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ORIGINAL PAPER

Longitudinal Relationship Between Food Insecurity, Engagement in Care, and ART Adherence Among US Women Living with HIV

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Abstract

Food insecurity disproportionately affects people with HIV and women in the United States (US). More evidence is needed to understand the interplay between levels of food insecurity and levels of antiretroviral therapy (ART) adherence over time, as well as how food insecurity relates to engagement in HIV care. We used random effects models with longitudinal data from the US Women's Interagency HIV Study to estimate the (1) adjusted associations of current and 6-month lagged food security with ART adherence categories (n = 1646), and (2) adjusted associations of food security with engagement-in-care (n = 1733). Very low food security was associated with a higher relative risk of ART non-adherence at prior and current visits compared with food security, and this association increased across non-adherence categories. Very low food security was associated with lower odds of receiving HIV care and higher odds of a missed visit. Food insecurity among US women with HIV is associated with poorer engagement in care and degree of ART non-adherence over time.

Keywords Women · Food security · Nutrition · Adherence · Engagement in car

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Introduction

Sustained adherence to antiretroviral therapy (ART) and engagement in care is crucial to achieve HIV viral suppression [1, 2]. Viral suppression in turn leads to dramatic reductions in morbidity and mortality [3–5], and virtually eliminates risk of HIV transmission [6, 7]. Identifying modifiable factors that may undermine ART adherence and engagement in HIV care is therefore critical to achieve individual and public health benefits of ART. Factors that may contribute to low adherence in vulnerable populations are especially important to identify given the persistence of HIV health inequities along lines of race, income and gender [8–10].

Food insecurity is defined as having limited or uncertain availability of nutritionally adequate, safe foods, or the inability to acquire personally acceptable foods in socially acceptable ways [11], and is highly prevalent among people living with HIV [12–15]. In the United States (US), food insecurity disproportionately affects women, Black/African American and Hispanic/Latinx households [16], as well as people living with HIV [17, 18].

Over the past decade, food insecurity has emerged as a prominent contextual barrier to adherence to HIV treatment and care in both resource-rich [17, 19–26] and resource-limited settings [14, 27–32], yet meaningful gaps in evidence remain. While studies of food insecurity and ART adherence have found associations at various thresholds of adherence considered dichotomously (including 80%, 90% and 95% adherence), none have investigated the patterning of associations with food insecurity across different degrees of non-adherence. In addition, understanding how the timing and persistence of food insecurity interplays with adherence difficulties can help to illuminate the dynamic relationship between food insecurity and adherence. Identifying how food insecurity is related to adherence over time and across degrees of non-adherence can help identify the priority population, timing and duration of food security interventions most likely to improve adherence. Finally, while a growing number of studies link food insecurity with engagement in HIV care, and particularly with loss-to-follow-up and care retention, these studies tend to be relatively small and localized (i.e. tied to a city, region or hospital) [25, 26, 30–35], or focus on a targeted population such as hospitalized patients with co-occurring substance use [24].

To advance scientific understanding of the relationship between food insecurity, ART adherence and engagement in HIV care, we conducted a longitudinal study in a national sample of women living with HIV in the US. We hypothesized that prior- and current-visit food insecurity would each be independently associated with higher ART non-adherence, and that food insecurity persisting over the prior and current study visits would have the greatest association with non-adherence compared to food insecurity that was not persistent or non-existent. We also hypothesized that the association between food insecurity with non-adherence would vary by the degree of non-adherence, with stronger associations at lower adherence levels. Finally, we hypothesized that food insecurity would be associated with poor engagement in HIV care, including not receiving HIV care and missing routine HIV visits.

Methods

Data and Population

Data for this study are from the Women's Interagency HIV Study (WIHS) (now known as the MACS-WIHS Combined Cohort Study) [36], the largest ongoing prospective cohort study of HIV among women in the US. WIHS includes both women living with HIV and sero-negative controls, reflecting the age and race profiles of US women living with HIV [37, 38]. Biological, clinical, sociodemographic and behavioral data were collected every six months in 9 sites: Bronx, NY; Brooklyn, NY; Washington, D.C.; Chicago, IL; San Francisco, CA; Chapel Hill, NC; Miami, FL; Birmingham, AL/Jackson, MS; and Atlanta, GA. Assessments included interviews, physical exams, and laboratory tests. Participants provided written informed consent and were compensated for participation. This study was approved by the Institutional Review Board at each study site's institution and by the WIHS Executive Committee. After the end of our study, WIHS was combined with the Multicenter AIDS Cohort Study (MACS), renamed the MACS-WIHS Combined Cohort Study, and now includes both men and women.

The Food Insecurity Sub-Study was implemented in the WIHS from 2013 to 2016 to investigate the role of food insecurity on HIV-related health among women. The Food Insecurity Sub-Study added data on comprehensive measures of food security, dietary intake, household savings, HIV stigma, and food support among all WIHS women. The first sub-study visit for WIHS women started in 2013; the median number of visits completed was 5 (interquartile range 3, 6) out of a maximum of six study visits. There were 8336 person-visits among women living with HIV, of which 1807 unique women comprising 7523 person-visits (90%) reported taking ARTs. Among these women, food insecurity data was available for 1687 women comprising 7427 person visits; i.e., food insecurity data was missing among 1.3% of all eligible person-visits. Thus the analytic sample for the adherence analysis included 1687 unique women currently prescribed and reported taking ART; while the analytic sample for the engagement in care analysis included 1733

unique women living with HIV. Observations for any study visit attended in the study window from 2013 to 2016 were included; a person-visit with missing data on at least one variable was excluded.

Measures

Outcome Variables

Our primary outcome was self-reported ART medication adherence in the previous six months, assessed at each of six biannual WIHS visits in our study period. Participants on ART were asked how often they took their antiretroviral medications as prescribed over the past six months (100%, 95–99%, 75–94%, or < 75% of the time, or "I haven't taken any of my prescribed medications"). To characterize the different levels of non-adherence, we created a 4-level categorical variable combining the final two categories into a < 75% category: Perfect adherence (100%), mild-non-adherence (95–99%), moderate non-adherence (75–94%), and severe non-adherence (< 75%). We analyzed the associations between food insecurity and different thresholds of adherence available in the data for several reasons. Self-reported adherence is predictive of viral suppression [39, 40] and 95% is a common cut-off for non-adherence associated with poor HIV outcomes. Adherence < 75% is an additional threshold that has been found to significantly increase the risk of drug resistance [41]. Finally, we considered the full spectrum of non-adherence as a behavioral outcome nested within the broader concept of self-management [42], with importance beyond its direct, immediate clinical impact linked to any particular threshold. For instance, adherence has been linked both conceptually [42] and empirically [43] to patient activation, a key component of self-management, which may relate to contextual factors such as food insecurity across the full adherence gradient. Thus, non-adherence at any level–even one of sub-clinical importance (e.g., 95–99%) may signal possible challenges to optimal self-management beyond medication taking behaviors (e.g., following doctor recommendations, comorbidity management) [44] which may be affected by food insecurity.

We assessed secondary outcomes related to engagement in HIV care, measured by two variables: (1) self-report of any HIV-care visit in the previous 6 months [39] and (2) self-reported missed clinic visits (i.e. missing at least one HIV-care visit that was not rescheduled in the previous 6 months). These measures were available annually (i.e. for 3 visits) rather than biannually.

Explanatory Variable

Food security was assessed using the 18-item US Department of Agriculture (USDA) Household Food Security Survey Module (HFSSM). The HFSSM is a validated scale [45] supported by ethnographic work [46–48] and is used as the reference measure of population food security in the US [49]. Domains of food insecurity covered by the HFSSM include uncertainty about food supplies, inadequate diet quality, and food insufficiency at the household level due to inability to afford food over the previous 6 months. We used the HFSSM scoring algorithm to categorize individuals as having high, marginal (some uncertainty about food supplies, but little or no change in diet or reduced intake), low (reduced diet quality, but little or no reduced food intake), or very low food security (disrupted eating patterns and reduced food intake). Cronbach's alpha for the HFSSM in our sample was 0.88, indicating high internal consistency.

Covariates

Based on our previous research and the literature, we included as potential confounders the following fixed covariates: race/ethnicity (non-Hispanic white (reference), non-Hispanic Black, Hispanic or other); high school education (vs. < high school) and CD4 nadir (continuous). We also included the following time-updated covariates as potential confounders: age at visit (years, continuous); annual household income ($12,000 or less (reference), $12,001–$24,000, $24,001–$36,000, $36,001–75,000, > $75,000); health insurance status (any, including public and private, vs. none); time on ART (years, continuous); illicit substance use, defined as self-reported cocaine, crack, heroin, methamphetamine, hallucinogens, club drugs, non-prescribed narcotics, or any other illicit recreational drugs since last visit not including marijuana (vs. none); heavy drinking, defined as > 7 alcoholic drinks per week (vs. ≤ 7) [50]; and any household dependents under age 18 (vs. none) [51]. No covariates were lagged as these were not posited to be consequence of food insecurity. We also assessed ART use defined as self-reporting using ARV medications since the last study visit.

Analysis

To understand the independent association of food insecurity with non-adherence, we used longitudinal multinomial logistic regression with the 4-category adherence variable as the outcome and food insecurity as the explanatory variable, controlling for covariates and using complete case analysis. The resulting adjusted relative-risk ratios (RRRs) [52–54], as described in our previous published work [55], are interpreted as the association of food insecurity with each non-adherence category (< 75%, 75–94%, and 95–99% adherence) versus 100% adherence. All regressions included random effects to allow for unexplained individual-level variation. First, we modeled adherence and food insecurity at

the current visit. Next, we regressed adherence on food insecurity at the current and prior visit simultaneously, yielding independent associations of current and prior food insecurity with adherence (the Pearson's correlation coefficient between current and prior food insecurity was 0.57). We calculated the association of persistent food insecurity (i.e., over two consecutive visits) with adherence by summing the unexponentiated adjusted regression coefficients for the current and prior visits. For these analyses, we limited our analytic sample to women who reported taking ART since the last study visit. Finally, we conducted two sensitivity analyses to take into account the possible effects of clinical status: (1) in addition to controlling for CD4 nadir as in the original models, we re-ran models including time updated CD4 count as a covariate, and (2) we stratified our models by CD4 status (≥ 200 cells/μL vs. < 200). A final set of sensitivity analyses adjusted for calendar time (year and, separately, month-year) to account for possible secular trends that could confound the relationship between food insecurity and adherence during the study period.

To investigate the association between food insecurity and engagement in HIV care, we modeled the association between food insecurity and two outcomes: (1) received HIV care, and (2) missed HIV care visits. We used logistic regression with random effects and included food insecurity assessed concurrently with the outcomes, i.e. food insecurity and engagement in care were assessed at the same study visit and have the same 6-month recall period. We did not model the lagged relationship between food insecurity and HIV care engagement in our main models because these outcomes are only collected annually, and we considered a one-year lag to be too long to be meaningful. For example, qualitative work suggests that people living with HIV who are currently food-insecure may miss current HIV appointments because they are hungry and/or need to spend time or resources getting food [56]. Models were stratified by ART status in recognition that ART influences engagement in HIV care in unique ways, and food insecurity may play a substantively different role in engagement in HIV care depending on ART status. For analyses of engagement in care, we included all women with HIV. All analyses were conducted using Stata 14 (College Station, TX: StataCorp LP).

Results

We analyzed longitudinal data on 1687 unique women reporting ART use in the previous 6 months and 294 women who did not report ART use in the previous 6 months. Forty-three percent of women on ART and 49% of women not on ART were food insecure. Among women on ART, median age was 48 years, 70.8% identified as non-Hispanic Black/African American, and over half had an annual household income under $12,000. Women not on ART were more likely to have household income under $12,000 per year, identify as Black/African American, and have child dependents compared to women on ART. About 1 in 10 women on ART reported illicit substance use and/or heavy drinking since the last study visit, compared to almost 2 in 10 women not on ART.

At baseline, 29.6% of women on ART reported mild non-adherence (95–99%), 12.3% reported moderate non-adherence (75–94%), and 5.2% reported severe non-adherence (< 75%) (Table 1). Among women on ART, 92.6% reported receiving HIV care in the previous 6 months and 18.1% reported missing at least one HIV care visit, compared to 67.2% and 26.6% of women not on ART.

ART Adherence

ART adherence models included 1646 unique women on ART (7430 person visits), with 41 women on ART excluded due to missing data on at least one variable. These women did not systematically differ from women who were included in the analysis on key demographic variables. At baseline, women on ART with perfect adherence had higher food security (Table 1). Both illicit substance use and heavy drinking at baseline were close to 20 percentage points higher among women with severe non-adherence, compared to women with perfect adherence ($p < 0.001$).

Mild Non-adherence

Marginal (RRR = 1.67; 95% confidence interval [CI] 1.25, 2.23), low (RRR = 1.61; 95% CI 1.18, 2.19), and very low (RRR = 3.07; 95% CI 2.07, 4.55) food security at the *current visit* were associated with greater relative risk of mild non-adherence, compared to high food security at the current visit (all $p < 0.01$) (Table 2). Independent of current food security, low and very low food security at the *prior visit* were associated with 1.36 (95% CI 1.00, 1.84) and 1.60 (95% CI 1.11, 2.31) higher relative risk of mild non-adherence (both $p < 0.05$), compared to high food security at the prior visit. Persistent marginal, low, or very low food security at both the current and prior visit (Table 3) was associated with 1.91 (95% CI 1.27, 2.86; $p < 0.01$), 2.18 (95% CI 1.43, 3.33; $p < 0.001$), and 4.91 (95% CI 3.03, 795; $p < 0.001$) greater relative risk of mild non-adherence, respectively, compared to women who were food-secure at both visits, exhibiting a dose–response relationship.

Moderate Non-adherence

Compared to high food security, marginal (RRR = 2.05, 95% CI 1.17, 3.58; $p < 0.05$), low (RRR = 2.66; 95% CI

Table 1 Baseline characteristics by ART status and ART adherence category (n = 1981)

	On ART	Not on ART	On ART, by adherence %				
			100% (perfect adherence)	95–99% (mild non-adherence)	75–94% (moderate non-adherence)	< 75% (severe non-adherence)	x^2 p-value
	1687	294	*891 (53.0%)*	*497 (29.6%)*	*206 (12.3%)*	*88 (5.2%)*	
Food security, %							
High	57.0	51.0	62.9	51.7	47.1	50.0	< 0.001
Marginal	15.4	18.4	12.9	17.5	17.0	25.0	
Low	14.7	12.9	14.4	15.5	14.6	14.8	
Very low	12.9	17.7	9.9	15.3	21.4	10.2	
In HIV care, previous 6 mo	92.6	67.2	93.8	93.6	86.0	78.6	< 0.001
Missed visit, previous 6 mo	18.1	26.6	8.8	16.5	22.1	37.7	< 0.001
Age at visit[a]	48.3 (41.4, 54.2)	45.6 (37.1, 51.4)	48.9 (42.3, 54.6)	48.6 (40.9, 54.4)	46.0 (40.3, 52.8)	45.6 (37.9, 50.7)	< 0.001[d]
Race/ethnicity, %							
White, non-Hispanic	11.3	7.5	10.7	14.7	7.3	8.0	0.034
Hispanic	14.9	11.9	15.6	15.9	10.2	13.6	
Black/African American, non-Hispanic	70.8	77.6	70.7	66.0	80.1	76.1	
Other	3.0	3.1	3.0	3.4	2.4	2.3	
HH income (annual), %							
< $12,000	52.9	62.2	56.2	46.6	52.8	55.4	0.01
$12,001–24,000	22.4	17.0	23.0	23.0	19.1	20.5	
$24,001–$36,000	11.1	8.1	9.9	12.0	13.6	13.3	
$36,001–75,000	8.9	8.5	7.8	11.2	10.1	6.0	
$75,001	4.7	4.2	3.3	7.3	4.5	4.8	
≥ High school education, %	67.1	62.5	64.8	72.0	65.1	67.1	0.047
Has health insurance, %	94.2	85.4	94.1	94.6	94.2	95.5	0.94
Has child dependents, %	35.9	49.0	32.0	39.6	40.3	44.3	0.004
Time on ART[l]	8.0 (3.0, 14.7)	0 (0, 9)	7.2 (2.7, 14.5)	8.4 (3.2, 14.6)	10.8 (3.4, 15.2)	9.4 (3.5, 14.9)	0.005[d]
CD4 nadir[a]	279 (157, 414)	388 (245, 540.5)	283 (169, 419)	278 (147, 409)	265 (139, 387)	279 (190.5, 394)	0.26 [d]
Illicit substance use[b], %	10.4	19.1	5.7	11.9	19.4	28.4	< 0.001
Heavy drinker[c], %	11.7	19.1	8.9	12.7	14.1	28.4	< 0.001

[a]Median and interquartile range shown

[b]Illicit drugs defined as crack, cocaine, heroin, methamphetamines, non-prescribed methadone, hallucinogens, club drugs, and non-prescribed prescription drugs

[c]More than 7 drinks per week

[d]Prob > F

1.47, 4.79; p < 0.01), and very low (RRR = 6.99, 95% CI 3.40, 14.36; p < 0.001) food security at the *current visit* were associated with greater relative risk of moderate non-adherence. Independent of associations with current food security, marginal, and very low food security at the *prior visit* were also associated with 2.23 (95% CI 1.32, 3.78; p < 0.01) and 2.20 (95% CI 1.11, 4.33; p < 0.05) greater

Table 2 Longitudinal associations between food insecurity and ART adherence categories from a multinomial logistic regression model (n = 1646)[a]

	Mild non-adherence (95–99%)	Moderate non-adherence (75–94%)	Severe non-adherence (≤ 75%)
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Food security at current study visit			
High	Ref (1.0)	Ref (1.0)	Ref (1.0)
Marginal	1.67*** (1.25–2.23)	2.05* (1.17–3.58)	1.70 (0.68–4.25)
Low	1.61** (1.18–2.19)	2.66** (1.47–4.79)	4.13** (1.73–9.84)
Very Low	3.07*** (2.07–4.55)	6.99*** (3.40–14.36)	11.09*** (3.93–31.31)
Food security at prior study visit (i.e. food security lagged by 6 months)			
High	Ref (1.0)	Ref (1.0)	Ref (1.0)
Marginal	1.14 (0.86–1.51)	2.23** (1.32–3.78)	0.83 (0.33–2.12)
Low	1.36* (1.00–1.84)	1.32 (0.74–2.37)	0.86 (0.36–2.09)
Very Low	1.60* (1.11–2.31)	2.20* (1.11–4.33)	2.91* (1.14–7.45)
Person-visits	4499	3380	3001

[a]The sample for Table analyses is women with HIV who reported being prescribed ART in the last 6 months. Results are relative risk ratios (RRR) with 95% confidence intervals (CI) from a multinomial random effects logistic regression model, with perfect (i.e. 100%) adherence as the reference category. The number of women in each column (Unique IDs) is the number of women with perfect adherence (ref category) plus the number of women with the category of non-adherence being modeled. The total number of women included in the full longitudinal multinomial model was 1646 women; 41 women on ART with baseline data were excluded from the longitudinal models because of missing data. Models controlled for the following covariates: age at visit, race/ethnicity, annual household income, high school education, health insurance, number of years on ART, CD4 nadir, illicit substance use, heavy drinking, and having child dependents

***p < 0.001, **p < 0.01, *p < 0.05

Table 3 Association of persistent food security over the previous year with ART non-adherence categories (n = 1646)[a]

	Mild non-adherence	Moderate non-adherence	Severe non-adherence
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Food security (current visit + prior visit)			
High	Ref (1.0)	Ref (1.0)	Ref (1.0)
Marginal	1.91** (1.27, 2.86)	4.58*** (2.10, 10.0)	1.42 (0.413, 4.87)
Low	2.18*** (1.43, 3.33)	3.52** (1.58, 7.83)	3.57* (1.11, 11.5)
Very low	4.91*** (3.03, 7.95)	15.38*** (6.28, 37.5)	32.27*** (9.82, 106.2)
Person-visits	4499	3380	3001

[a]This Table results are the exponentiated linear combinations of the natural log of the adjusted relative risk ratios for current and prior food security within each level (i.e. marginal, low and very low) from Table 2, i.e. Persistent FS = e^(ln($RRR_{current}$) + ln(RRR_{prior})). Estimates, confidence intervals and p-values obtained through post-estimation commands for linear combinations in Stata. Models controlled for the following covariates: age at visit, race/ethnicity, annual household income, high school education, health insurance, years on ART, CD4 nadir, illicit substance use, heavy drinking, and having child dependents

***p < 0.001, **p < 0.01, *p < 0.05

relative risk of moderate non-adherence, compared to high food security at the prior visit. Persistent marginal, low, or very low food security at both the current and prior visit (Table 3) was associated with 4.58 (95% CI 2.10, 10.0; p < 0.001), 3.52 (95% CI 1.58, 7.83; p < 0.01), and 15.38 (95% CI 6.28, 37.5; p < 0.001) greater relative risk of moderate non-adherence compared to women who were food-secure at both visits.

Severe Non-adherence

Compared to high food security, low (RRR = 4.13; 95% CI 1.73, 9.84; p < 0.01) and very low (RRR = 11.09, 95% CI 3.93, 31.31; p < 0.001) food security at the *current visit* were associated with greater relative risk of severe non-adherence. Above and beyond associations with current food security, very low food security at the *prior visit* was independently associated with almost 3 times greater relative

risk (RRR = 2.91; 95% CI 1.14, 7.45; p < 0.05) of severe non-adherence, compared to high security. Finally, persistent marginal, low, and very low food security at both the current and prior visit were associated with 1.42 (95% CI 0.68, 4.25; p = 0.58), 3.57 (95% CI 1.11, 11.5; p < 0.05), and 32.27 (95% CI 9.82, 106.2; p < 0.001) greater relative risk of severe non-adherence, compared to women who were food-secure at both visits.

Sensitivity Analyses

Adding CD4 as a covariate in addition to CD4 nadir did not meaningfully change the magnitude, confidence in, or patterning of the results, with the exception of the severe non-adherence category where associations with current food insecurity were slightly lower. Similarly, stratifying the regressions by CD4 status ≥ 200 mm/μL did not meaningfully change the results, particularly for the high CD4 group which comprised > 90% of the analytic sample. The magnitudes and dose–response patterning remained mostly consistent with the original models; however, associations between current food insecurity and moderate non-adherence became weaker. Finally, in models adjusting for calendar time, the magnitude of and confidence in our results did not meaningfully change.

Engagement in Care

We modeled associations between food insecurity and engagement in HIV care (receipt of HIV care and missed routine HIV care visits) among 1733 women with HIV (6424 person-visits). In adjusted models among women on ART (Table 4), marginal and very low food security were associated with 1.43 (95% CI 1.06, 1.94; p < 0.05) and 2.10 (95% CI 1.51, 2.92; p < 0.001) greater odds of one or more missed visit, compared to high food security. For women *not* on ART, low and very low food security were associated with greater odds of a missed HIV care visit in the previous 6 months, compared with high food security (AOR = 3.01, 95% CI 1.02, 8.91, p < 0.05 and AOR = 4.92, 95% CI 1.41, 17.16; p < 0.05, respectively). In addition, among women not on ART, very low food security was associated with 80% lower odds of receiving HIV care in the previous 6 months (AOR = 0.19; 95% CI 0.05, 0.74; p < 0.05), compared to high food security (Table 4). Food security was not associated with the odds of receiving HIV care among women receiving ART.

Discussion

In this study of women living with HIV in the US, food insecurity was associated with lower ART adherence and engagement in care. Food insecurity and ART non-adherence were associated in a dose-dependent manner: within any given non-adherence category, associations with adherence increased across levels of food insecurity. Overall magnitudes of association between food insecurity and adherence also generally increased across degrees of non-adherence in the multinomial model. Furthermore, both current and prior food insecurity were independently associated with ART non-adherence, suggesting that past limitations in food access may be important to understand future adherence. Persistent, severe food insecurity appeared to be particularly detrimental for ART non-adherence. Finally, food insecurity was associated with lower odds of being in HIV care and higher odds of missing HIV care visits, particularly for women not on ART. These results underscore the importance of developing and testing sustainable approaches to addressing both short- and long-term food insecurity among women with HIV to support optimal clinical outcomes.

Food insecurity may undermine HIV treatment adherence and engagement in care for several reasons. Some food-insecure individuals may forgo their ART medications due

Table 4 Longitudinal associations between food insecurity and engagement in HIV care, by ART status (n = 1733)

	Received HIV Care ≤ 6 months		Missed ≥ 1 HIV care visit ≤ 6 months	
	On ART	Not on ART	On ART	Not on ART
Food security				
High	Ref (1.0)	Ref (1.0)	Ref (1.0)	Ref (1.0)
Marginal	0.88 (0.63–1.23)	0.70 (0.18–2.71)	1.43* (1.06–1.94)	0.74 (0.22–2.50)
Low	0.81 (0.57–1.13)	0.41 (0.12–1.44)	1.27 (0.93–1.75)	3.01* (1.02–8.91)
Very low	0.77 (0.54–1.12)	0.19* (0.05–0.74)	2.10*** (1.51–2.92)	4.92* (1.41–17.16)
Person-Visits	5714	270	5709	243

Results are adjusted odds ratios (aOR) with 95% confidence intervals (CI) from a binary random effects logistic regression model. Models controlled for the following covariates: age at visit, race/ethnicity, annual household income, high school education, health insurance, years on ART, CD4 nadir, illicit substance use, heavy drinking, and having child dependents

***p < 0.001, **p < 0.01, *p < 0.05

to worries of adverse side effects associated with taking the medications on an empty stomach [56, 57], particularly if they have been prescribed an ART regimen meant to be taken with food. In addition, competing demands between spending money on food and spending money on health care, including fees for going to doctor appointments and refilling medications, may lead to lower adherence and care engagement for food-insecure individuals [56, 58]. Food insecurity may also lead to psychosocial issues such as anxiety [59], depression [56, 60] and intimate partner violence [61] that may have lingering effects on adherence [62], even if a person is not currently food-insecure.

Previous epidemiological studies of food insecurity and ART non-adherence in resource-rich settings have primarily examined a single adherence threshold, demonstrating associations at < 80% [17, 63], 85% [64], and < 90% [17, 23] adherence. Understanding patterns of associations between food insecurity across different levels of adherence is important, as lower thresholds may be important to identify risk for viral non-suppression and viral resistance [65] as well as individuals with significant barriers to engaging in and adhering to medical care [66]. This is particularly true as current ART regimens are becoming more forgiving, with lower levels of ART adherence needed to achieve viral suppression [67]. Evidence suggests that structural barriers, such as inability to afford medications, may differentiate severe from moderate non-adherence and may be more important for those with severe non-adherence than cognitive barriers such as forgetting [66]. In the context of the literature, our findings suggest that addressing food insecurity among women with severe non-adherence may be a crucial target for intervention.

Our study provides insight into the persistent, detrimental role of food insecurity on ART adherence by identifying independent effects for prior and current food insecurity. A study conducted by Pellowski et al. among food-insecure persons living with HIV in Atlanta found that reporting being hungry but unable to afford food on a given day predicted daily missed medication doses on the next day [19]. These results support our finding that severe and current food insecurity are highly associated with non-adherence and suggest that day-to-day circumstances may play a key role; however, they do not explain our finding that food insecurity in the prior 6 months is associated with non-adherence independent of current food insecurity. We consider several explanations for the association of recent past food insecurity with later non-adherence. First, food insecurity may undermine adherence partially through depression [60, 62], with qualitative research indicating that depression related to food insecurity can linger and continue to affect health behaviors including adherence even after the individual is no longer food insecure [56]. In addition, it is possible that food insecurity may undermine renewal and/or pharmacy pick-up of ART prescriptions if, as our results suggest, food-insecure women are more likely to miss HIV care visits. Future studies should test mediating pathways between food insecurity and HIV treatment and care behaviors, with attention to the potential impact of food insecurity on psychosocial factors which may make it difficult to engage in and adhere to care.

Our study also contributes to understanding of how extended periods of food insecurity are related to ART adherence. Our finding that food insecurity lasting over at least two visits (i.e. lasting at least 1 year) is more strongly associated with non-adherence compared to intermittent food insecurity echoes previous findings that "consistent" food insufficiency (i.e., inadequate quantities of food during the last two program assessments) is strongly associated with detectable viral load [68], while inconsistent food insufficiency is not. Our study expands this result by showing that even less severe forms of persistent food insecurity than food insufficiency, encompassing persistently poor-quality diets or worry over food supplies, are also associated with poor HIV health outcomes.

This study used a large longitudinal dataset, and was representative by age and race of women with HIV in the U.S. The data were observational, limiting causal inference on the relationship between food insecurity and non-adherence. Despite evidence of independent associations between ART adherence and current and prior food insecurity, food insecurity and adherence are likely to have a cyclical relationship and our study cannot determine which came first. For engagement in care outcomes, these were assessed concurrently with food insecurity within the same 6-month recall period; therefore, it is possible that missed visits occurred before experiences of food insecurity within those six months. In addition, although we have included a number of socioeconomic and demographic covariates, there may be other unmeasured factors that could confound the observed associations, such as job loss. Rigorously designed intervention studies are needed to assess causal relationships between improving food security and adherence in the US context. Generalizability to all women with HIV in the US may also be limited if there are systematic differences among women living in geographic areas without a WIHS site, or selection bias related to the opportunity or decision to enroll in WIHS in areas with a recruitment site. Finally, relying on self-reported adherence is a limitation and may have resulted in the appearance of higher overall levels of adherence.

Conclusion

While the provision of nutritional services has long been included in the notion of comprehensive HIV care in the US via the Ryan White Care Act (Part A), people with HIV

remain disproportionately food insecure compared to the general population [17, 18]. In recognition of the negative health effects of food insecurity on HIV health, including among women, there is increasing policy attention directed at addressing food insecurity among people with HIV in both community and healthcare settings [69, 70]. Our study provides important evidence to inform these food security programming and policy efforts, finding that food insecurity may undermine HIV treatment and care goals among women living with HIV in the US, particularly among those with severe food insecurity and severe non-adherence, and with worsening effects over longer durations of food insecurity. Efforts to better target and tailor food security programming for women with HIV in resource-rich settings including the US, may help support optimal HIV outcomes in this population.

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Data availability Access to individual-level data from the MACS/WIHS Combined Cohort Study Data (MWCCS) may be obtained upon review and approval of a MWCCS concept sheet. Links and instructions for online concept sheet submission are on the study website: https://statepi.jhsph.edu/mwccs/work-with-us/

Code Availability Stata 14 (Stata Corp., College Station, TX, USA) was used for all analyses. Study code has been shared with the main MACS/WIHS Combined Cohort Study Data Center. We are willing to share our study code upon request.

Declarations

Conflict of interest The authors declare that they have no competing interests.

Ethical Approval This study was approved by the Institutional Review Board at each study site's institution and by the WIHS Executive Committee.

Consent to Participate Written informed consent was obtained for all participants in the study.

Consent for Publication Written informed consent obtained for the study included publication of the results, with the assurance that no individually identifiable data would be included in publications.

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