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Food Is Medicine for Human Immunodeficiency Virus: Improved Health and Hospitalizations in the Changing Health Through Food Support (CHEFS-HIV) Pragmatic Randomized Trial

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Background. Policy support for "food is medicine"—medically tailored meals or groceries to improve health—is rapidly growing. No randomized trials have heretofore investigated the benefits of medically tailored food programs for people with human immunodeficiency virus (PWH).

Methods. The CHEFS-HIV pragmatic randomized trial included PWH who were clients of Project Open Hand (POH), a San Francisco–based nonprofit food organization. The intervention arm (n = 93) received comprehensive medically tailored meals, groceries, and nutritional education. Control participants (n = 98) received less intensive (POH "standard of care") food services. Health, nutrition, and behavioral outcomes were assessed at baseline and 6 months later. Primary outcomes measured were viral nonsuppression and health-related quality of life. Mixed models estimated treatment effects as differences-in-differences between arms.

Results. The intervention arm had lower odds of hospitalization (odds ratio [OR], 0.11), food insecurity (OR, 0.23), depressive symptoms (OR, 0.32), antiretroviral therapy adherence <90% (OR, 0.18), and unprotected sex (OR, 0.18), as well as less fatty food consumption ($\beta = -.170$ servings/day) over 6 months, compared to the control arm. There was no difference between study arms in viral nonsuppression and health-related quality of life over 6 months.

Conclusions. A "food is medicine" intervention reduced hospitalizations and improved mental and physical health among PWH, despite no impact on viral suppression.

Clinical Trials Registration. NCT03191253.

Keywords. ART adherence; depression; nutrition; food security; HIV; food is medicine; hospitalizations; randomized controlled trial.

Inconsistent access to healthy food is a key determinant of poor health among people with human immunodeficiency virus (PWH) [1]. Food insecurity in resource-rich settings, including the United States (US), is associated with poorer diet quality; higher rates of depression, anxiety, and other mental health conditions; increased risk of human immunodeficiency virus (HIV) and other sexually transmitted infections (STIs); worse adherence to HIV medications; and lower CD4 cell counts, higher viral load, and higher mortality among PWH [2–4]. Additionally, food insecurity and HIV both disproportionately affect low-income and racially/ethnically minoritized communities [5, 6], highlighting the potential importance of reducing food insecurity to improve HIV outcomes and reduce disparities.

The landscape of food and nutrition supports for PWH in the US encompasses an interlocking patchwork of governmental programs (eg, Supplemental Nutrition Assistance Program), nongovernmental, nonprofit nutrition agencies (eg, Feeding America's food banks, Project Open Hand [POH]), and community-based programs (eg, church-based food pantries and soup kitchens) serving the general population. Additionally, the federal Ryan White HIV/AIDS CARE Act provides HIV-specific funding for food and nutrition assistance via local nutrition safety-net programs. Traditional nutrition safety-net approaches focus on preventing hunger and reducing economic distress but sometimes have unintended consequences undermining health, such as providing foods high in salt or sugar [7]. Aligning food support with

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health and medical needs (an approach termed "food is medicine" [FIM]), particularly for populations with chronic illnesses, has the potential to address twin goals of improving food security and health [8]. The proposition is that FIM will improve health and reduce healthcare costs for people with chronic illnesses affected by social vulnerabilities, such as food insecurity, social isolation, or limited mobility [8].

Several early FIM studies included substantial representation of PWH [9, 10], building on evidence linking food insecurity to poor HIV outcomes and leveraging the availability of data on HIV-related food support. Our pre-post pilot study of 72 individuals with HIV and/or diabetes found improvements in food security, depressive symptoms, and antiretroviral therapy (ART) adherence [10] after an FIM intervention. However, it did not assess viral load or other clinical HIV markers, had a small sample size, and no control arm. To address these limitations, we conducted the Changing Health through Food Support for HIV (CHEFS-HIV) Study, a randomized controlled trial (RCT) of medically tailored food support for PWH in a real-world setting, to investigate its impact on viral load and other health and utilization outcomes among PWH. We hypothesized that the intensive CHEFS-HIV intervention would improve viral load and health-related quality of life (HRQoL), as well as nutritional, mental health, behavioral, and healthcare utilization outcomes, compared to standard food support services.

METHODS

The CHEFS-HIV Study was a pragmatic RCT conducted in 2016–2017 by the University of California, San Francisco (UCSF), in partnership with POH, a nonprofit nutrition agency based in the San Francisco Bay area. The study was approved by the UCSF Institutional Review Board (#14-15488) and registered at ClinicalTrials.gov (NCT03191253).

Study Setting

POH was founded in 1985 and currently provides free medically tailored food support and nutritional counseling to >1000 PWH in San Francisco and Alameda counties, with significant funding by the Ryan White HIV/AIDS Care Act. POH facilities include space for meal preparation, storage, and distribution and a grocery center where clients select healthy foods.

Participants and Recruitment

Between May 2016 and January 2017, we recruited POH clients living with HIV into the CHEFS-HIV trial. They were receiving either 1 meal equivalent (ME) (Level 1) or 2 MEs daily (Level 2) through groceries or prepared meals. The study sample sought to maximize the number of participants while maintaining feasibility for POH, informed by our pilot study. Recruitment, enrollment, and randomization were conducted in 3 waves of 60–70 participants, each wave staggered by 2 months.

Inclusion criteria were age ≥18 years, had a provider-certified HIV diagnosis, were a current POH client for ≥1 year, were English or Spanish speaking, and had household income <200% of the federal poverty level (proxy for food insecurity risk). Participation also required the ability to store and reheat perishable food. Exclusion criteria were special diet requirements POH could not accommodate (eg, vegan diet), severe food allergies, currently pregnant or <6 months postpartum, previous violence (verbal or physical) toward POH staff or other clients, or physically or cognitively unable to engage in interviews. Only 1 person per household was eligible for study participation.

Eligibility criteria were assessed initially by POH staff using administrative records. UCSF research staff then randomly contacted potential participants for additional screening and, if eligible, study enrollment. Study staff trained in human research conducted informed consent procedures in the participant's preferred language (English or Spanish).

In response to unexpectedly high food security and viral suppression in our first recruitment wave, we adjusted our enrollment procedures in subsequent waves to preferentially recruit individuals who screened positive for food insecurity and/or had indications of possible viral nonsuppression or poor ART adherence using information collected by POH during service enrollment or recertification and/or by working with POH caseworkers to identify potential participants.

Randomization

After baseline assessments, participants were randomized 1:1 to control or intervention arms in a parallel design, stratified by service location (Oakland vs San Francisco) and prestudy POH service level (Level 1 vs 2). Arm assignment numbers were randomly generated within each stratum by a co-investigator (E. A. F.) using Excel, sealed in individual nontransparent envelopes, and provided to participants, who opened their envelope in view of the interviewer.

Intervention

The CHEFS-HIV intervention (Figure 1) was designed by POH's registered dietitians (RDs), POH leadership, and study investigators, incorporating lessons learned from the pilot study such as allowing a more flexible balance of meals versus groceries, based on participant preference. In addition, participants could reduce the amount of food received if they could not store or did not need it, as long as they received more food than their previous POH service level ("standard of care").

The intervention consisted of the following:

1. Medically tailored meals and groceries (MTM+): Participants received medically tailored food support for 6 months designed to meet up to 100% of daily energy requirements through a flexible mix of prepared meals and groceries. Group-level tailoring was consistent with medically tailored meal guidelines for HIV

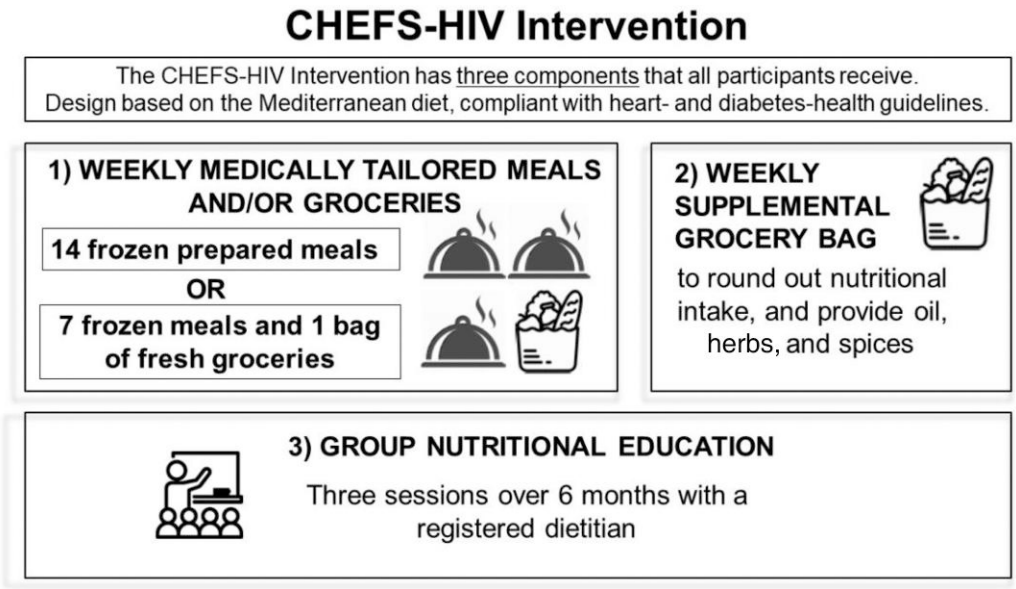

Figure 1. The Changing Health through Food Support for HIV (CHEFS-HIV) intervention.

[11] and informed by carbohydrate guidelines from the American Diabetes Association and saturated fat and sodium guidelines from the American Heart Association, with individual tailoring for calories and specialized diets (eg, mechanical soft foods, vegetarian). Average energy requirements used to design the intervention (including meals, groceries, and supplemental bag) were 1965–2359 kcal/day (8222–9870 kJ/day), depending on the participant's size and metabolic needs. The food plan (which varied each week) was low in refined sugars and saturated fats, featuring fresh fruits and vegetables, lean proteins, healthy fats (eg, olive oil), and whole grains, consistent with the Dietary Approaches to Stop Hypertension (DASH) and Mediterranean diets. A supplemental bag of groceries (eg, olive oil, herbs, spices, soups, grain, beans) was provided to ensure all food groups and daily nutrients were included. Participants (or a surrogate) obtained their food twice per week at designated times from POH facilities or received food delivery (if physically unable to pick up their food). Additional food was offered for dependents, if applicable.

2. Nutritional education: Participants received 1 individual in-person nutritional counseling session at baseline and another at 5–6 months, one 15-minute check-in call at 3 months, and three 2-hour small-group nutrition education classes. Group classes were participatory; addressed HIV, nutrition, portion size, food labels, and goal setting; and included hands-on cooking demonstrations. All sessions were conducted by RDs at POH.

Control Arm

Participants were randomized to an active control arm ("POH standard of care"). Depending on their POH service level determined by a client's health status, control clients could receive 1 or 2 MEs/day (vs 3 MEs/day in the intervention arm). Control participants also met briefly with POH RDs every 6 months as part of client recertification, but did not receive group nutritional education.

Data Collection

Study visits were conducted at baseline and at 6 months from May 2016 to July 2017. At both visits, participants completed an interviewer-administered questionnaire, anthropometric assessment, and blood tests. Data were collected using Research Electronic Data Capture, a secure, Health Insurance Portability and Accountability Act (HIPAA)–compliant, web-based system.

Outcomes

All outcome measures were collected at baseline and 6-month follow-up, described below:

Primary Outcomes

Viral load was measured using the COBAS AmpliPrep/COBAS TaqMan assay, with a lower detection limit of 20 copies/mL. Viral load was classified as viral nonsuppression (vs suppression) using 20 copies/mL as the threshold. HRQoL was assessed using Short Form-36 (SF-36) and analyzed as a continuous variable from 0 to 100, with higher scores indicating better health [12, 13].

Secondary and Exploratory Outcomes

Food security, depressive symptoms, and ART adherence were prespecified as secondary outcomes based on our conceptual framework and pilot results [10, 14]. Food security was assessed using the 18-item US Department of Agriculture's (USDA) Household Food Security Survey Module [15], the reference measure of population food security in the US [16], and

categorized as very low, low, marginal, or full based on the standard USDA scoring algorithm. Diet quality was evaluated as servings per day using an adapted version of the 2000 National Health Interview Survey multifactor screener [17]. Dietary intake variables were transformed to square roots to satisfy the assumption of normality. Depressive symptom severity was measured using the Patient Health Questionnare-9 [18], a 9-item instrument assessing depression symptom severity. Depressive symptom severity scores were categorized as none to minimal (score = 0–4), mild (score = 5–9), moderate (score = 10–14), moderately severe (score = 15–19), and severe (score = 20–27) [18]. ART adherence was evaluated using a visual analog scale of the percentage of prescribed medications taken in the previous 7 days. We dichotomized ART adherence as ≥90% versus <90%, a threshold shown to predict viral suppression [19], including using self-reported adherence data [20]. Number of hospitalizations and number of times having unprotected penetrative sex in the past 90 days were assessed by self-report, dichotomized as ≥1 event versus none, and were exploratory outcomes based on suggestive evidence from our pilot [10, 21].

Statistical Analysis

To test for intervention effects, we used an intent-to-treat difference-in-differences method, employing 2-level mixed models with participant as the random effect. We assessed differences between study arms in changes from baseline to follow-up using an interaction term between visit and arm. This analytic approach controls for any baseline differences in the outcome variable between study arms. Three types of regression models were used: linear for continuous variables (diet, HRQoL), binary logistic for dichotomous variables (unsuppressed viral load, adherence <90%, overnight hospitalization, unprotected sex), and ordinal logistic for ordered multiple category variables (food insecurity, depressive symptom severity). The ordinal logistic regression does not produce separate estimates for each transition between specific ordinal categories; instead, it gives the odds of moving to a more severe category within the respective variable. As a pragmatic study to evaluate a real-world program with limited funding using an RCT design, this study was not powered to detect small differences in unsuppressed viral load. However, a sample size of 168 provided 80% power to detect a 0.20 difference in the proportion of patients with nonsuppressed viral load at $\alpha = .05$. All analyses were conducted using Stata 2014 (StataCorp).

RESULTS

Baseline Characteristics

Among the 191 participants enrolled in the study, 98 (51%) were assigned to the control arm and 93 (49%) to the intervention arm (Figure 2). Most participants were male, >50 years of age, from racial and ethnic minoritized groups, and had more than a high school education (Table 1). Most participants (79%) were served by the San Francisco POH location. Many participants used controlled substances in the past 30 days (30%) and most had a self-reported mental health diagnosis (60%). The median time since HIV diagnosis was 22 years. Forty percent had self-reported diabetes, hypertension, or cardiovascular disease. At baseline, 39% had nonsuppressed viral loads (compared to 27%–33% of San Francisco's general population of PWH in 2015), and the mean HRQoL score was 52.4 (compared to an average score of 50 for US adults) (Table 2). Almost two-thirds of participants (63%) were food insecure, 46% had depressive symptoms, 22% had <90% ART adherence, 8% had ≥1 overnight hospitalization in the past 90 days, and 61% had unprotected sex in the previous 90 days.

At baseline, participants were receiving 1.08 MEs/day from POH (average entitlement of 1.41 MEs/day × food receipt rate of 76.7%).

Six-Month Outcomes

At 6-month follow-up, 168 participants (88%) remained in the study. Study retention was similar in both study arms (intervention, 89%; control, 87%). Baseline characteristics of participants lost to follow-up were similar to those of participants who completed the study, except for a lower monthly income.

The prevalence of nonsuppressed viral load decreased in both study arms over the 6-month study period, with no difference between arms (Table 2). There was no difference in HRQoL scores between the arms over 6 months.

Intervention arm participants had 77% lower odds of a more severe food insecurity category (odds ratio [OR], 0.23 [95% confidence interval {CI}, .087–.617]; $P = .003$) over 6 months, compared to the control arm, and 68% lower odds of a more severe depressive symptoms category (OR, 0.32 [95% CI, .125–.834]; $P = .020$). The intervention arm exhibited a greater decrease in fatty food consumption than the control arm ($\beta = -.170$, standard error [SE] = 0.085; $P = .044$), but there was no difference in fruit and vegetable consumption between arms ($\beta = .062$, SE = 0.079; $P = .430$) over 6 months.

Intervention arm participants had 82% lower odds of <90% ART adherence (OR, 0.18 [95% CI, .0389–.821]; $P = .030$) over 6 months, compared to the control arm. The intervention arm also had 95% lower odds of unprotected sex in the previous 90 days (OR, 0.05 [95% CI, .00385–.528]; $P = .014$) over 6 months.

The percentage of participants with overnight hospitalizations in the past 90 days decreased from 11% to 5% in the intervention arm over 6 months but increased from 6% to 11% in the control arm, translating to 89% lower odds of hospitalization (OR, 0.11

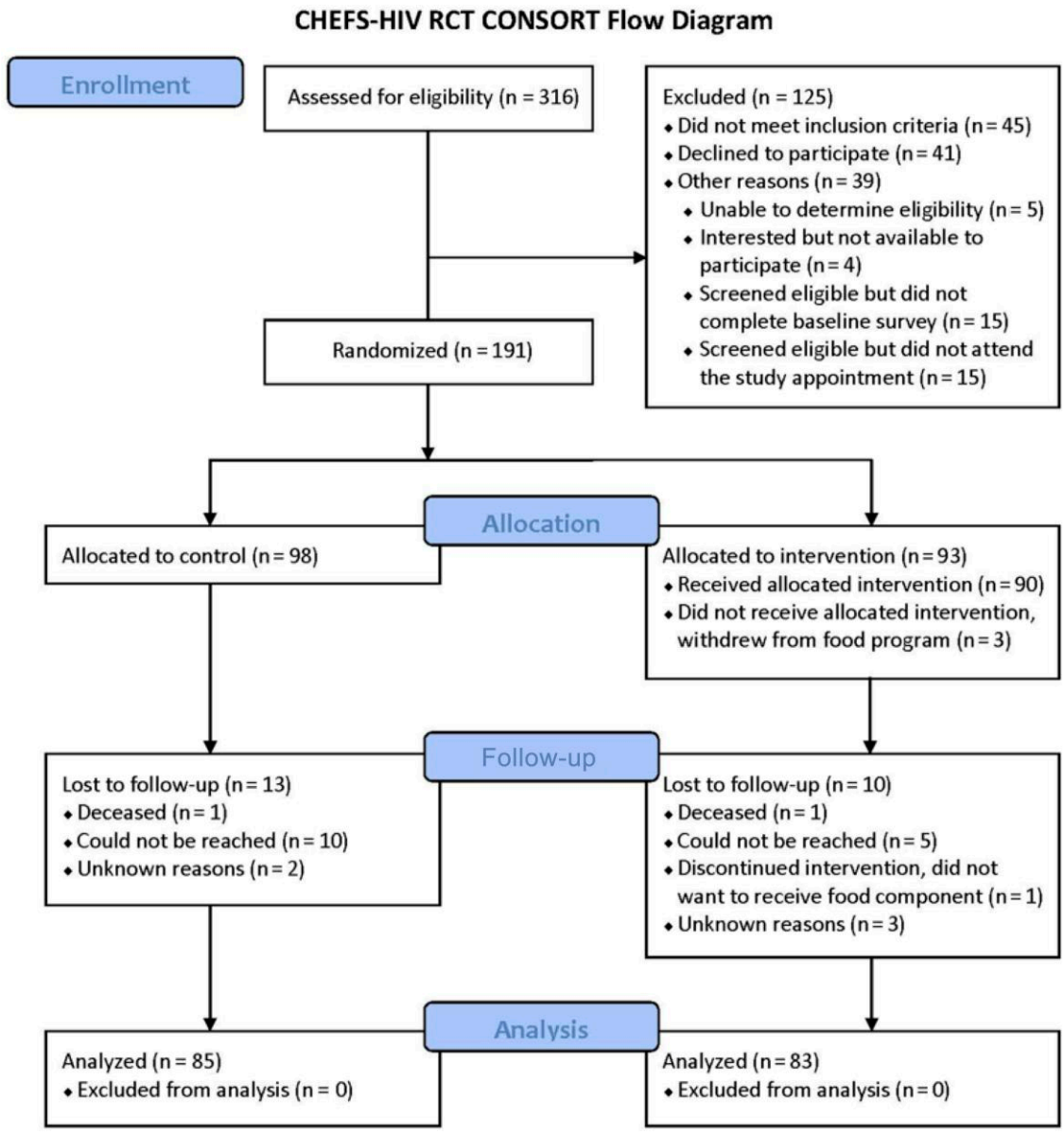

Figure 2. Consolidated Standards for Reporting Trials (CONSORT) diagram for the Changing Health through Food Support for HIV (CHEFS-HIV) pragmatic randomized controlled trial (RCT).

[95% CI, .0134–.960]; $P = .046$) in the intervention arm, compared to the control arm.

Exposure to the Intervention

Intervention arm participants received a median of 75.7% of the total CHEFS-HIV food they were offered over the 6-month study (interquartile range [IQR], 59.5%–89.7%), or 2.26 MEs/day. Control participants had no measurable change in average MEs/day over the course of the study. Participants received at least some CHEFS-HIV food during a median 82.1% of weeks (IQR, 60.7%–92.9%) and the complete CHEFS-HIV package (equivalent of 3 meals/day) during a median 61.5% of weeks (IQR, 37.5%–78.6%).

DISCUSSION

The 6-month CHEFS-HIV intervention, pairing an intensive community-based program of MTM+ with RD-led nutrition education, did not impact HIV viral suppression or HRQoL. However, it improved food security and ART adherence, and reduced depressive symptom severity, unprotected sexual encounters, and overnight hospitalizations, compared to controls. As the comparator was an active control arm receiving standard POH services, intervention effects may have been even stronger, compared to no intervention. The RCT design improves the rigor of evidence for FIM programs serving PWH, as previous prospective studies neither included a control

Table 1. Baseline Characteristics of Enrolled Participants, Stratified by Study Arm

Characteristic	Intervention Arm (n = 93)	Control Arm (n = 98)
Female sex at birth	19	17
Identifies as transgender or genderqueer	8	7
Age, y	55.2 (50.7–60.4)	55.8 (50.7–59.9)
Education		
Less than high school/GED	14	13
High school/GED	19	12
More than high school/GED	67	74
Income in the previous month, USD	1073.00 (898.00–1354.00)	1003.6 (889.00–1304.00)
Any child dependents	3	3
"Partnered" relationship status	25	22
Race/ethnicity		
American Indian, Native American, Alaska Native, Indigenous	2	3
Asian or Pacific Islander	3	4
Black/African American	26	25
White	39	34
Latino/Hispanic	8	13
Multiracial or other race, ethnicity, or origin	23	19
Body mass index, kg/m^2	26.2 (22.5–30.5)	25.0 (21.8–28.5)
Substance use in the past 30 d[a]	26	35
Years as Project Open Hand client	13 (7–20)	11 (6–19)
Years since HIV diagnosis	22 (15–27)	21.5 (15–28)
Self-reported diabetes, hypertension, or cardiovascular disease	38	40
Self-reported mental health diagnosis[b]	54	66

Data are presented as percentage or median (interquartile range).

Abbreviations: GED, General Educational Development (high school equivalency test); HIV, human immunodeficiency virus; USD, United States dollars.

[a]Includes crystal, methamphetamine, speed, heroin, cocaine, or crack; does not include marijuana or opioid analgesics.

[b]Participants reported being told by a doctor that they have depression, anxiety disorder, bipolar disorder, and/or another mental health condition.

arm nor measured HIV clinical outcomes. Furthermore, quasi-experimental studies using observational data examined only healthcare cost and utilization outcomes. Our results support the proposition that FIM programs can improve physical and mental health outcomes among PWH.

There are several possibilities as to why we did not observe an impact on viral suppression. One is that we could not recruit based on viral load, and most participants were virally suppressed at baseline, making improvements in viral load difficult to detect. Furthermore, our study was only powered to detect a 20 percentage point difference in viral nonsuppression, whereas much smaller differences are clinically meaningful. Additionally, during the timeframe of the study, intensive county-level "Getting to Zero" initiatives sought to improve local rates of viral suppression and other HIV outcomes by increasing outreach and services. The decrease in nonsuppressed viral load observed in both study arms may reflect those environmental changes. Larger studies involving populations with lower rates of viral suppression are warranted to further understand the impact of FIM programs on HIV viral suppression. While suppressed viral load is critical for the health of PWH and for reducing HIV transmission, social factors linked to food insecurity (eg, homelessness, substance use) are often strong contributors to emergency department use, hospitalization, and death in San Francisco [22]. These factors may explain the decreased odds of hospitalization with the intervention, despite the lack of impact on viral suppression.

Reducing costly and avoidable hospitalizations is of primary interest to healthcare payers and is a main policy lever targeted by FIM proponents. Our finding that intensive MTM+ plus nutrition education reduced the odds of overnight hospitalizations contributes to understanding the potential role of MTM+ in improving health and reducing costs. As the first RCT to evaluate use of MTM (with or without added groceries) among PWH, our results are consistent with the lower rates of hospitalization among MTM recipients reported in quasi-experimental studies [9, 23]. Analysis of an all-payer claims database from Massachusetts found that receiving MTM (with PWH comprising one-fifth of recipients) was associated with significantly fewer inpatient admissions and admissions to skilled nursing facilities, with potential $753 mean monthly savings per person [23]. Our findings also corroborate our pilot study in which hospitalizations decreased from 15.7% to 5.7% with a similar MTM + intervention. In the current study, there were 11 fewer hospitalizations in the intervention arm than the control arm over 6 months. Given an average daily cost of $3535 for hospitalization

Table 2. Impact of Changing Health through Food Support for HIV (CHEFS-HIV) Intervention on Primary and Secondary Outcomes (Intent-to-Treat Analysis)

	Intervention Arm		Control Arm		Difference-in-Differences Estimate[a]	
Outcome	Baseline	Follow-up	Baseline	Follow-up	Estimate	*P* Value
Unsuppressed viral load	37	26	35	19	OR, 1.55 (95% CI, .47–5.11)	.47
HRQoL, mean (SD)	53.8 (21.5)	52.9 (23.0)	51.0 (20.5)	52.7 (22.2)	β = −1.97, SE = 2.29	.39
Food security category					OR, 0.23 (95% CI, .087–.617)	.003
High	20	54	19	34		
Marginal	18	17	15	20		
Low	20	13	24	16		
Very low	41	16	41	29		
Consumption of fatty foods, servings/d	3.3 (2.0–5.2)	2.9 (1.8–4.3)	3.6 (2.0–5.3)	3.3 (2.1–5.8)	β = −.170[b], SE = 0.085	.044
Fruit and vegetable consumption, servings/d	1.3 (0.9–2.4)	1.7 (1.0–2.9)	1.4 (0.6–2.0)	1.4 (0.9–2.6)	β = .062[b], SE = 0.079	.43
Depressive symptom severity category					OR, 0.32 (95% CI, .125–.834)	.020
None to minimal	56	60	52	45		
Mild	20	24	29	26		
Moderate	11	11	8	24		
Moderately severe	6	5	8	2		
Severe	6	0	3	4		
<90% ART adherence	26	18	19[‡]	19	OR, 0.18 (95% CI, .0389–.821)	.030
Overnight hospitalization (past 90 d)	11	5	6	11	OR, 0.11 (95% CI, .0134–.960)	.046
Unprotected sex (past 90 d)	69	51	52	67	OR, 0.05 (95% CI, .00385–.528)	.014
No.	93	83	95	85	168	

Data are presented as percentage or median (interquartile range), except where otherwise indicated.

Abbreviations: ART, antiretroviral therapy; CI, confidence interval; HRQoL, Health-Related Quality of Life; OR, odds ratio; SD, standard deviation; SE, standard error.

[a]Differences-in-difference model estimates represent the difference in change over time of the outcome in the intervention arm, compared to the control arm, based on 2-level mixed models, with participants as the random effect. Regression models included terms for time (baseline and 6 months), study arm (intervention and control), and an interaction term for time × study arm. Shown are the ORs or β-coefficients from the interaction terms for the intervention minus control arm differences in changes over time. Ordinal logistic regression was used for food insecurity and depressive symptom severity; logistic regression was used for nonsuppressed viral load, adherence, overnight hospitalization, and unprotected sex; and linear regression was used for diet and HRQoL.

[b]These analyses involved square root transformation of outcomes to account for their nonnormal distribution.

and mean length of stay of 4.6 days in California in 2018 [24], this intervention could have reduced hospitalization costs by $178 781 among study participants.

This study also addresses key literature gaps by demonstrating the impact of MTM+ on depressive symptoms and ART adherence among PWH. Food insecurity contributes to poor mental health, including depression, stress, and anxiety, in the general population and among PWH [14, 25–30]. Similarly, food insecurity is a well-recognized barrier to ART adherence [31], with higher food insecurity associated with greater difficulties accessing and adhering to medications [1, 2, 32, 33]. Prior qualitative research in our study population revealed how food insecurity undermines mental health and ART adherence synergistically, making it difficult for PWH to access material and psychological resources for their condition [14]. Despite an increasing number of intervention studies suggesting that addressing food insecurity via direct food support can improve adherence for PWH, much of this evidence is from low- and middle-income countries [34], primarily in sub-Saharan Africa [35–37] and the Caribbean/Latin America [38, 39]. Furthermore, food support in these settings focuses on insufficient food intake and hunger and is not usually medically tailored. To our knowledge, no RCTs of medically tailored food support have assessed mental health outcomes or ART adherence among PWH. Our findings that MTM+ reduces depressive symptoms and improves ART adherence contributes to understanding the benefits of these programs for PWH.

A novel finding was that providing comprehensive, medically tailored food support may reduce unprotected sex, although the intervention did not address sexual behavior. This finding aligns with robust literature linking food insecurity with risky sexual behavior, including reduced condom use and increased transactional sex, as well as increased prevalence of HIV and other STIs [40–45], possibly operating via poor mental health and substance use or via pressures to engage in unprotected sex if doing so could secure food or resources for food [42, 43, 46, 47]. In our prior qualitative study, PWH described how safer sex practices were outweighed by the short-term need for food, often in the context of transactional sex [21]. Thus, medically tailored food programs may contribute to population efforts to reduce STIs by reducing unprotected sex among individuals for whom food insecurity affects sexual decision-making.

There were limitations to this study. Given the widespread use of POH services among PWH in our geographic region, we could not logistically or ethically compare our intervention to a control arm receiving no food services. Instead, the control group arm

received regular POH services and was compared to participants receiving more intensive intervention (MTM+). Additionally, only individuals able to store and reheat food were included, potentially excluding patients with greater housing insecurity. We also used self-reported measures of ART adherence and healthcare utilization, including emergency department visits and hospitalizations. Furthermore, the Getting to Zero campaign in San Francisco implemented during our study period likely reduced our ability to detect intervention-related changes in viral suppression. Finally, while the data are several years old, as the first FIM randomized trial for PWH, the results are still highly relevant to the field. The strengths of our study included its RCT design and high retention rate in both arms (88%), particularly given the high burden of mental and physical health comorbidities in our study population.

Medically tailored meals and groceries, combined with nutritional education, reduced hospitalizations, improved mental health and medication adherence, and decreased unprotected sex among PWH at high risk for food insecurity. These findings underscore the promise of MTM+ to improve multiple domains of health for PWH and reduce healthcare costs through lower healthcare utilization. With the current expansion and endorsement of FIM programs and policies at the US federal level as well as in many states [48, 49], our data can inform evidence-based design of medically supportive food programs locally and nationally. Larger studies are warranted to understand how different modalities of implementing food support programs impact HIV and non-HIV clinical outcomes.

Notes

Author contributions. K. P., S. D. W., S. P., M. R., and K. M. led conception and design of the intervention. K. P. and S. D. W. led the design and implementation of the research. Data collection was led by A. A. O. D., T. M. N., and B. P. Data analysis and interpretation of results was led by L. A. S., E. A. F., K. P., S. D. W., and E. D. R. Drafting of the manuscript was led by K. P., with support from S. D. W. and A. A. O. D. Critical revision of the article and final approval of the version to be published was conducted by all authors.

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Kalichman SC, Cherry C, Amaral C, et al. Health and treatment implications of food insufficiency among people living with HIV/AIDS, Atlanta, Georgia. J Urban Health **2010**; 87:631–41.
2. Weiser SD, Yuan C, Guzman D, et al. Food insecurity and HIV clinical outcomes in a longitudinal study of urban homeless and marginally housed HIV-infected individuals. AIDS **2013**; 27:2953–8.
3. Wang EA, McGinnis KA, Fiellin DA, et al. Food insecurity is associated with poor virologic response among HIV-infected patients receiving antiretroviral medications. J Gen Intern Med **2011**; 26:1012–8.
4. Chen C, Yang X, Zeng C, Li X, Qiao S, Zhou Y. The role of mental health on the relationship between food insecurity and immunologic outcome among people living with HIV in Guangxi, China. Health Psychol Behav Med **2020**; 8: 636–48.
5. Wilson EC, Turner C, Arayasirikul S, et al. Housing and income effects on HIV-related health outcomes in the San Francisco Bay Area—findings from the SPNS transwomen of color initiative. AIDS Care **2018**; 30:1356–9.
6. Odoms-Young A, Bruce MA. Examining the impact of structural racism on food insecurity: implications for addressing racial/ethnic disparities. Fam Community Health **2018**; 41:S3–6.
7. Ginossar T, Oetzel J, Van Meter L, Gans AA, Gallant JE. The Ryan White HIV/AIDS Program after the Patient Protection and Affordable Care Act full implementation: a critical review of predictions, evidence, and future directions. Top Antivir Med **2019**; 27:91–100.

8. Ellwood M, Downer S, Leib EB, et al. Food is medicine opportunities in public and private health care for supporting nutritional counseling and medically-tailored, home-delivered meals: Center for Health Law and Policy Innovation. Cambridge, MA: Harvard Law School, **2014**.
9. Gurvey J, Rand K, Daugherty S, Dinger C, Schmeling J, Laverty N. Examining health care costs among MANNA clients and a comparison group. J Prim Care Community Health **2013**; 4:311–7.
10. Palar K, Napoles T, Hufstedler LL, et al. Comprehensive and medically appropriate food support is associated with improved HIV and diabetes health. J Urban Health **2017**; 94:87–99.
11. Food is Medicine Coalition. Nutrition standards. United States: Food is Medicine Coalition, **2023**.
12. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care **1992**; 30:473–83.
13. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-item short-form health survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care **1993**; 31:247–63.
14. Whittle HJ, Palar K, Seligman HK, Napoles T, Frongillo EA, Weiser SD. How food insecurity contributes to poor HIV health outcomes: qualitative evidence from the San Francisco Bay Area. Soc Sci Med **2016**; 170:228–36.
15. Frongillo EA Jr. Validation of measures of food insecurity and hunger. J Nutr **1999**; 129:506S–9S.
16. Bickel G, Nord M, Price C, Hamilton W, Cook J. Guide to measuring household food security, revised 2000. Alexandria, VA: Food and Nutrition Service, US Department of Agriculture, **2000**.
17. National Cancer Institute. Multifactor screener in the 2000 national health interview survey cancer control supplement: overview. https://epi.grants.cancer.gov/nhis/multifactor/. Accessed 16 February 2021.
18. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med **2001**; 16:606–13.
19. Byrd KK, Hou JG, Hazen R, et al. Antiretroviral adherence level necessary for HIV viral suppression using real-world data. J Acquir Immune Defic Syndr **2019**; 82:245–51.
20. Almeida-Brasil CC, Moodie EEM, Cardoso TS, Nascimento ED, Ceccato M. Comparison of the predictive performance of adherence measures for virologic failure detection in people living with HIV: a systematic review and pairwise meta-analysis. AIDS Care **2019**; 31:647–59.
21. Whittle HJ, Palar K, Napoles T, et al. Experiences with food insecurity and risky sex among low-income people living with HIV/AIDS in a resource-rich setting. J Int AIDS Soc **2015**; 18:20293.
22. Hickey MD, Imbert E, Appa A, et al. HIV treatment outcomes in POP-UP: drop-in HIV primary care model for people experiencing homelessness. J Infect Dis **2022**; 226: S353–62.
23. Berkowitz SA, Terranova J, Randall L, Cranston K, Waters DB, Hsu J. Association between receipt of a medically tailored meal program and health care use. JAMA Intern Med **2019**; 179:786–93.
24. Agency for Healthcare Research and Quality. HCUP visualization of inpatient trends in COVID-19 and other conditions. Healthcare Cost and Utilization Project (HCUP). 2021. www.hcup-us.ahrq.gov/datavisualizations/covid-19-inpatient-trends.jsp. Accessed 16 February 2021.
25. Carter KN, Kruse K, Blakely T, Collings S. The association of food security with psychological distress in New Zealand and any gender differences. Soc Sci Med **2011**; 72:1463–71.
26. Palar K, Kushel M, Frongillo EA, et al. Food insecurity is longitudinally associated with depressive symptoms among homeless and marginally-housed individuals living with HIV. AIDS Behav **2015**; 19:1527–34.
27. Palar K, Frongillo EA, Escobar J, et al. Food insecurity, internalized stigma, and depressive symptoms among women living with HIV in the United States. AIDS Behav **2018**; 22:3869–78.
28. Tuthill EL, Sheira LA, Palar K, et al. Persistent food insecurity is associated with adverse mental health among women living with or at risk of HIV in the United States. J Nutr **2019**; 149:240–8.
29. Heflin CM, Siefert K, Williams DR. Food insufficiency and women's mental health: findings from a 3-year panel of welfare recipients. Soc Sci Med **2005**; 61:1971–82.
30. Whittle HJ, Sheira LA, Wolfe WR, et al. Food insecurity is associated with anxiety, stress, and symptoms of posttraumatic stress disorder in a cohort of women with or at risk of HIV in the United States. J Nutr **2019**; 149:1393–403.
31. Singer AW, Weiser SD, McCoy SI. Does food insecurity undermine adherence to antiretroviral therapy? A systematic review. AIDS Behav **2015**; 19:1510–26.
32. Weiser SD, Palar K, Frongillo EA, et al. Longitudinal assessment of associations between food insecurity, antiretroviral adherence and HIV treatment outcomes in rural Uganda. AIDS **2014**; 28:115–20.
33. Franke MF, Murray MB, Munoz M, et al. Food insufficiency is a risk factor for suboptimal antiretroviral therapy adherence among HIV-infected adults in urban Peru. AIDS Behav **2011**; 15:1483–9.
34. de Pee S, Grede N, Mehra D, Bloem MW. The enabling effect of food assistance in improving adherence and/or treatment completion for antiretroviral therapy and tuberculosis treatment: a literature review. AIDS Behav **2014**; 18:S531–41.
35. Cantrell RA, Sinkala M, Megazinni K, et al. A pilot study of food supplementation to improve adherence to

antiretroviral therapy among food-insecure adults in Lusaka, Zambia. J Acquir Immune Defic Syndr **2008**; 49: 190–5.
36. Tirivayi N, Koethe JR, Groot W. Clinic-based food assistance is associated with increased medication adherence among HIV-infected adults on long-term antiretroviral therapy in Zambia. J AIDS Clin Res **2012**; 3:171.
37. Posse M, Tirivayi N, Saha UR, Baltussen R. The effect of food assistance on adherence to antiretroviral therapy among HIV/AIDS patients in Sofala Province, in Mozambique: a retrospective study. J AIDS Clin Res **2013**; 4:1000198.
38. Martinez H, Palar K, Linnemayr S, et al. Tailored nutrition education and food assistance improve adherence to HIV antiretroviral therapy: evidence from Honduras. AIDS Behav **2014**; 18:S566–77.
39. Ivers LC, Chang Y, Gregory Jerome J, Freedberg KA. Food assistance is associated with improved body mass index, food security and attendance at clinic in an HIV program in central Haiti: a prospective observational cohort study. AIDS Res Ther **2010**; 7:33.
40. Palar K, Laraia B, Tsai AC, Johnson MO, Weiser SD. Food insecurity is associated with HIV, sexually transmitted infections and drug use among men in the United States. AIDS **2016**; 30:1457–65.
41. Weiser SD, Leiter K, Bangsberg DR, et al. Food insufficiency is associated with high-risk sexual behavior among women in Botswana and Swaziland. PLoS Med **2007**; 4: 1589–97; discussion 1598.
42. Vogenthaler NS, Kushel MB, Hadley C, et al. Food insecurity and risky sexual behaviors among homeless and marginally housed HIV-infected individuals in San Francisco. AIDS Behav **2013**; 17:1688–93.
43. Wang EA, Zhu GA, Evans L, Carroll-Scott A, Desai R, Fiellin LE. A pilot study examining food insecurity and HIV risk behaviors among individuals recently released from prison. AIDS Educ Prev **2013**; 25:112–23.
44. Justman J, Befus M, Hughes J, et al. Sexual behaviors of US women at risk of HIV acquisition: a longitudinal analysis of findings from HPTN 064. AIDS Behav **2015**; 19:1327–37.
45. Eaton LA, Cain DN, Pitpitan EV, et al. Exploring the relationships among food insecurity, alcohol use, and sexual risk taking among men and women living in South African townships. J Prim Prev **2014**; 35:255–65.
46. Tsai AC, Weiser SD. Population-based study of food insecurity and HIV transmission risk behaviors and symptoms of sexually transmitted infections among linked couples in Nepal. AIDS Behav **2014**; 18:2187–97.
47. Raja A, Heeren TC, Walley AY, Winter MR, Mesic A, Saitz R. Food insecurity and substance use in people with HIV infection and substance use disorder. Subst Abus **2022**; 1:104–12.
48. The White House. Fact sheet: The Biden-Harris administration announces more than $8 billion in new commitments as part of call to action for White House conference on hunger, nutrition, and health. 2022. https://www.whitehouse.gov/briefing-room/statements-releases/2022/09/28/fact-sheet-the-biden-harris-administration-announces-more-than-8-billion-in-new-commitments-as-part-of-call-to-action-for-white-house-conference-on-hunger-nutrition-and-health/. Accessed 4 June 2023.
49. Weintraub K; USA Today. Food as medicine: White House pilot program would bring medically tailored meals under Medicare. 2022. https://www.usatoday.com/story/news/health/2022/09/27/white-house-conference-on-hunger-medically-tailored-meals/8090011001/. Accessed 4 June 2023.