Title

Brief Report

Journal

JAIDS Journal of Acquired Immune Deficiency Syndromes, 71(3)

ISSN

1525-4135

Authors

Koss, Catherine A

Natureeba, Paul

Nyafwono, Dorcas

et al.

Publication Date

2016-03-01

DOI

10.1097/qai.0000000000000860

Peer reviewed

Food Insufficiency Is Associated With Lack of Sustained Viral Suppression Among HIV-Infected Pregnant and Breastfeeding Ugandan Women

Catherine A. Koss, MD,† Paul Natureeba, MBChB,† Dorcas Nyafwono,† Albert Plenty, MSPH,†‡ Julia Mwesigwa, MBChB, MSc,†§ Bridget Nzarubara, MBChB, MSc,† Tamara D. Clark, MHS,*† Theodore D. Ruel, MD,†‖ Jane Achan, MBChB, MMed, PhD,†§ Edwin D. Charlebois, MPH, PhD,†‡ Deborah Cohan, MD, MPH,†¶ Moses R. Kamya, MBChB, MMed, MPH, PhD,†# Diane V. Havlir, MD,*† and Sera L. Young, MA, PhD***

Abstract: Food insecurity is associated with poor virologic outcomes, but this has not been studied during pregnancy and breastfeeding. We assessed sustained viral suppression from 8 weeks on antiretroviral therapy to 48 weeks postpartum among 171 pregnant and breastfeeding Ugandan women; 74.9% experienced food insufficiency. In multivariable analysis, food insufficiency [adjusted odds ratio (aOR) 0.38, 95% confidence interval (CI): 0.16 to 0.91], higher pretreatment HIV-1 RNA (aOR 0.55 per 10-fold increase, 95% CI: 0.37 to 0.82), and lopinavir/ritonavir versus efavirenz (aOR 0.49, 95% CI: 0.24 to 0.96) were associated with lower odds of sustained viral suppression. Interventions to address food security may improve virologic outcomes among HIV-infected women.

Key Words: food insecurity, nutrition, perinatal transmission, pregnancy, household hunger, virologic outcomes

(*J Acquir Immune Defic Syndr* 2016;71:310–315)

Received for publication June 5, 2015; accepted August 21, 2015.

From the *Division of HIV, Infectious Diseases, and Global Medicine, Department of Medicine, San Francisco General Hospital, University of California, San Francisco, San Francisco, CA; †Makerere University-University of California, San Francisco Research Collaboration, Kampala, Uganda; ‡Center for AIDS Prevention Studies, Department of Medicine, University of California, San Francisco, San Francisco, CA; §Medical Research Council Unit, The Gambia, Serrekunda, Gambia; ‖Department of Pediatrics, University of California, San Francisco, San Francisco, CA; ¶Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, San Francisco, CA; #Department of Medicine, Makerere University College of Health Sciences, Kampala, Uganda; and **Department of Population Medicine and Diagnostic Sciences, Program in International Nutrition, Cornell University, Ithaca, NY.

This work was supported by grants from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (P01 HD059454, D.V.H. and K23 HD60459, T.D.R.), the National Institute of Allergy and Infectious Diseases (T32 AI060530, D.V.H./C.A.K.), and the National Institute of Mental Health (K01 MH098902, S.L.Y.) at the National Institutes of Health. The nutritional substudy was supported by the President's Emergency Plan For AIDS Relief, the Office of the Global AIDS Coordinator, and the Office of AIDS Research.

AbbVie Pharmaceuticals donated lopinavir/ritonavir (Aluvia) for the parent study but had no role in study design, data accrual and analysis, or manuscript preparation. Gilead donates medications for participants in a separate NIH-funded study led by D.V.H. but provides no financial support. The other authors have no conflicts of interest to disclose.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jaids.com).

D.C., E.D.C., M.R.K., and D.V.H. conceived and designed the parent study. S.L.Y. and D.C. designed this substudy. P.N., D.N., J.M., B.N., T.D.C., T.D.R., and J.A. contributed significantly to the acquisition of data. C.A.K., A.P., E.D.C., D.V.H., and S.L.Y. analyzed and interpreted the data. C.A.K. and S.L.Y. authored the manuscript with input and important revisions from all authors, including P.N., D.N., A.P., J.M., B.N., T.D.C., T.D.R., J.A., E.D.C., D.C., M.R.K., and D.V.H.

Correspondence to: Catherine A. Koss, MD, Division of HIV, Infectious Diseases, and Global Medicine, San Francisco General Hospital, University of California, San Francisco, Box 0874, San Francisco, CA 94143-0874 (e-mail: catherine.koss@ucsf.edu).

INTRODUCTION

Food insecurity, defined as uncertain access to safe and nutritious foods,[1] and food insufficiency (FI), in which inadequate quantities of food are available,[2–4] have been associated with poor health outcomes in HIV-infected populations, including reduced adherence to antiretroviral therapy (ART) and mortality.[5–7] Moreover, food insecurity has been associated with lower rates of viral suppression among HIV-infected adults in the United States[8–10] and rural Uganda.[11]

Pregnant and breastfeeding women may be particularly vulnerable to food insecurity and insufficiency because of increased nutritional demands[12,13] at a time of reduced physical ability to generate income and obtain and prepare food.[14] Poor nutritional status and food insecurity have been associated with adverse pregnancy outcomes among HIV-infected women and reduced uptake of interventions to prevent perinatal transmission.[15–19] Among pregnant women treated with combination ART, food insecurity has been associated with reduced pharmacokinetic exposure to antiretrovirals (ARVs), inadequate maternal weight gain during pregnancy, low birth weight, and preterm delivery.[20–22] Furthermore, food insecurity may also be a barrier to exclusive breastfeeding.[23,24]

World Health Organization guidelines now recommend that all pregnant and breastfeeding HIV-infected women initiate combination ART and encourage lifelong therapy.[25] Achieving and maintaining viral suppression during pregnancy and breastfeeding will be critical to attaining the dual

goals of preserving maternal health and eliminating perinatal HIV infections. Viral suppression, in turn, is dependent on adequate ARV adherence and pharmacokinetic exposure, both of which may be influenced by insufficient food intake.[6,7,20,26–28]

Although food insecurity and insufficiency may be major drivers of virologic outcomes among childbearing HIV-infected women in resource-limited settings, this relationship has not yet been examined. In Uganda, where the prevalence of HIV is 7.3%[29] and 48% of households are food energy deficient,[30] food security and sufficiency may impact HIV outcomes. Therefore, we examined the association between household FI and viral suppression during pregnancy and breastfeeding in a cohort of HIV-infected women in rural Uganda.

METHODS

Study Design and Population

We performed a secondary analysis of data from the PROMOTE-Pregnant Women and Infants study (NCT00993031), which was designed to test the hypothesis that lopinavir/ritonavir would reduce the prevalence of placental malaria. Study procedures[31] and results[20–22,24,31–35] are described elsewhere. Briefly, the study enrolled HIV-infected, ART-naive pregnant women between 12 and 28 weeks gestation in Tororo, Uganda from December 2009 to September 2012. Women initiated ART at enrollment and were randomized to receive lopinavir/ritonavir or efavirenz, in combination with lamivudine/zidovudine. Participants received multivitamins containing iron and folic acid, iron supplements, mebendazole, and trimethoprim/sulfamethoxazole prophylaxis. Women were seen at the study clinic every 4 weeks; participants continued ART and were followed for up to 1 year postpartum. Women were counseled to breastfeed their infants for 1 year, with exclusive breastfeeding for the first 6 months of life. One participant switched from lopinavir/ritonavir to efavirenz because of the need for tuberculosis treatment; all other participants remained on their assigned study drug.

This analysis includes women who participated in assessments of food security, which were performed among all participants actively enrolled from September 11, 2011, to February 4, 2012. The study protocol was approved by the Makerere University School of Medicine Research and Ethics Committee, the Uganda National Council for Science and Technology, Cornell University Institutional Review Board, and the University of California, San Francisco Committee on Human Research. Participants provided written informed consent in their preferred language.

Measurements

HIV-1 RNA was measured at screening, 8 weeks after ART initiation, delivery, 8, 24, and 48 weeks postpartum, and at other intervals for clinical management. HIV-1 RNA polymerase chain reaction testing was performed using COBAS AMPLICOR version 1.5 (Roche Molecular Diagnostics, Pleasanton, CA) until September 2012, and thereafter with the *m*2000 RealTi*m*e HIV-1 assay (Abbott Laboratories, Abbott Park, IL). The primary outcome for this analysis was sustained viral suppression from 8 weeks after ART initiation to 48 weeks postpartum. Viral suppression was dichotomized as "sustained" if HIV-1 RNA $\leq$400 copies per milliliter (the lower limit of detection of the assays) at all measured time points and "not sustained" if HIV-1 RNA $>$400 copies per milliliter at any measured time point. Sixteen participants had missing HIV-1 RNA measurements at 8 weeks on ART (N = 8) or 48 weeks postpartum (N = 8).

FI was operationalized using the Household Hunger Scale (HHS),[36] a subset of 3 questions about insufficient food quantities from the 9-item Household Food Insecurity Access Scale,[37] which has been previously been validated for cross-cultural use[38] and measured among HIV-infected adults in rural Uganda.[28,39] The HHS asks the frequency over the previous 4 weeks of (1) having no food to eat of any kind in one's household, (2) going to sleep at night hungry, and (3) going a whole day and whole night without eating. A response of "never" received 0 points, "rarely or sometimes" received 1 point, and "often" received 2 points; points were summed as a score, with a maximum score of 6 points for a response of "often" to all 3 questions. For logistic regression analyses, FI was dichotomized as no household hunger (HH) versus any HH (any positive response, indicating the presence of FI). FI was assessed once, in the season when food is most abundant in Tororo, such that FI scores would be the most conservative and have the least seasonal variation. FI interviews were conducted among 197 women, at a median of 5.6 months postpartum (interquartile range 2.2–9.2); 18 participants were interviewed before delivery.

A household wealth index was generated by performing a principal component analysis of questions regarding household possession of assets, including a radio, telephone, television, motorcycle, or bicycle, among all PROMOTE participants.[22] The first principal component was used to create the index. Tertiles of the wealth index were used to categorize individual household wealth relative to the cohort. Participants in the middle and highest tertiles of wealth were grouped together for comparison with those in the lowest wealth tertile. Residence within the town of Tororo was defined as urban based on GPS coordinates; other residences in Tororo district were classified as rural. Gestational age at enrollment was determined based on last menstrual period and fetal ultrasound.[21] For calculation of body mass index (BMI), maternal height was measured using a wall-mounted measuring tape (Seca 206; Seca, Hamburg, Germany); maternal weight was measured using a Seca 876 mechanical scale until September 2011 and thereafter using a Seca 874 digital scale. Participants were asked whether they were breastfeeding every 4 weeks postpartum. The end of breastfeeding was defined as the last period in which a participant reported any breastfeeding (exclusive or partial). ART adherence was assessed by self-reported recall of the number of pills taken of the expected number of pills over the 3 days before each study visit.

Statistical Analysis

Characteristics of enrolled participants with and without FI were compared using the χ^2 test or Fisher's exact test for categorical variables and the Wilcoxon rank-sum test for

continuous variables. The proportion of participants with and without FI who achieved viral suppression at individual time points was evaluated using Fisher's exact test because of the small number of participants who did not achieve viral suppression at each time point. A 4-week measurement window was used for virologic outcomes.

Logistic regression models were used to evaluate the association between sustained viral suppression, FI, and covariates in our causal model (see Figure S1, Supplemental Digital Content, http://links.lww.com/QAI/A755). We postulated that the association between FI and sustained viral suppression is mediated through effects on adherence, absorption/pharmacokinetics/bioavailability, BMI, depression, poor nutrition, and reduced protein binding of drug. ART regimen and pretreatment HIV-1 RNA were included in the multivariable model as independent predictors of sustained viral suppression. Household wealth was included in the model as a confounder of the relationship between FI and viral suppression. Age was evaluated as a potential confounder. Using the causal model as a guide, we evaluated the effect of individual predictors and confounders, and assessed overall model fit to achieve the final model. Inclusion of age in the multivariable model did not alter the association between FI and viral suppression and did not improve overall model fit; thus, age was excluded from the final model. Statistical analyses were performed using SAS software version 9.3 (SAS Institute, Cary, NC).

RESULTS

Participant Characteristics by Food Insufficiency Status

Of 197 women in the PROMOTE study who underwent FI assessment, 26 were excluded from this analysis: 2 did not deliver, 8 were withdrawn before 48 weeks postpartum, and 16 had missing HIV-1 RNA measurements. There were no statistically significant differences between included and excluded participants in any predictor variables, including FI status and pretreatment HIV-1 RNA, and viral suppression at delivery. Among 171 participants, 43 (25.1%) reported no FI (score 0) and 128 (74.9%) reported FI (any HH) (Table 1). Of 128 participants with FI, 12 (9.4%) reported severe HH (score 4–6), 70 (54.7%) reported moderate HH (score 2–3), and 46 (35.9%) had little HH (score 1). At baseline, characteristics were similar between participants with and without FI, including maternal age, gestational age, CD4 cell count, and $\log_{10}$ HIV-1 RNA. At 24 weeks postpartum, 99.2% of food insufficient participants and 100% of food sufficient participants were breastfeeding their infants; 68.6% (food insufficient) and 80.5% (food sufficient) reported exclusive breastfeeding. At 48 weeks postpartum, 91.7% of food insufficient participants and 95.1% of food-sufficient participants reported partial breastfeeding. Two infants acquired HIV; both of their mothers reported FI (one moderate and one severe HH).

Virologic Outcomes

Overall, a high proportion of participants achieved viral suppression at individual time points throughout the study

TABLE 1. Characteristics of 171 HIV-Infected Pregnant Women in the PROMOTE Trial at Enrollment and During Study Follow-Up, by Food Insufficiency Status

	Food Insufficiency	
Characteristics	**Any (N = 128)**	**None (N = 43)**
Enrollment		
Age, mean (SD), yrs	29.4 (5.6)	29.3 (5.3)
Education completed, n (%)		
Less than primary	14 (10.9)	8 (18.6)
Primary or higher	114 (89.1)	35 (81.4)
Household wealth, n (%)		
Lowest	50 (39.7)	11 (25.6)
Middle/highest	76 (60.3)	32 (74.4)
Urban residence (versus rural), n (%)	20 (16.0)	10 (24.4)
No. previous pregnancies, n (%)		
0	9 (7.0)	5 (9.8)
1–2	29 (22.7)	11 (25.6)
3 or more	90 (70.3)	27 (62.8)
No. living children, median (IQR)	3.0 (1.5–4.0)	3.0 (1.0–5.0)
Gestational age, median (IQR), wk	20.1 (17.7–24.5)	22.1 (17.4–24.4)
BMI, median (IQR), kg/m^2	21.1 (19.9–22.9)	21.9 (20.4–24.1)
HIV diagnosed in current pregnancy, n (%)	54 (42.2)	17 (39.6)
WHO stage 1, n (%)	123 (96.1)	42 (97.7)
CD4 cell count, median (IQR), $cells/mm^3$	386 (271–487)	423 (261–559)
Pretreatment HIV-1 RNA, median (IQR), $\log_{10}$ copies/mL	4.3 (3.4–4.9)	4.2 (3.5–4.8)
During Study Follow-Up		
Efavirenz-based ART regimen (versus lopinavir/ritonavir), n (%)	68 (53.1)	18 (41.9)
Self-reported ART adherence, mean (SD), %		
During pregnancy	97.2 (8.8)	99.1 (3.0)
During breastfeeding	99.2 (2.4)	99.6 (1.5)
During pregnancy and breastfeeding	98.8 (2.5)	99.5 (1.6)
Grade 1 or 2 nausea or vomiting during pregnancy or breastfeeding, n (%)	45 (35.2)	14 (32.6)
Grade 1 or 2 diarrhea during pregnancy or breastfeeding, n (%)	64 (50.0)	13 (30.2)*
Breastfeeding, n/N (%)		
24 wk postpartum, partial or exclusive	119/120 (99.2)	41/41 (100)
24 wk postpartum, exclusive	83/121 (68.6)	33/41 (80.5)
48 wk postpartum, partial	110/120 (91.7)	39/41 (95.1)
Viral suppression, n/N (%)		
8 wk after ART initiation	111/128 (86.9)	42/43 (97.7)
Delivery	109/121 (90.1)	37/40 (92.5)
8 wk postpartum	110/124 (88.7)	36/40 (90.0)
24 wk postpartum	101/116 (87.1)	40/40 (100)
48 wk postpartum	112/128 (87.5)	41/43 (95.4)
Sustained viral suppression, n/N (%)†	77/128 (60.2)	34/43 (79.1)‡

*$P = 0.02$.
†At all measured time points from 8 weeks after ART initiation to 48 weeks postpartum.
‡$P = 0.03$.
IQR, interquartile range; WHO, World Health Organization.

(Table 1); 90.1% of food insufficient women and 92.5% of food sufficient women were virologically suppressed at delivery. A total of 77 women (60.2%) with FI achieved sustained viral suppression, compared with 79.1% of women reporting no FI ($P = 0.03$). The proportion of participants who achieved sustained viral suppression by HH status was 34 of 43 (79.1%, no HH), 29 of 46 (63%, little HH), 39 of 70 (55.7%, moderate HH), and 9 of 12 (75%, severe HH).

In a multivariable model of sustained viral suppression, FI [adjusted odds ratio (aOR) 0.38, 95% confidence interval (CI): 0.16 to 0.91, $P = 0.03$], pretreatment HIV-1 RNA (aOR 0.55 per 10-fold increase, 95% CI: 0.37 to 0.82, $P < 0.01$), and ART regimen of lopinavir/ritonavir versus efavirenz (aOR 0.49, 95% CI: 0.24 to 0.96, $P = 0.04$) were associated with lower odds of viral suppression (Table 2).

DISCUSSION

In this cohort of HIV-infected women in rural Uganda who initiated ART during pregnancy, FI was highly prevalent, consistent with previous estimates among nonpregnant HIV-infected Ugandan adults.[11] Although the proportion of women who achieved viral suppression was high overall in this cohort, with more than 90% virologically suppressed at delivery,[33] FI was associated with 62% lower odds of achieving and sustaining viral suppression during pregnancy and breastfeeding. To our knowledge, this is the first study to evaluate the association between FI and virologic outcomes during pregnancy and breastfeeding, when viral suppression has implications both for preserving maternal health and reducing the risk of perinatal transmission. Thus, in this cohort of women with high median CD4 cell count, the strong association between FI and lack of sustained viral suppression suggests that FI may be an important and modifiable risk factor for virologic failure.

The results of this study are consistent with previously published reports of poor virologic outcomes among nonpregnant food insecure individuals in the United States and Uganda, in whom food insecurity was associated with 40%–77% lower odds of viral suppression.[8–11] The consistency of these findings across diverse settings and the modifiable nature of food insecurity underscore the need to understand the mechanisms by which FI and food insecurity may lead to virologic failure, such that appropriate interventions can be implemented. Potential causal pathways include behavioral[7] (eg, decreased adherence due to lack of food with which to take medicines, competing resource demands precluding access to medicines), psychological[6,40] (eg, depression and anxiety associated with FI, leading to decreased adherence), and pharmacokinetic alterations[26] (eg, altered ARV absorption and reduced bioavailability in food insecure individuals).

Nutritional supplements, ready to use supplementary foods, and other strategies may reduce FI and are increasingly being studied and implemented programmatically in nonpregnant HIV-infected populations.[41–43] In a pilot study in Zambia, food supplementation led to increased ART adherence.[44] Similarly, food supplementation was associated with improved clinic attendance, BMI, and food security in Haiti.[45] Another study in Haiti that randomized nonpregnant HIV-infected adults on ART to ready to use supplementary foods or a corn-soy blend supplement found similar improvements in CD4 cell count, ART adherence, and household wealth index in each arm.[46] Nonetheless, the optimal components, quantity, and duration of supplementation are not yet known.[43,47,48]

Whereas several studies have addressed micronutrient (vitamin/mineral) supplementation among HIV-infected pregnant women,[49] few studies of macronutrient (carbohydrate/protein/fat) supplementation have been conducted in this population, such that little is known about the impact on viral suppression. A trial in Malawi found that a lipid-based nutrient supplement plus maize reduced weight loss during breastfeeding among HIV-infected women compared with those receiving a maize provision alone, but did not affect infant weight gain.[50,51] The first study of macronutrient supplementation among HIV-infected pregnant women (a subgroup of PROMOTE participants not included in this analysis) found that a lipid-based nutrient supplement and instant soy porridge were highly acceptable.[48]

This study has several important strengths, including being the first to investigate the role of FI in virologic outcomes among pregnant and lactating women and the repeated measures of HIV-1 RNA. A limitation of this study

TABLE 2. Factors Associated With Sustained Viral Suppression From 8 Weeks After ART Initiation to 48 Weeks Postpartum, Among 171 HIV-Infected Pregnant and Breastfeeding Women in the PROMOTE Trial

Variable	Unadjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Food insufficiency				
Any household hunger versus none	0.40 (0.18 to 0.90)	0.03	0.38 (0.16 to 0.91)	0.03
Pretreatment HIV-1 RNA				
Per 10-fold increase	0.55 (0.38 to 0.82)	<0.01	0.55 (0.37 to 0.82)	<0.01
ART regimen				
Lopinavir/ritonavir versus efavirenz	0.59 (0.31 to 1.11)	0.10	0.49 (0.24 to 0.96)	0.04
Household wealth				
Lowest versus middle/highest	0.69 (0.36 to 1.32)	0.26	0.76 (0.38 to 1.53)	0.45
Age				
Per year	1.06 (1.00 to 1.12)	0.06		

OR, odds ratio.

is that FI was measured only once, and the HHS only assessed experiences in the 4 weeks before FI interviews. In addition, FI was generally not measured at the beginning of the period during which virologic outcomes were measured. Thus, it is possible that variation in FI occurred throughout the study period that we were unable to measure. Repeated measurements of FI would have provided stronger evidence of causality. However, because FI was measured in the season of greatest food security (ie, when FI is lowest in Tororo), the strength of the relationship between FI and viral suppression may be underestimated. Participants received resources that are protective against some of the potential pathways by which FI may be deleterious (ie, reimbursement for transportation to the study clinic, free provision of ART and medical care); this may have also attenuated the strength of the observed association between FI and virologic outcomes. In addition, we do not have data on quantity or quality of diet.

In summary, FI may be an important and modifiable determinant of adverse virologic outcomes among pregnant and lactating women. As millions of HIV-infected women worldwide initiate and continue ART during pregnancy and breastfeeding, there is a pressing need to address barriers to achieving and maintaining viral suppression. Interventions to reduce FI may result in improved health outcomes among HIV-infected women and their children and merit further attention from the research and programmatic communities. Future research should elucidate the mechanisms driving this association, such that efficacious and cost-effective interventions can be implemented.

ACKNOWLEDGMENTS

The authors thank the participants in the PROMOTE-Pregnant Women and Infants study, the dedicated PROMOTE study staff and members of the Infectious Diseases Research Collaboration, and the practitioners at Tororo District Hospital.

REFERENCES

1. Food and Agricultural Organization. Rome declaration on world food security and world food summit plan of action. Rome: FAO, 1996. Available from: http://www.fao.org/docrep/003/w3613e/w3613e00.HTM. Accessed July 20, 2015.
2. Jones AD, Ngure FM, Pelto G, et al. What are we assessing when we measure food security? A compendium and review of current metrics. *Adv Nutr.* 2013;4:481–505.
3. Anema A, Fielden SJ, Castleman T, et al. Food security in the context of HIV: towards harmonized definitions and indicators. *AIDS Behav.* 2014; 18(suppl 5):S476–S489.
4. Briefel RR, Woteki CE. Development of food sufficiency questions for the 3rd National Health and Nutrition Examination Survey. *J Nutr Educ.* 1992;24:S24–S28.
5. Weiser SD, Fernandes KA, Brandson EK, et al. The association between food insecurity and mortality among HIV-infected individuals on HAART. *J Acquir Immune Defic Syndr.* 2009;52:342–349.
6. Weiser SD, Young SL, Cohen CR, et al. Conceptual framework for understanding the bidirectional links between food insecurity and HIV/AIDS. *Am J Clin Nutr.* 2011;94:1729S–1739S.
7. Young S, Wheeler AC, McCoy SI, et al. A review of the role of food insecurity in adherence to care and treatment among adult and pediatric populations living with HIV and AIDS. *AIDS Behav.* 2014;18(suppl 5): S505–S515.
8. Feldman MB, Alexy ER, Thomas JA, et al. The association between food insufficiency and HIV treatment outcomes in a longitudinal analysis of HIV-infected individuals in New York City. *J Acquir Immune Defic Syndr.* 2015;69:329–337.
9. 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;26:1012–1018.
10. Weiser SD, Frongillo EA, Ragland K, et al. Food insecurity is associated with incomplete HIV RNA suppression among homeless and marginally housed HIV-infected individuals in San Francisco. *J Gen Intern Med.* 2009;24:14–20.
11. 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;28:115–120.
12. Institute of Medicine and National Research Council. *Weight Gain During Pregnancy: Reexamining the Guidelines*. Washington, DC: The National Academies Press; 2009.
13. Institute of Medicine. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, DC: The National Academies Press; 2006.
14. Laraia BA, Siega-Riz AM, Gundersen C, et al. Psychosocial factors and socioeconomic indicators are associated with household food insecurity among pregnant women. *J Nutr.* 2006;136:177–182.
15. McCoy SI, Buzdugan R, Mushavi A, et al. Food insecurity is a barrier to prevention of mother-to-child HIV transmission services in Zimbabwe: a cross-sectional study. *BMC Public Health.* 2015;15:420.
16. Mehta S, Manji KP, Young AM, et al. Nutritional indicators of adverse pregnancy outcomes and mother-to-child transmission of HIV among HIV-infected women. *Am J Clin Nutr.* 2008;87:1639–1649.
17. Ramlal RT, Tembo M, Soko A, et al. Maternal mid-upper arm circumference is associated with birth weight among HIV-infected Malawians. *Nutr Clin Pract.* 2012;27:416–421.
18. Villamor E, Dreyfuss ML, Baylin A, et al. Weight loss during pregnancy is associated with adverse pregnancy outcomes among HIV-1 infected women. *J Nutr.* 2004;134:1424–1431.
19. Villamor E, Saathoff E, Msamanga G, et al. Wasting during pregnancy increases the risk of mother-to-child HIV-1 transmission. *J Acquir Immune Defic Syndr.* 2005;38:622–626.
20. Bartelink IH, Savic RM, Mwesigwa J, et al. Pharmacokinetics of lopinavir/ritonavir and efavirenz in food insecure HIV-infected pregnant and breastfeeding women in Tororo, Uganda. *J Clin Pharmacol.* 2014; 54:121–132.
21. Koss CA, Natureeba P, Plenty A, et al. Risk factors for preterm birth among HIV-infected pregnant Ugandan women randomized to lopinavir/ritonavir- or efavirenz-based antiretroviral therapy. *J Acquir Immune Defic Syndr.* 2014;67:128–135.
22. Young S, Murray K, Mwesigwa J, et al. Maternal nutritional status predicts adverse birth outcomes among HIV-infected rural Ugandan women receiving combination antiretroviral therapy. *PLoS One*. 2012;7: e41934.
23. Webb-Girard A, Cherobon A, Mbugua S, et al. Food insecurity is associated with attitudes towards exclusive breastfeeding among women in urban Kenya. *Matern Child Nutr.* 2012;8:199–214.
24. Young SL, Plenty AH, Luwedde FA, et al. Household food insecurity, maternal nutritional status, and infant feeding practices among HIV-infected Ugandan women receiving combination antiretroviral therapy. *Matern Child Health J.* 2014;18:2044–2053.
25. World Health Organization. *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach*. Geneva, Switzerland: World Health Organization, 2013.
26. Bartelink IH, Savic RM, Dorsey G, et al. The effect of malnutrition on the pharmacokinetics and virologic outcomes of lopinavir, efavirenz and nevirapine in food insecure HIV-infected children in Tororo, Uganda. *Pediatr Infect Dis J.* 2015;34:e63–e70.
27. Kalichman SC, Washington C, Grebler T, et al. Medication adherence and health outcomes of people living with HIV who are food insecure and prescribed antiretrovirals that should be taken with food. *Infect Dis Ther.* 2015;4:79–91.
28. Weiser SD, Tuller DM, Frongillo EA, et al. Food insecurity as a barrier to sustained antiretroviral therapy adherence in Uganda. *PLoS One*. 2010;5:e10340.

29. UNAIDS. *How AIDS Changed Everything. MDG 6: 15 Years, 15 Lessons of Hope from the AIDS Response*. Geneva, Switzerland: UNAIDS, 2015.
30. World Food Programme. *Comprehensive Food Security and Vulnerability Analysis: Uganda*. 2013. Available from: https://www.wfp.org/content/uganda-comprehensive-food-security-and-vulnerability-analysis-cfsva-april-2013. Accessed July 20, 2015.
31. Natureeba P, Ades V, Luwedde F, et al. Lopinavir/ritonavir-based antiretroviral treatment (ART) versus efavirenz-based ART for the prevention of malaria among HIV-infected pregnant women. *J Infect Dis*. 2014;210:1938–1945.
32. Ades V, Mwesigwa J, Natureeba P, et al. Neonatal mortality in HIV-exposed infants born to women receiving combination antiretroviral therapy in rural Uganda. *J Trop Pediatr*. 2013;59:441–446.
33. Cohan D, Natureeba P, Koss CA, et al. Efficacy and safety of lopinavir/ritonavir versus efavirenz-based antiretroviral therapy in HIV-infected pregnant Ugandan women. *AIDS*. 2015;29:183–191.
34. Gandhi M, Mwesigwa J, Aweeka F, et al. Hair and plasma data show that lopinavir, ritonavir, and efavirenz all transfer from mother to infant in utero, but only efavirenz transfers via breastfeeding. *J Acquir Immune Defic Syndr*. 2013;63:578–584.
35. Koss CA, Natureeba P, Mwesigwa J, et al. Hair concentrations of antiretrovirals predict viral suppression in HIV-infected pregnant and breastfeeding Ugandan women. *AIDS*. 2015;29:825–830.
36. Deitchler M, Ballard T, Swindale A, et al. *Introducing a Simple Measure of Household Hunger for Cross-Cultural Use*. Washington, DC: Food and Nutrition Technical Assistance II Project (FANTA-2), AED, 2011.
37. Coates C, Swindale A, Bilinsky P. *Household Food Insecurity Access Scale (HFIAS) for Measurement of Food Access: Indicator Guide (v. 3)*. Washington, DC: Food and Nutrition Technical Assistance Project, Academy for Educational Development, August; 2007.
38. Deitchler M, Ballard T, Swindale A, et al. Validation of a measure of household hunger for cross-cultural use. Washington, DC: Food and Nutrition Technical Assistance II Project (FANTA-2), FHI 360; 2010.
39. Weiser SD, Tsai AC, Gupta R, et al. Food insecurity is associated with morbidity and patterns of healthcare utilization among HIV-infected individuals in a resource-poor setting. *AIDS*. 2012;26:67–75.
40. Mills EJ, Nachega JB, Buchan I, et al. Adherence to antiretroviral therapy in sub-Saharan Africa and North America: a meta-analysis. *JAMA*. 2006; 296:679–690.
41. Cohen CR, Steinfeld RL, Weke E, et al. Shamba Maisha: pilot agricultural intervention for food security and HIV health outcomes in Kenya: design, methods, baseline results and process evaluation of a cluster-randomized controlled trial. *Springerplus*. 2015;4:122.
42. Grobler L, Siegfried N, Visser ME, et al. Nutritional interventions for reducing morbidity and mortality in people with HIV. *Cochrane Database Syst Rev*. 2013;2:CD004536.
43. Nagata JM, Cohen CR, Young SL, et al. Descriptive characteristics and health outcomes of the food by prescription nutrition supplementation program for adults living with HIV in Nyanza Province, Kenya. *PLoS One*. 2014;9:e91403.
44. 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;49:190–195.
45. Ivers LC, Chang Y, Gregory Jerome J, et al. 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.
46. Ivers LC, Teng JE, Jerome JG, et al. A randomized trial of ready-to-use supplementary food versus corn-soy blend plus as food rations for HIV-infected adults on antiretroviral therapy in rural Haiti. *Clin Infect Dis*. 2014;58:1176–1184.
47. Ivers LC, Cullen KA, Freedberg KA, et al. HIV/AIDS, undernutrition, and food insecurity. *Clin Infect Dis*. 2009;49:1096–1102.
48. Young S, Natamba B, Luwedde F, et al. "I have remained strong because of that food": acceptability and use of lipid-based nutrient supplements among pregnant HIV-infected ugandan women receiving combination antiretroviral therapy. *AIDS Behav*. 2015;19:1535–1547.
49. Siegfried N, Irlam JH, Visser ME, et al. Micronutrient supplementation in pregnant women with HIV infection. *Cochrane Database Syst Rev*. 2012;3:CD009755.
50. Flax VL, Bentley ME, Chasela CS, et al. Use of lipid-based nutrient supplements by HIV-infected Malawian women during lactation has no effect on infant growth from 0 to 24 weeks. *J Nutr*. 2012;142: 1350–1356.
51. Kayira D, Bentley ME, Wiener J, et al. A lipid-based nutrient supplement mitigates weight loss among HIV-infected women in a factorial randomized trial to prevent mother-to-child transmission during exclusive breastfeeding. *Am J Clin Nutr*. 2012;95:759–765.