



Body composition, energy expenditure and physical activity

# HIV infection and increased food insecurity are associated with adverse body composition changes among pregnant and lactating Kenyan women

Elizabeth M. Widen<sup>1</sup> · Irene Tsai<sup>2</sup> · Shalean M. Collins<sup>3</sup> · Pauline Wekesa<sup>4</sup> · Joy China<sup>4</sup> · Natalie Krumdieck<sup>5</sup> · Joshua D. Miller<sup>3</sup> · Sheri D. Weiser<sup>6</sup> · Maricianah Onono<sup>4</sup> · Sera L. Young<sup>3,7</sup>

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## Abstract

**Background/objectives** Body composition changes markedly during reproduction. In sub-Saharan Africa, impacts of HIV infection on body composition across pregnancy and lactation in the context of Option B+ antiretroviral therapy are unknown. Therefore, we sought to evaluate the role of HIV infection on body composition during pregnancy and lactation among Kenyan women.

**Subjects/methods** A cohort of pregnant women ( $n = 333$ ; 50.5% HIV+, receiving ART) were enrolled at seven clinics in western Kenya. Two prenatal (mean  $\pm$  SD:  $23.6 \pm 4.4$  and  $33.4 \pm 2.0$  weeks gestation) and three postpartum (6, 14, and 36 weeks) measurements included: individual-level food insecurity, height, weight, fat mass (FM), and fat-free mass (FFM) by bioimpedance analysis (BIA), mid-upper arm circumference (MUAC), and triceps skinfold (TSF), allowing for AMA (arm muscle area) and AFA (arm fat area) derivation. Multivariable longitudinal regression models were used to relate HIV to body composition changes.

**Results** In longitudinal models, HIV-infected women had lower weight ( $\beta = -3.0$  kg,  $p = 0.003$ ), fat mass ( $\beta = -1.5$  kg,  $p = 0.02$ ), fat-free mass ( $\beta = -1.5$  kg,  $p = 0.01$ ), TSF ( $\beta = -2.6$  mm,  $p < 0.001$ ), AFA ( $\beta = -3.9$  cm<sup>3</sup>,  $p < 0.001$ ), and MUAC ( $\beta = -1.0$  cm,  $p = 0.001$ ), but not AMA ( $p = 0.34$ ), across all observations. Food insecurity was inversely associated with AMA and MUAC postpartum (AMA  $\beta$ -range =  $-0.47$  to  $-0.92$  cm<sup>3</sup>; MUAC  $\beta$ -range =  $-0.09$  to  $-0.15$  cm, all  $p < 0.05$ ).

**Conclusions** HIV infection was associated with lower weight, fat mass, fat-free mass, TSF, AFA, and MUAC values during pregnancy and lactation, while food insecurity was intermittently associated with body composition. This suggests that pregnant and lactating women living with HIV and food insecurity could benefit from nutritional support.

## Introduction

Body composition is an important indicator of nutritional status and health. Across life stages, body composition is

influenced by both diet and infection. During pregnancy and lactation, maternal body composition changes dynamically to support the growing fetus and breastfeeding [1, 2]. During pregnancy, women gain fat and fat-free mass with concomitant shifts in regional body fat depots, typified by gains in the arm fat area (AFA) in early and mid-pregnancy, followed by declines thereafter [1, 3, 4]. Body composition changes are highly variable during lactation; most women

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✉ Sera L. Young  
sera.young@northwestern.edu

<sup>1</sup> Department of Nutritional Sciences, University of Texas at Austin, Austin, TX, USA

<sup>2</sup> School of General Studies, Columbia University, New York, NY, USA

<sup>3</sup> Department of Anthropology, Northwestern University,

Evanston, IL, USA

<sup>4</sup> Kenya Medical Research Institute, Nairobi, Kenya

<sup>5</sup> Weill Cornell Medical College, New York, NY, USA

<sup>6</sup> School of Medicine, University of California San Francisco, San Francisco, CA, USA

<sup>7</sup> Institute for Policy Research, Northwestern University, Evanston, IL, USA

experience mild and gradual weight loss, while some remain relatively weight-stable or gain weight [2].

HIV infection is associated with body composition changes. Among HIV+ women, thinness and lower anthropometry values have been linked to adverse pregnancy outcomes [5–7], sub-optimal infant growth [8], and increased mother-to-child transmission of HIV [9]. Additionally, postnatal antiretroviral therapy (ART) may exacerbate weight loss during 6 months of exclusive breastfeeding (EBF) [10]. However, no studies have examined body composition changes across pregnancy and lactation among HIV-infected (HIV+) and HIV-uninfected (HIV–) women in a single cohort in the context of widespread adoption of Option B+ ART [11]. Given that ART is now widely administered in accordance with World Health Organization (WHO) recommendations (e.g. initiation of lifelong ART “Option B+” at HIV diagnosis), understanding its role in body composition is important [11].

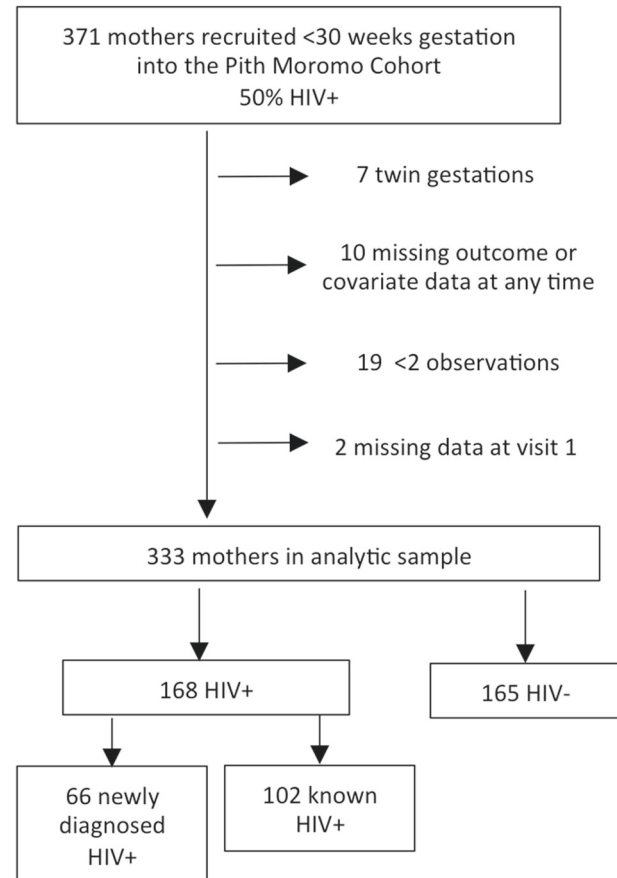
Timing of HIV diagnosis relative to pregnancy, as well as the initiation and duration of ART, could also influence body composition, but to date there are no data supporting this. Further, newly diagnosed women may experience emotional distress and disengagement from care, which can be deleterious for nutritional status [12].

Food insecurity, HIV, and nutrition are linked in a multi-directional relationship, which is intensified during periods of heightened nutritional needs, such as reproduction or HIV infection [13, 14]. For example, among HIV+ and HIV– Ugandan women, food insecurity was associated with adverse changes in postpartum weight and AFA [15].

We examined whether HIV infection was associated with body composition changes during pregnancy and lactation among Kenyan women of mixed HIV status. We hypothesized that HIV+ women receiving ART would exhibit lower weight and greater loss of overall and regional lean mass than HIV-negative women. Relatedly, we examined how HIV diagnosis during the index pregnancy and concomitant initiation of Option B+ influenced body composition compared to HIV diagnosis prior to the index pregnancy. Our second objective was to evaluate how food insecurity influenced body composition. We hypothesized that food insecurity would be inversely associated with body composition.

## Methods

Data are from the Pith Moromo Study, a longitudinal observational cohort designed to examine the health consequences of food insecurity in HIV+ and HIV– women in Nyanza Region, Kenya (NCT02974972). Study enrollment was between August 2014 and February 2015, and follow-up visits were conducted through April 2016.



**Fig. 1** Participant flow diagram of HIV+ and HIV– Kenyan women. HIV–, HIV-uninfected; HIV+, HIV-infected

All participants received antenatal care (ANC) at Family AIDS Care and Educational Services (FACES) clinics in Kisumu, Nyahera, Rongo, Ongo, Migori, Macalder, or Nyamara. These clinics deliver integrated, comprehensive HIV care, treatment, and prevention services. HIV+ women received comprehensive HIV services, including Option B + ART. At the first ANC visit, women were invited to participate if they met the following criteria: gestational age <30 weeks (assessed using last menstrual period abstracted from ANC cards), living within the study area and not planning to move, and known HIV status (assessed at ANC). Food insecurity in the past month was determined using the 9-item Individual Food Insecurity Access Scale (range: 0–27) [16]. Sampling was purposive by HIV and food insecurity status (Fig. 1, Supplemental Table 1), such that equal numbers of HIV+ and HIV– women by tertiles of food insecurity scores (low 0–9, moderate 10–18, and severe 19–27) were enrolled. Approximately equal numbers of women with a known HIV+ status (Known Positive (KP); HIV diagnosis prior to index pregnancy) and a new HIV+ diagnosis (Newly Diagnosed (ND); HIV diagnosis during index pregnancy) were enrolled. Three hundred

seventy-one women were enrolled into the parent study, which was determined to be sufficient to detect differences in the primary outcomes of the study (e.g. maternal BMI) by food insecurity status at a power of 0.8.

Visits antenatally were at enrollment (Mean  $\pm$  SD:  $23.7 \pm 4.4$  weeks gestation) and follow-up ( $33.4 \pm 2.0$  weeks gestation), and postnatally at 6 ( $6.5 \pm 0.91$  weeks) and 14 weeks ( $14.6 \pm 0.88$  weeks) and 9 months ( $39.8 \pm 1.8$  weeks), with two phone calls at 1 week and 6 months. Measurements obtained by trained research staff included: weight (Seca 874, Seca North America, Chino, CA), height (Seca 206, Seca North America, Chino, CA), mid-upper arm circumference (MUAC) with a non-stretchable retractable tape measure, and triceps skinfold thickness (TSF) (Harpenden calipers, Baty International, United Kingdom). Arm muscle area (AMA) and AFA were calculated [15]. Bioelectrical impedance analysis (BIA) [BIA 450, Biodynamics, Seattle, Washington] was used to estimate fat-free mass and fat mass. Meeting water needs is often challenging in sub-Saharan Africa [17] and many women in this cohort reported at least one experience of water insecurity in the previous month [18]. To ensure hydration and minimize dehydration, which results in underestimation of fat mass by BIA [19], participants consumed approximately 8 oz of water and BIA was conducted approximately 90 min later.

At enrollment, self-report of education, marital status, and age were obtained. Household socioeconomic status was derived using principal components analysis from self-report of household assets adapted from the Kenya Integrated Household Budget Survey questionnaire [20], where higher scores indicate greater wealth. Measures at all visits included the Center for Epidemiologic Studies Depression (CES-D) scale [21], self-report of breastfeeding, morbidity (symptoms experienced at the time of visit), and dietary diversity [22] and time use activities (heavy/light work/sleep/leisure) within the last 24 h. For HIV+ women, ART regimen and WHO clinical staging [23] were abstracted from clinical records and ANC cards.

Institutional Review Boards at Cornell University, Northwestern University, and Kenya Medical Research Institute approved study procedures for Pith Moromo. All mothers provided written informed consent.

## Statistical analyses

Statistical analyses were conducted using Stata 14.0 software with an  $\alpha$  of  $< 0.05$ . Singleton participants were included in analyses if they had  $\geq 2$  study visits and enrollment body composition data (Fig. 1). Baseline characteristics were compared between HIV+ and HIV– mothers using parametric tests for continuous, normally distributed variables, and non-parametric tests for skewed

variables. Enrollment occurred at varying gestational ages, so a constructed prenatal visit timing was derived for analyses: early second trimester ( $< 21$  weeks); late second trimester (21 to  $< 28$  weeks); early third trimester (28 to  $< 32$  weeks); mid-third trimester (32 to  $< 36$  weeks); and late third trimester ( $\geq 36$  weeks).

Random-effects longitudinal models were fit for each body composition outcome with the constructed indicator variables for visit timing and study site. Primary exposures were HIV status and time-varying individual food insecurity (continuous score). We evaluated if body composition changes varied by HIV status or food insecurity by including interaction terms between these factors and visit.

Covariates were included if the HIV  $\beta$ -coefficient changed by  $> 10\%$  in one or more of the multivariable models. Time-independent variables included: maternal height (cm), age (years), education [categorical:  $\leq$ primary (ref), secondary,  $\geq$ tertiary], parity (continuous), asset index (continuous), and probable depression at enrollment (CES-D score  $\geq 17$ ). Time-varying variables included: fever (yes/no, categorical), gastrointestinal distress (report of nausea or diarrhea), dietary diversity (score), hunger season in the previous month (e.g. February to May), and proportion of heavy work to light work.

We conducted several secondary analyses. A second set of longitudinal random-effects models evaluated associations between the timing of HIV diagnosis and body composition. In HIV+ women with WHO clinical staging data ( $n = 141$ , 84% of HIV+), we conducted a sensitivity analysis with adjustment for clinical stage [categorical: Stage 1 (Asymptomatic, reference); Stage  $\geq 2$  (Mild-Severe)]. To evaluate, whether breastfeeding impacted body composition changes postpartum, we also conducted a sensitivity analysis using postpartum body composition models with adjustment for EBF linked to concurrent measurements at 6 and 14 weeks, and lagged at 9 months (i.e. EBF at 6 months used at 9 months visit).

## Results

Body composition data were available for 333 mothers (Fig. 1). The characteristics of included women were not different from those not included, except that included women had a lower fat mass at enrollment ( $18.5 \pm 5.8$  vs.  $21.5 \pm 13.8$  kg,  $p = 0.02$ ).

Most characteristics were similar between HIV+ and HIV– women (Table 1), with differences in age, parity, reported fever, and EBF. The majority of HIV+ women were classified as WHO clinical stage I (52.4%) and II (36.7%) HIV infection, and were receiving tenofovir/

**Table 1** Characteristics of HIV+ and HIV- Kenyan women ( $n = 333$ )

	All ( $n = 333$ )	HIV+ ( $n = 168$ )	HIV- ( $n = 165$ )	$p$ -value <sup>a</sup>
Age, years	24.9 ± 4.9	26.2 ± 5.0	23.6 ± 4.4	<0.001
Married, %	91.0	88.7	93.3	0.14
Education, %				
≤Primary	59.2	64.5	53.9	0.09
Secondary	31.5	29.0	34.0	
≥Tertiary	9.3	6.5	12.2	
Asset index <sup>b</sup>	6.8 ± 3.1	6.8 ± 3.2	6.9 ± 2.9	0.61
Gestational age at enrollment, weeks	23.6 ± 4.4	22.9 ± 4.7	24.3 ± 4.0	0.001
Gestational age at enrollment, %				
Early 2nd trimester (<21)	26.4	32.1	20.6	0.05
Late 2nd trimester (≥21, <28)	47.5	44.6	50.3	
Early 3rd trimester (≥28, <32)	26.1	23.2	29.1	
Parity, $n$	2.0 ± 1.7	2.3 ± 1.7	1.6 ± 1.7	<0.001
Maternal BMI at enrollment, kg/m <sup>2</sup>	24.0 ± 3.5	23.8 ± 3.5	24.2 ± 3.5	0.38
Maternal height at enrollment, cm	162.3 ± 6.2	161.8 ± 6.1	162.8 ± 6.3	0.15
Gastrointestinal ailments at enrollment, %	23.7	25.6	21.8	0.42
Fever-related illness at enrollment, %	15.9	11.3	20.6	0.02
Probable depression at enrollment, <sup>c</sup> %	59.8	61.9	57.6	0.42
Dietary diversity (0–8) at enrollment, score	4.2 ± 1.2	4.1 ± 1.3	4.3 ± 1.2	0.29
Food insecurity (0–27) at enrollment, score	13.0 ± 5.1	12.9 ± 5.0	13.1 ± 5.2	0.75
Time allocation at enrollment (h)				
Heavy work	1.9 ± 2.4	1.9 ± 2.4	1.9 ± 2.4	0.82
Light work	10.6 ± 3.2	10.6 ± 3.0	10.7 ± 3.3	0.86
Leisure	2.5 ± 2.4	2.6 ± 2.5	2.5 ± 2.4	0.55
Sleep	8.9 ± 1.3	8.8 ± 0.9	9.0 ± 1.6	0.24
Breastfeeding status postpartum				
Exclusive, %				
6 weeks	59.5	64.9	53.9	0.04
14 weeks	56.46	67.9	44.9	<0.001
6 months	21.3	31.6	10.9	<0.001
Breastfeeding at 9 months, <sup>d</sup> %	95.9	91.8	100	0.002

**Table 1** (continued)

	All ( $n = 333$ )	HIV+ ( $n = 168$ )	HIV- ( $n = 165$ )	$p$ -value <sup>a</sup>
Clinic site, %				
Kisumu	19.5	22.0	17.0	0.08
Macalder	10.8	10.7	10.9	
Migori	11.1	11.3	10.9	
Nyahera	14.4	12.5	16.4	
Nyamaraga	11.7	11.9	11.5	
Ongo	15.0	13.1	17.0	
Rongo	17.4	18.5	16.4	

Mean ± SD, all such values

*CES-D* Center for Epidemiologic Studies Depression Scale, *BMI* body mass index, *KEDH* Kisumu East District Hospital

<sup>a</sup>Comparison between HIV+ and HIV- women

<sup>b</sup>Asset index derived from principal components analysis of possession of twenty different household assets, where households with higher values represent greater household wealth relative to others in the sample

<sup>c</sup>*CES-D* score ≥17

<sup>d</sup>Breastfeeding at 9 months available for 221 women

lamivudine/efavirenz (TDF/3TC/EVF) (57.7%) ART regimen (Supplemental Table 2).

Generally, HIV+ women exhibited lower mean body composition values over time, with more pronounced differences postnatally (Table 2). While some differences were not statistically significant (e.g. weight and AMA) by HIV status, values for TSF, AFA, and fat-free mass were lower in late pregnancy and postpartum for HIV+.

In models of overall maternal body composition over time (Supplemental Table 3), we observed increases in weight during pregnancy, decreases in weight and fat-free mass postpartum, and no significant changes in fat mass. For regional body composition (Supplemental Table 4), we observed decreases in TSF and AFA across pregnancy and postpartum, and increases in AMA at visits ≥36 weeks and MUAC at 9 months.

The interaction between time and HIV status was not significant, thus HIV was included as a covariate. HIV was negatively associated with most body composition values (Fig. 2a). Specifically, HIV infection was associated with lower weight, fat mass, fat-free mass, TSF, AFA, and MUAC from pregnancy to 9 months postpartum, and was not associated with AMA.

Effects of food insecurity varied over time for TSF, AMA, and MUAC (Fig. 2b). Specifically, greater food insecurity was associated with marginally lower TSF and higher AMA at the early second trimester visit, whereas during lactation, food insecurity was associated with lower AMA and MUAC, and greater TSF, suggesting muscle loss

**Table 2** Maternal body composition values among HIV+ and HIV- Kenyan mothers across pregnancy and lactation<sup>a</sup>

	Weight, kg		BMI, kg/m <sup>2</sup>		FM, kg		FFM, kg		AFA, cm <sup>3</sup>		AMA, cm <sup>3</sup>		TSF, mm		MUAC, cm	
	HIV- (n)	HIV+ (n)	HIV- (n)	HIV+ (n)	HIV- (n)	HIV+ (n)	HIV- (n)	HIV+ (n)	HIV- (n)	HIV+ (n)	HIV- (n)	HIV+ (n)	HIV- (n)	HIV+ (n)	HIV- (n)	HIV+ (n)
<b>Pregnancy</b>																
Early second Tri.	34	54	66.1 (12.8)	61.7 (8.4)	24.5 (4.4)	23.5 (3.0)	19.9 (6.5)	18.8 (5.2)	18.3 (6.6)	23.7 (10.2)	19.8 (9.0)	41.2 (12.6)	18.3 (6.6)	15.6 (6.0) <sup>b</sup>	28.3 (3.9)	27.4 (3.1)
Late second Tri.	83	75	62.7 (9.6)	61.7 (10.0)	23.8 (3.2)	24.0 (4.0)	18.1 (5.7)	17.8 (6.0)	16.2 (6.6)	20.5 (9.7)	18.2 (9.6)	39.5 (5.6)	16.2 (6.6)	14.7 (6.3)	27.3 (2.8)	26.8 (3.0)
Early third Tri.	66	53	65.1 (10.2)	64.1 (10.9)	24.6 (3.4)	24.1 (3.2)	19.5 (5.5)	18.9 (6.8)	15.6 (6.8)	19.4 (10.1)	17.4 (6.4)	38.2 (8.3)	15.6 (6.8)	14.1 (4.3)	26.7 (3.4)	26.6 (3.3)
Mid third Tri.	111	123	67.2 (10.6)	64.7 (8.9)	25.5 (3.4)	24.8 (3.0)	20.8 (5.9)	19.7 (4.9)	14.8 (5.5)	18.6 (8.4)	16.5 (6.8) <sup>b</sup>	40.1 (9.0)	14.8 (5.5)	13.3 (4.7) <sup>b</sup>	27.0 (3.2)	26.5 (3.1)
Late third Tri.	16	19	66.0 (7.9)	64.4 (6.9)	25.0 (3.0)	24.7 (2.0)	18.9 (5.0)	18.3 (3.9)	15.2 (5.6)	18.7 (7.2)	14.0 (6.5)	40.0 (9.2)	15.2 (5.6)	11.1 (4.7) <sup>b</sup>	27.1 (2.5)	26.7 (4.3)
<b>Postpartum</b>																
6 weeks	134	130	62.2 (11.1)	60.0 (9.9)	23.8 (3.6)	22.9 (3.5) <sup>b</sup>	19.9 (10.0)	18.2 (6.3)	14.5 (5.7)	18.5 (8.6)	16.1 (7.2) <sup>c</sup>	42.1 (9.7)	14.5 (5.7)	13.0 (5.0) <sup>b</sup>	27.4 (3.3)	26.4 (3.4) <sup>b</sup>
14 weeks	136	124	62.7 (14.1)	60.0 (9.0)	24.0 (4.7)	22.9 (3.2) <sup>b</sup>	20.3 (10.8)	17.7 (5.1) <sup>c</sup>	15.7 (7.2)	19.9 (10.2)	16.6 (8.7) <sup>c</sup>	40.7 (9.2)	15.7 (7.2)	13.2 (6.0) <sup>c</sup>	27.4 (3.2)	26.9 (3.2)
36 weeks	116	120	62.4 (14.8)	59.8 (11.0)	23.9 (5.3)	22.7 (3.9)	18.1 (7.0)	18.9 (14.7)	12.9 (8.1)	16.9 (11.4)	13.4 (9.9) <sup>c</sup>	46.3 (15.9)	12.9 (8.1)	10.5 (7.2) <sup>b</sup>	27.9 (4.0)	27.1 (3.4)

*BMI* body mass index, *FM* fat mass, *FFM* fat-free mass, *AFA* arm fat area, *AMA* arm muscle area, *TSF* triceps skinfold, *Tri.* trimester, *MUAC* mid-upper arm circumference

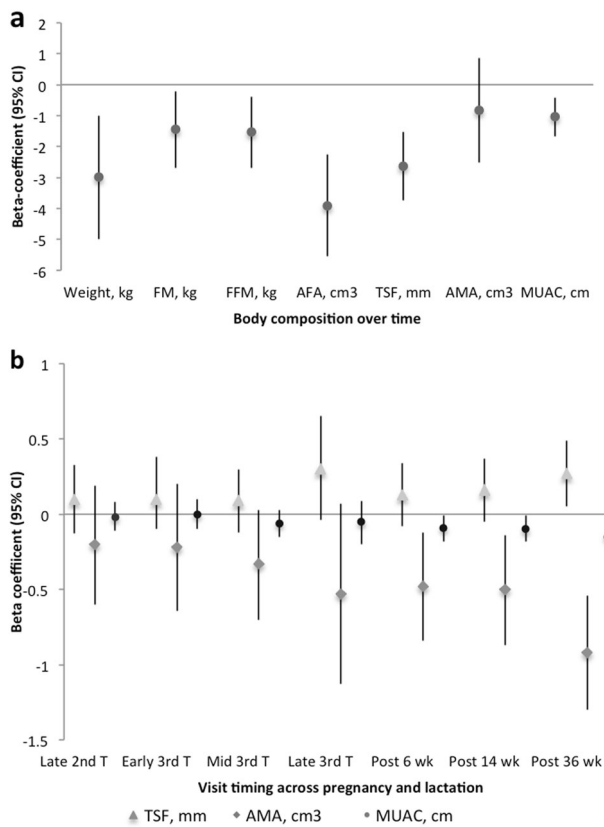
<sup>a</sup>Mean±SD

<sup>b</sup>Comparison by HIV status:  $p < 0.05$

<sup>c</sup>Comparison by HIV status:  $p \leq 0.01$

Bolding indicates values are significantly different from HIV- women





**Fig. 2** Predicted  $\beta$  (95% CI) effects of HIV (a) and food insecurity (b) on maternal body composition over time across pregnancy and lactation. Results shown are estimated from multivariable random-effects longitudinal models that adjust for maternal height and covariates. Results for food insecurity include an interaction term between study visit timing and food insecurity. **A)** Predicted effects comparing women with HIV+ infection to HIV- women on body composition across pregnancy and lactation. **B)** Predicted effects of a 1-unit increase in individual food insecurity access score on TSF, AMA and MUAC at each observation

over time. Food insecurity was not associated with other outcomes.

Other factors associated with body composition included maternal age, height, probable depression, light and heavy work, hunger season in the previous month, and gastrointestinal distress (Supplemental Tables 3 and 4; descriptive summary available on the Online Supplemental Materials page 7).

Further, we examined the timing of HIV diagnosis as the primary exposure. Among HIV+, some maternal characteristics differed depending on the timing of diagnoses (Supplemental Table 5). In the models (Supplemental Table 6), newly diagnosed women did not have significant differences in body composition compared to women diagnosed prior to the index pregnancy. However, the effect sizes for body composition values were predominately negative among newly diagnosed women. In our sensitivity analysis evaluating the role of HIV clinical staging on body

composition across pregnancy and lactation in the subset with staging data ( $n = 141$ ), we found that WHO clinical stage  $\geq 2$  was associated with lower AFA and TSF over time [AFA  $b = -2.8 \text{ cm}^3$  (95% CI:  $-5.2, -0.3$ ),  $p = 0.03$ ; TSF  $b = -1.9 \text{ mm}$  (95% CI:  $-3.5, -0.2$ ),  $p = 0.03$ ], but not with overall body composition (weight, fat mass, fat-free mass) or other regional measures (AMA, MUAC) (data not shown).

We conducted additional analyses to explore if breastfeeding influenced postpartum body composition. Adjustment for breastfeeding did not appreciably alter associations between HIV and maternal body composition (data not shown). Furthermore, EBF did not predict changes in body composition (data not shown).

## Discussion

In this first study of body composition changes across both pregnancy and lactation among women of mixed HIV status, HIV infection was associated with lower weight, fat mass, fat-free mass, TSF, AFA, and MUAC values over time. This is in support of our first hypothesis that HIV would be associated with adverse changes in body composition. Regarding the timing of HIV diagnosis relative to the pregnancy, we observed that a HIV diagnosis in the index pregnancy was associated with a trend towards worse body composition measures over time. This suggests that newly diagnosed women may need increased nutritional support during pregnancy and lactation.

Our second hypothesis, that food insecurity would lead to adverse changes in body composition, was only supported by some of our findings. Greater food insecurity was associated intermittently with regional changes in body composition in the arm (TSF, AMA, and MUAC), suggesting muscle tissue loss over time. However, food insecurity was not associated with most body composition outcomes, including overall body composition (weight, fat mass, and fat-free mass) and regional arm fat depots.

Similar to other reports in HIV+ [4, 24, 25] and HIV- populations [3, 26], participants exhibited changes in overall and regional body composition. For overall body composition, in longitudinal multivariate models, we observed increases in weight during pregnancy and decreases postpartum. Interestingly, we observed only significant decreases in lean mass during postpartum visits, and observed no significant differences in fat mass over time. This suggests that maternal weight changes were a proportional change in fat and lean mass during pregnancy, and that the weight changes were largely leaner mass during lactation. These decreases in overall lean mass postpartum are likely due to the large decreases in body water and shifts in other supporting tissues after delivery (e.g. uterus) [1, 2].

For regional body composition, TSF and AFA decreased across pregnancy and lactation, with the largest decrease at 9 months postpartum, suggesting arm fat was mobilized to support breastfeeding; this is similar to a report in HIV-uninfected rural Taiwanese women [3]. AMA increased from late pregnancy and across lactation, which is comparable to a previous study reporting effects in ART-naive HIV+ Malawian women during pregnancy [4]. At 9 months postpartum, MUAC was higher in our cohort of Kenyan women, which is similar to our findings in Ugandan HIV+ and HIV- women [15].

Unadjusted overall body composition values were not markedly different across pregnancy and lactation by maternal HIV status, although some differences by HIV were observed for regional measures of arm fat (TSF and AFA). When adjusting for maternal height and covariates, maternal HIV infection was associated with lower overall body composition values (weight, fat mass, and lean mass), and also regional body composition values (TSF and AFA) across pregnancy and postpartum; while no association was found between HIV and regional arm muscle depots (AMA). Overall, this suggests that HIV+ women may be more prone to adverse changes in body composition during pregnancy and lactation. It is difficult to compare these findings to other studies, because prior work has only examined body composition changes during lactation by HIV status. In these two previous studies, there were no observable differences by HIV status in overall [15, 24] or regional body composition [15] at 8–24 wk postpartum [24] and 1 week to 12 months postpartum [15].

In addition to the main effects of HIV infection, we also evaluated if timing of HIV diagnosis and ART initiation were associated with changes in body composition. Although most body composition effects were lower for new HIV diagnoses, suggesting a trend towards lower values in this group, there were no significant differences between newly diagnosed and known positive groups. To our knowledge, there are no data on timing of HIV diagnosis and body composition during pregnancy and lactation to which we can compare these observations.

Similar to our previous work, in which food insecurity was inversely associated with weight and AFA among HIV+ and HIV- postpartum Ugandan women receiving ART [15], we observed some adverse effects of higher food insecurity scores on body composition during lactation. However, in contrast to our previous study in Uganda [15], food insecurity was not associated with overall body composition in our Kenyan cohort. Instead, we found that food insecurity was intermittently associated with regional body composition values. Specifically, food insecurity was associated with lower AMA and MUAC postpartum, suggesting muscle tissue loss. These differential findings could be attributable to different periods of follow up (9 vs.

12 months), hunger season exposure, or more pronounced food insecurity in Nyanza, Kenya.

In our sensitivity analysis with adjustment for EBF, associations between HIV and postpartum body composition were not altered. This is similar to our previous findings in HIV+ and HIV- Ugandan women [15], and among well-nourished HIV+ women receiving ART from Kenya, Burkina Faso, and South Africa, where breastfeeding was not associated with weight loss [27].

We identified several other predictors of body composition changes (Supplemental Tables 3 and 4). Maternal age was positively associated with several body composition measures, suggesting that younger women may be at higher risk for poor nutritional outcomes. Probable maternal depression during pregnancy was associated with lower weight across pregnancy and lactation and trended toward lower fat and lean mass over time. Previously, in HIV+ and HIV- Ugandan women, maternal depression was associated with weight and lean mass loss postpartum [15]. Together, these findings suggest that women with impaired mental health may be more vulnerable to adverse nutrition outcomes.

Finally, we observed that exposure to the hunger season (e.g. February to May), when food stores run low, was associated with lower AMA and MUAC over time. This suggests that this period may be particularly important for nutritional interventions. This relationship is supported by findings from Uganda, where exposure to hunger season was associated with lower AMA during breastfeeding [15]. While exposure to hunger season was associated with lower AMA during pregnancy in the HIV+ Malawian cohort [4], the longer enrollment and follow-up timing in this Malawian cohort (2003–2009) may have allowed for more robust examinations of the effects of food shortages on body composition compared to our study, where women were enrolled during a relatively short period of time (~6 months: August 2014–February 2015).

The strengths of this study include evaluation of many indicators of body composition along with a variety of environmental and demographic characteristics. Limitations include the differential enrollment timing across study participants during pregnancy, which precluded adjustment for most initial body composition values in the longitudinal models. The rurality of some of the clinics and distance between study sites necessitated the use of a portable BIA, which precluded us from using more robust body composition assessment methods. There are concerns with the validity of BIA during pregnancy [1]; however, BIA has been used in many other studies of body composition during pregnancy [28–31] and it has been shown to predict total body water during pregnancy [32], which is the primary factor used in deriving fat-free mass. The Biodynamics BIA 450 does not have race-specific proprietary equations for predicting body fat, and developed equations from a range of body types,

weights, percentage fat, and ethnic heritage (Personal communications with Biodynamics Corporation, July 19, 2018). It is unknown whether race-specific equations would improve our body composition estimates.

There may also be unaccounted confounders that could explain differences between HIV+ and HIV- women. Although we used WHO clinical staging, viral load and HIV-specific co-morbidities would have provided a more comprehensive picture. Due to the breadth of ART regimens, we were unable to evaluate how specific ART regimens related to body composition. Although we measured dietary diversity, we were unable to measure dietary and energy intakes. Furthermore, we assessed time use activities such as heavy or light work, but were unable to robustly measure physical activity with a gold-standard method such as accelerometry. Finally, because HIV status was determined in ANC clinics, we may have had imprecise dates of diagnoses.

In conclusion, HIV infection was associated with adverse changes in overall and regional body composition across pregnancy and lactation. Food insecurity was associated with greater loss of arm muscle and MUAC during lactation. Adverse changes in body composition were associated with HIV, lower maternal age, physical exertion, and depression. Taken together, this suggests that women with these characteristics may need nutritional support to ensure adequate reserves to support breast milk production, and maintain maternal health during pregnancy and lactation.

## Disclaimer

The content is solely the responsibility of the authors and does not necessarily represent the views of the National Institutes of Health.

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## Compliance with ethical standards

**Conflict of interest** Research activities and Sera Young were supported by the National Institute of Mental Health. EMW has received

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