one-years worth of follow-up data, only 36 (42%) remained severely food insecure after one year on ART.

At baseline, the mean PHS was 43.1 (SD = 11.9) and this increased subsequent to ART initiation (Table 3). After statistical adjustment for baseline sociodemographic and clinical variables, the mean PHS was greater at every time point,

TABLE 1. Characteristics of Participants at Baseline (N = 228)

Characteristic	Mean or Percentage (±SD or n)
Sociodemographic characteristics	
Age (yrs)	34.4 (±8.7)
Female	70.60% (161)
Secondary education or higher	23.30% (53)
Marital status	44.30% (101)
Household size	3.4 (±2.8)
Asset index	0 (±2.2)
Time to clinic (min)	51.5 (±40.8)
Alcohol use disorder (male >3, female >2)	13.60% (31)
CD4	185.1 (±122.4)
Food insecurity	
Mean HFIAS score	8.8 (±6.7)
HFIAS quartiles	
Food secure	18.90% (43)
Mild FI	6.10% (14)
Moderate FI	32.50% (74)
Severe FI	42.50% (97)
Physical health status	
MOS-HIV physical health status score	43.4 (±11.9)
Nutritional status	
Mean BMI	21.8 (±3.7)
BMI	
Severely underweight <16.5	1.80% (4)
Underweight 16.5–18.5	11.80% (27)
Normal 18.5–25	72.40% (165)
Overweight 25–30	11.40% (26)
Obese >30	2.60% (6)
Mid-upper arm circumference (MUAC)	26 (±3.2)
Malnourished (MUAC <22 cm males, <23 cm females)	11.00% (25)

FI, food insecurity; MOS-HIV, Medical Outcomes Study HIV Quality of Life survey; SD, standard deviation.

TABLE 2. Time Trends in Food Insecurity (HFIAS) Subsequent to ART Initiation Among Adults in Rural Uganda (N = 228)

	Regression Coefficient (95% CI)		
Characteristics	Adjusted for Sociodemographic and Clinical Covariates Alone	Additionally Adjusted for Physical Health Status	Additionally Adjusted for Social Support
Time on ART (mo)			
3	−0.80 (−2.02 to 0.43)	−0.22 (−1.49 to 1.05)	−0.70 (−1.96 to 0.56)
6	−1.72 (−2.84 to −0.61)*	−0.91 (−2.09 to 0.28)	−1.73 (−2.85 to −0.61)*
9	−2.07 (−3.29 to −0.86)*	−1.20 (−2.52 to 0.99)	−2.08 (−3.29 to −0.87)*
12	−2.32 (−3.59 to −1.05)†	−1.33 (−2.69 to 0.31)	−2.27 (−3.52 to −1.02)†
15	−2.36 (−3.75 to −0.98)*	−1.35 (−2.78 to −0.84)	−2.37 (−3.72 to −1.01)*
18	−2.25 (−3.57 to −0.94)*	−1.11 (−2,54 to 0.32)	−2.26 (−3.55 to −0.96)*
21	−2.51 (−3.96 to −1.17)†	−1.46 (−2.93 to 0.12)	−2.57 (−3.89 to −1.23)†
24	−2.72 (−4.21 to −1.22)†	−1.49 (−3.08 to 0.94)	−2.80 (−4.26 to −1.33)†
27	−3.12 (−5.28 to −0.96)*	−2.19 (−4.33 to −0.50)‡	−3.31 (−5.39 to −1.23)*
30	−3.42 (−5.38 to −1.46)*	−2.42 (−4.54 to −0.31)‡	−4.18 (−6.28 to −2.09)†
33	−4.76 (−8.22 to −1.29)*	−3.55 (−6.70 to −4.17)‡	−4.88 (−8.06 to −1.71)*
36	−6.51 (−10.36 to −2.65)*	−5.28 (−10.10 to −0.46)‡	−6.16 (−9.70 to −2.62)*
Covariates			
Age	0.51 (0.08 to 0.93)‡	0.45 (0.04 to 0.86)‡	0.49 (0.07 to 0.90)‡
Sex (female)	2.89 (1.70 to 4.07)†	2.67 (1.54 to 3.82)†	2.47 (1.33 to 3.61)†
Secondary education or higher	−1.01 (−2.31 to 0.28)	−0.93 (−2.3 to 038)	−0.72 (−2.0 to 0.57)
Married	1.25 (−0.04 to 2.53)	1.15 (−0.12 to 2.42)	1.16 (−0.76 to 2.41)
Household size	−0.16 (−0.36 to 0.05)	−0.17 (−0.38 to 0.34)	−0.13 (−0.33 to 0.07)
Asset index	−0.56 (−0.90 to −0.23)*	−0.51 (−0.84 to −0.17)*	−0.53 (−0.86 to −0.19)*
Time to clinic (h)	0.23 (−0.48 to 0.94)	0.25 (−0.46 to 0.96)	0.18 (−0.54 to 0.90)
Heavy drinking	−0.34 (−1.85 to 1.17)	−0.37 (−1.81 to 1.06)	−0.38 (−1.82 to 1.06)
CD4	0.03 (−0.44 to 0.49)	0.08 (−0.37 to 0.52)	−0.00 (−0.44 to 0.44)
Physical health status	—	−0.11 (−0.16 to −0.67)†	—
Social support	—	—	−2.48 (−3.46 to −1.50)†
Constant	3.50	—	—

*$P < 0.01$.
†$P < 0.001$.
‡$P < 0.05$.

beginning with the first quarter (b = 5.2; 95% CI: 3.1 to 7.4) and ending with the last quarter (b = 11.9; 95% CI: 3.1 to 20.6). F tests for the joint statistical significance of the time indicator variables and for a linear trend in them were statistically significant ($P < 0.001$).

Nutritional status improved over time after ART initiation (Table 3). In adjusted analysis, BMI increased at nearly every time point, beginning with the second quarter (b = 0.7; 95% CI: 0.2 to 1.1) and ending with the last quarter (b = 5.3; 95% CI: 0.1 to 10.5). Similarly, MUAC increased at nearly every time point, beginning with the second quarter (b = 0.9; 95% CI: 0.4 to 1.4) and ending with the last quarter (b = 1.4; 95% CI: 0.1 to 2.7). F tests for the joint statistical significance of time indicator variables and for a linear trend in them for both nutritional outcomes were also statistically significant ($P < 0.001$).

Improvements in physical health status partially explained the decreases in food insecurity over time. When PHS was added to the regression models examining trends in food insecurity over time, the time indicator variables were no longer statistically significant as a group (P = 0.37) and the magnitude of the regression coefficients decreased by approximately 40% (Table 2, column 3). Conversely, when social support was added to the regression models examining trends in food security over time, the time indicator variables were still statistically significant as a group, and the regression coefficients were not attenuated, suggesting no mediation (Table 2, column 4). For BMI or MUAC, when either PHS or food insecurity were added to the models, the time indicator variables were still statistically significant as a group, and the regression coefficients were only minimally attenuated suggesting minimal mediation (Table 4, columns 2 and 4).

DISCUSSION

In this analysis of data from people living with HIV/AIDS initiating ART in rural Uganda, we found that food insecurity decreased and nutritional status increased after initiation of ART. Physical health status also improved, and changes in physical health status partially explained the observed trends in food insecurity but not in nutritional status. These findings have several important implications for food-insecurity programming and for policies on early initiation of ART in resource poor settings.

The striking declines in food insecurity that we observed subsequent to ART initiation are of substantive importance

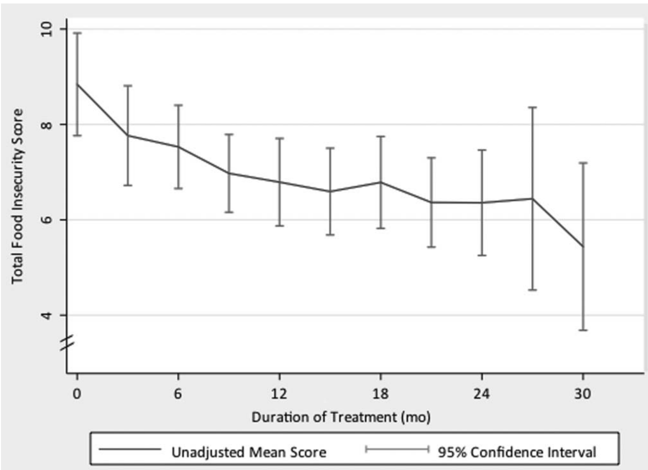

FIGURE 1. Unadjusted trends in food insecurity after initiation of ART.

given the high prevalence of food insecurity among HIV-infected individuals, as well as the known negative impacts of food insecurity on HIV/AIDS morbidity and mortality.[1,2,11,14] HIV/AIDS devastates affected households economically, by debilitating prime-working age household members and by increasing out-of-pocket medical expenses and caregiver burden.[4,15,16,20] Our results suggest that ART may be able to reverse some of these negative trends in food insecurity and are consistent with recent work in India showing substantial improvements in employment and income within the first 2 years after ART initiation[47] with a study in Kenya showing a 20% increase in the likelihood of being employed, and a 35% increase in hours worked within 6 months after ART initiation.[48] The attenuation of food insecurity on ART seen in this study also highlights that a substantial proportion of food insecurity among HIV-infected individuals in the region is likely HIV related.

TABLE 3. Time Trends in Physical Health Status (MOS-HIV) Subsequent to ART Initiation among Adults in Rural Uganda (N = 228)

Characteristics	Regression Coefficient (95% CI)
Time on ART (mo)	
3	5.24 (3.10 to 7.39)*
6	7.18 (5.08 to 9.27)*
9	8.4 (6.19 to 10.62)*
12	9.19 (7.10 to 11.32)*
15	9.47 (7.26 to 11.68)*
18	10.24 (8.02 to 12.45)*
21	10.35 (8.24 to 12.46)*
24	11.34 (9.23 to 13.45)*
27	8.44 (4.82 to 12.05)*
30	9.28 (5.87 to 12.69)*
33	10.91 (6.12 to 15.71)*
36	11.86 (3.09 to 20.61)†
Covariates	
Age	−0.51 (−0.98 to −0.04)‡
Sex	−2.2 (−4.07 to −0.34)‡
Secondary education or higher	0.18 (−1.92 to 2.28)
Married	−0.97 (−2.68 to 0.75)
Household size	−0.12 (−0.4 to 0.17)
Asset index	0.52 (0.09 to 0.94)‡
Time to clinic (h)	0.08 (−1.0 to 1.17)
Heavy drinking	−0.23 (−3.16 to 2.7)
CD4	0.47 (−0.05 to 0.98)
Constant	46.53

*$P < 0.001$.
†$P < 0.01$.
‡$P < 0.05$.

Our findings related to changes in physical health status for individuals on ART are consistent with studies from resource-rich settings that found substantial improvements in physical health status after initiation of ART, although these results have not been entirely consistent, and prior studies on this topic have been limited by shorter length of follow-up.[23–25,49,50] Our findings add to the literature by suggesting that these trends also apply to resource poor settings[26,51] and over longer follow-up durations.[24] Similarly, although our findings that nutritional status improves on ART are supported by previous studies, results have been inconsistent in different populations and settings, with weight loss and wasting persisting on ART among certain groups.[27–30]

The mechanisms underlying the changes in food insecurity remain unclear, but we hypothesized that improved physical health status contributes to improved food security by earlier return to work and engagement in food-generating activities. In our analysis, the time trend in food insecurity was no longer statistically significant after the addition of PHS to the model, consistent with this hypothesis. This finding fits with those of a qualitative study in Uganda suggesting that adherence to ART may be accompanied by decreased food insecurity as a result of improved physical health and ability to work.[10] Future studies should further evaluate this hypothesis by including changes in work status as a possible mediator of trends in food security. A second channel through which ART may decrease food insecurity is through social reintegration resulting in enhanced ability to draw on social networks for assistance during times of shortage.[19,41,52] We investigated whether changes in social support on ART partially explained the decreases in food insecurity on ART and saw no evidence of mediation by social support. In our analysis, improvements in measures of nutritional status did not seem to be mediated by improved physical health status or food insecurity as measured by the food security scale, suggesting other mechanisms such as the amelioration of HIV-associated wasting with suppressed viral loads on ART or dietary improvements, which are required for regaining lost tissues and are not well reflected in the food security scale. Future studies should examine these mechanisms more fully to help elucidate the pathways through which nutritional status improves on ART.

Our findings have several important policy implications. In countries with increasing availability of ART, maximizing quality of life and nutritional status are becoming increasing priorities as individuals live longer.[51,53] In view of the marked decreases seen in food insecurity and

TABLE 4. Time Trends in Nutritional Health Status Subsequent to ART Initiation Among Adults in Rural Uganda (N = 228)

	Regression Coefficient (95% CI)			
	Body Mass Index		Mid Upper Arm Circumference	
Characteristics	Adjusted for Sociodemographic and Clinical Covariates Alone	Additionally Adjusted for Food Security and Physical Health Status	Adjusted for Sociodemographic and Clinical Covariates Alone	Additionally Adjusted for Food Security and Physical Health Status
Time on ART (mo)				
3	0.27 (−0.18 to 0.72)	0.22 (−0.31 to 0.76)	0.46 (−0.02 to 0.94)	0.31 (−0.20 to 0.81)
6	0.67 (0.22 to 1.11)*	0.53 (0.02 to 1.03)†	0.91 (0.44 to 1.38)‡	0.67 (0.18 to 1.17)*
9	1.0 (0.53 to 1.47)‡	0.87 (0.32 to 1.41)*	1.15 (0.65 to 1.64)‡	0.95 (−0.42 to 1.48)*
12	1.04 (0.55 to 1.53)‡	0.87 (0.32 to 1.41)*	1.43 (0.78 to 2.08)‡	1.20 (0.51 to 1.90)*
15	1.27 (0.75 to 1.80)‡	1.14 (0.55 to 1.72)‡	1.13 (0.61 to 1.65)‡	0.90 (0.36 to 1.44)*
18	1.39 (0.86 to 1.92)‡	1.20 (0.55 to 1.85)‡	1.17 (0.65 to 1.68)‡	0.88 (0.31 to 1.45)*
21	1.18 (0.55 to 1.81)‡	0.99 (0.36 to 1.62)*	1.26 (0.73 to 1.80)‡	0.96 (0.39 to 1.52)*
24	0.93 (0.25 to 1.61)*	0.78 (0.11 to 1.45)†	0.91 (0.32 to 1.50)*	0.60 (−0.01 to 1.21)
27	0.47 (−0.60 to 1.53)	0.45 (−0.66 to 1.57)	0.91 (0.03 to 1.79)†	−0.79 (−0.16 to 1.74)
30	1.46 (0.31 to 2.61)†	1.35 (0.24 to 2.46)†	1.42 (0.42 to 2.43)*	1.22 (0.24 to 2.19)†
33	2.07 (−0.25 to 4.39)	1.98 (−0.30 to 4.26)	1.48 (−0.79 to 3.76)	1.26 (−1.02 to 3.53)
36	5.32 (0.13 to 10.52)†	5.27 (0.35 to 10.15)†	1.4 (0.14 to 2.65)†	1.21 (0.06 to 2.37)†
Covariates				
Age	0.18 (−1.64 to 0.52)	0.18 (−0.16 to 0.51)	−0.05 (−0.26 to 0.15)	−0.03 (−0.23 to 0.17)
Sex (female)	2.99 (2.07 to 3.91)‡	2.96 (2.08 (3.83)‡	1.03 (0.34 to 1.78)*	1.06 (0.33 to 1.79)*
Secondary education or higher	0.42 (−0.69 to 1.52)	0.46 (−0.65 to 1.58)	0.69 (−0.29 to 1.67)	0.67 (−0.31 to 1.65)
Married	−0.41 (−1.28 to 0.46)	−0.43 (−1.33 to 0.46)	−1.0 (−0.81 to 0.62)	−0.04 (−0.75 to 0.66)
Household size	−10.1 (−0.29 to 0.08)	−0.10 (−0.28 to 0.09)	0.01 (−0.11 to 0.14)	0.02 (−0.11 to 0.14)
Asset index	0.16 (−0.08 to 0.4)	0.17 (−0.07 to 0.41)	0.14 (−0.05 to 0.33)	0.14 (−0.05 to 0.33)
Time to clinic (h)	−0.23 (−0.77 to 0.3)	−0.23 (−0.77 to 0.30)	−0.04 (−0.57 to 0.48)	−0.06 (−0.60 to 0.47)
Heavy drinking	0.19 (−1.26 to 1.64)	0.21 (−1.24 to 1.66)	0.08 (−0.98 to 1.15)	0.18 (−0.90 to 1.25)
CD4	0.01 (−0.31 to 0.34)	−0.00 (−0.33 to 0.32)	−0.04 (−0.32 to 0.24)	−0.04 (−0.32 to 0.23)
Physical health status	—	0.18 (−0.17 to 0.53)	—	0.03 (−0.00 to 0.05)
Food security (HFIAS continuous)	—	0.29 (−0.03 to 0.09)	—	0.01 (−0.03 to 0.06)
Constant	18.93	17.99	25.12	23.70

*$P < 0.01$.
†$P < 0.05$.
‡$P < 0.001$.

improvements in nutritional status after ART initiation, programs aimed at decreasing food insecurity among HIV-infected individuals should consider earlier initiation of ART as part of their strategy. Although important barriers still exist for scaling up ART to reach all currently eligible individuals, recent studies have also shown that initiating ART at CD4 counts higher than current guidelines (≥350) show substantial benefits in terms of reducing morbidity and mortality among HIV-infected individuals and preventing secondary HIV transmission.[54–56] Our study also supports recent findings from a study in Malawi showing that prompt ART after an outpatient therapeutic feeding program for children improved nutritional recovery compared with individuals who did not receive prompt ART.[57] Future studies should also evaluate benefits of ART initiation on food insecurity, nutritional status, and physical health status among individuals with higher baseline CD4 cell counts.

Our findings should not be interpreted to mean that ART alone is sufficient to ensure adequate food and nutrition for HIV-infected patients. Even after 2 years on ART, a large proportion of the participants in our study were still food insecure. Other studies have shown that food insecurity and malnutrition are still highly prevalent among HIV-infected individuals stably on ART.[10,58] A recent study from Zambia and Kenya similarly reported that livelihoods and economic security still lag among individuals on ART.[59] Among individuals stably on ART, food insecurity is still associated with depression,[60] worse immunologic, and virologic outcomes, ART nonadherence, higher incidence of serious illness, and mortality.[1,9,12–14] These data support that ART treatment alone is insufficient for fully reversing the negative impacts of food insecurity on HIV/AIDS morbidity and mortality, and that in many settings interventions to improve food security and nutritional support are urgently needed regardless of timing of ART initiation.

Because food security, nutritional status, and physical health status were most compromised during the early phases of ART initiation among participants in our study, these findings lend support to claims by policymakers and program developers that provision of food and nutritional support may be most critical during the earlier phases of ART initiation, when health status is most compromised and engagement in livelihood programs may be more challenging.[61] This hypothesis requires further testing in controlled trials. Small trials from Haiti and Uganda have shown significant improvements in food security, nutritional status, adherence, and engagement in care among individuals receiving food supplementation during the first 12 months after ART initiation.[62,63] The optimal strategy to simultaneously reduce HIV/AIDS morbidity and improve food insecurity likely involves better integration of programs aimed to reduce food insecurity with HIV/AIDS treatment programs.

This study had several limitations. First, we did not have access to a comparison group that was not using ART. The observed trends in food security and nutritional or physical health status could theoretically be explained by secular trends over the 3-year period such as engagement in clinical care and associated programs. Yet, food prices have increased 50% in recent years in Uganda, suggesting higher, rather than lower, vulnerability to food insecurity.[64] In addition, in our sample, less than 1% of participants were receiving governmental or nongovernmental food aid either at baseline or during follow-up, suggesting that increased access to food aid is unlikely to account for the observed trends. Second, while there were no differences between included and excluded individuals in terms of our key outcomes of interest, we can not rule out that attrition from the cohort by some of the sickest and most food-insecure participants may have biased our findings away from the null. Third, assessment of mediation with the analytic strategy used in our analysis is subject to the assumptions that: (1) there is no unmeasured confounding, including confounding of the relationship between the mediator and the outcome when conditioning on the mediator, (2) the direction of causality is from physical health status to food insecurity as discussed above, and (3) there is no correlation of measurement errors for food insecurity and physical status, both of which were measured by self-report. If people who over-report food insecurity also over-report difficulties with physical health, this could bias our estimate of the extent to which improved physical health mediates the observed trends in food insecurity away from the null.[65–67] In addition, the small sample size may make it more difficult to fully assess mediation in this study.

In conclusion, we found that among HIV-infected individuals in rural Uganda, food insecurity declined and nutritional status improved continuously subsequent to initiation of ART. Changes in food insecurity, but not nutritional status, were largely explained by improvements in physical health status. Because food insecurity is associated with worse HIV health outcomes and increased risk of HIV transmission, our data further bolster the rationale for early initiation of ART in resource-poor settings coupled with measures to improve food and nutrition security.

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