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[1–4]

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ABSTRACT

Background: Breastfeeding increases metabolic demands on the mother, and excessive postnatal weight loss increases maternal mortality.

Objective: We evaluated the efficacy of a lipid-based nutrient supplement (LNS) for prevention of excess weight loss in breastfeeding, HIV-infected women.

Design: The BAN (Breastfeeding, Antiretrovirals, and Nutrition) Study was a randomized controlled trial in Lilongwe, Malawi. At delivery, HIV-infected mothers and their infants were randomly assigned according to a 2-arm (with and without LNS) by 3-arm (maternal triple-antiretroviral prophylaxis, infant-nevirapine prophylaxis, or neither) factorial design. The 28-wk LNS intervention provided daily energy (700 kcal), protein (20 g), and micronutrients (except for vitamin A) to meet lactation needs. Women were counseled to breastfeed exclusively for 24 wk and to wean by 28 wk. Weight change (0–28 wk) was tested in an intent-to-treat analysis by using 2-factor ANOVA and with longitudinal mixed-effects models.

Results: At delivery, the LNS (n = 1184) and control (n = 1185) groups had similar mean weights and BMIs. Women receiving the LNS had less 0–28-wk weight loss (−1.97 compared with −2.56 kg, P = 0.003). This difference remained significant after adjustment for maternal antiretroviral drug therapy and baseline BMI. Women receiving antiretroviral drugs had more weight loss than did those not receiving antiretroviral drugs (−2.93 compared with −1.90 kg, $P < 0.001$). The benefit of the LNS for reducing weight loss was observed both in those receiving antiretroviral drugs (−2.56 compared with −3.32 kg, P = 0.019) and in those not receiving antiretroviral drugs (−1.63 compared with −2.16 kg, P = 0.034).

Conclusions: The LNS reduced weight loss among HIV-infected, breastfeeding women, both in those taking maternal antiretroviral prophylaxis to prevent postnatal HIV transmission and in those not receiving antiretroviral prophylaxis. Provision of an LNS may benefit HIV-infected, breastfeeding women in resource-limited settings. This trial was registered at clinicaltrials.gov as NCT00164762. *Am J Clin Nutr* 2012;95:759–65.

INTRODUCTION

The promotion of breastfeeding is central to maternal and child health advocacy. Breastfeeding enhances maternal and child health through increased child spacing and optimal infant nutrition and protection against common childhood diseases (1–3). For the HIV-infected mother, however, breast-milk substitutes are recommended when feasible to prevent mother-to-child transmission. In resource-limited settings, replacement feeding is often not a feasible option. In settings in which national or subnational authorities have decided to promote and support breastfeeding and antiretroviral interventions (even when antiretroviral drugs are not immediately available), the WHO recommends that mothers known to be HIV infected and whose infants are HIV uninfected or are of unknown HIV status should exclusively breastfeed their infants for the first 6 mo of life and introduce appropriate complementary foods thereafter while continuing breastfeeding through 12 mo of life (4). Breastfeeding should then stop only once a nutritionally adequate and safe diet without breast milk can be provided. If infants are known to be HIV infected, mothers are strongly encouraged to exclusively

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[2] The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC.

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breastfeed for the first 6 mo of life and continue breastfeeding up to 2 y of age or beyond (4).

Breastfeeding increases the mother's energy and nutrient needs, and if diet during lactation is insufficient to meet the nutritional needs of the mother and infant, breastfeeding mothers may become nutritionally depleted (1, 5). In resource-limited countries, nutritional depletion from breastfeeding may be exacerbated by food shortages and high HIV infection rates, because HIV increases energy and nutrient needs (6). In a study in Zambia, >10% weight loss among HIV-infected women during lactation significantly increased subsequent mortality (7). Similarly, in a randomized trial in HIV-infected women in Kenya, breastfeeding mothers lost more weight and had higher rates of mortality than did mothers randomly assigned to formula feed (8). However, the higher mortality rate among the HIV-infected Kenyan cohort who breastfed for a median of 17 mo was not observed in an HIV-infected South African cohort who breastfed for a median of 6 mo (9).

HIV-infected women in resource-limited settings may benefit from a nutritional supplement during the breastfeeding period. The Breastfeeding, Antiretroviral, and Nutrition (BAN) Study was a randomized controlled trial designed to evaluate 3 objectives: *1*) the effectiveness of maternal or infant antiretroviral drugs in preventing postnatal HIV transmission (10); *2*) the effectiveness of a nutritional supplement for prevention of maternal depletion among breastfeeding, HIV-infected women; and *3*) the feasibility of exclusive breastfeeding followed by rapid weaning from 24 to 28 wk. The current article addresses the second study objective.

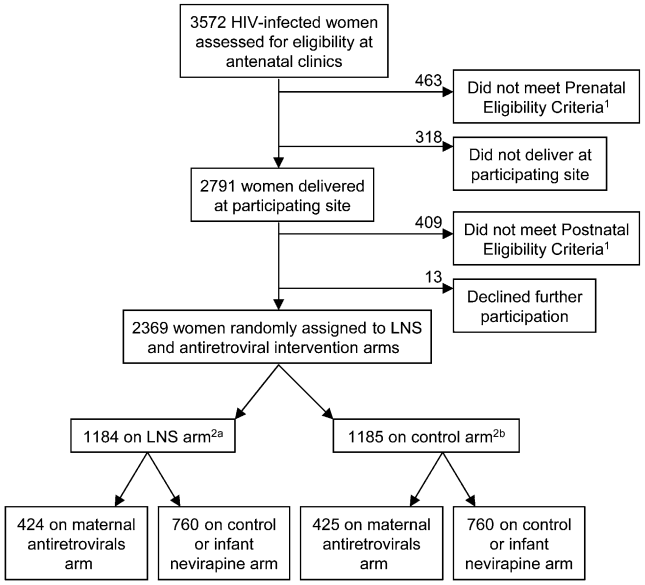

FIGURE 1. Flow of HIV-infected participants through each stage of the BAN Study. [1]Prenatal and postnatal eligibility criteria are described in Subjects and Methods. [2a]The 1184 women randomly assigned to receive the LNS were also randomly assigned to 1 of 3 antiretroviral interventions for prevention of postnatal HIV transmission: 424 to the maternal antiretroviral arm, 426 to the infant nevirapine arm, and 334 to the control arm; [2b]the 1185 women in the LNS control arm were also randomly assigned to 1 of the 3 antiretroviral arms: 425 to the maternal antiretroviral arm, 426 to the infant nevirapine arm, and 334 to the control arm. BAN, Breastfeeding, Antiretroviral, and Nutrition; LNS, lipid-based nutrient supplement.

SUBJECTS AND METHODS

The BAN Study (www.TheBANStudy.org) recruited HIV-infected, pregnant women at 4 antenatal clinics in Lilongwe, Malawi, from 2004 to 2009, and the screening outcomes have been reported (10, 11). Briefly, consenting, HIV-1–infected women (n = 3572) were screened against the following prenatal eligibility criteria: ≤30 wk gestation, intention to breastfeed, age ≥14 y, no serious coexisting infection, $CD4^+$ lymphocyte count of ≥250 cells/μL (≥200 cells/μL before 24 July 2006), hemoglobin ≥7 g/dL, and alanine aminotransferase <2.5 times the upper limit of normal (**Figure 1**). Of the 463 (13%) ineligible women, 289 (62%) had a CD4 count below the cutoff (10). All ineligible women were referred to a public HIV care facility. Eligible women who delivered at a participating site (n = 2791), along with their infants, received single-dose nevirapine peripartum plus twice-daily zidovudine and lamivudine for 7 d postpartum. After delivery, 2382 mother-infant pairs met the following postnatal eligibility criteria: presentation at the study site within 36 h of delivery, infant birth weight ≥2000 g, and no severe congenital malformations or other conditions incompatible with infant survival. The predominant reasons for postnatal exclusion (n = 409) were delayed presentation to the study site (46%) and low birth weight (20%). Thirteen women declined further participation, and 2369 mothers completed informed consent and were randomly assigned to treatment.

Mother-infant pairs were randomly assigned by using a permuted-block method to one of six 28-wk treatment conditions according to a 2-arm nutritional by 3-arm antiretroviral intervention factorial design and followed through 48 wk postpartum. The 3-arm intervention required a larger sample size, and the method used to calculate sample size has been reported (11). A data manager generated the random allocation sequence, study nurses screened and enrolled the women, and study pharmacists assigned participants to interventions via sequentially numbered envelopes. Antiretroviral drugs and lipid-based nutrient supplements (LNS) were distributed by the study pharmacists at scheduled visits occurring at 0, 1, 2, 4, 6, 8, 12, 18, 21, 24, and 28 wk postpartum.

All mother-infant pairs were randomly assigned to 1 of 2 nutritional intervention arms. Half of the women received an LNS of ready-to-use food, which when taken twice-daily supplied the estimated added energy (700 kcal), and protein (20 g) requirements for lactation and provided the full recommended daily allowance of micronutrients except for vitamin A (**Table 1**). Vitamin A was excluded from the LNS because of a reported association with increased postnatal HIV transmission (12). The LNS was manufactured by Nutriset in France (www.nutriset.fr) from peanut paste, vegetable oil, dry skimmed milk, dry whey, dextrin-maltose, sugar, and a mineral and vitamin complex. Nutrient content was tested regularly by chemical analysis. The LNS package label, in the local Chichewa language, indicated its use for the breastfeeding mothers. To buffer seasonal food shortages and to prevent potential sharing of the maternal LNS, all participants—regardless of treatment assignment—received a 2-kg/wk family maize supplement that provided ~200 kcal/person daily for a family of 5 (13). Adherence to the LNS was measured at 6 visits by standardized questions asked by trained staff about the number of missed LNS packets.

TABLE 1
Composition (per 70-g sachet) of the twice-daily maternal nutritional supplement used in the BAN Study[1]

Component	Provides
Energy (kcal)	373
Protein (g)	10.4
Lipids (g)	24.8
Iron (mg)	7.5
Zinc (mg)	9.5
Phosphorus (mg)	600
Potassium (mg)	572
Magnesium (mg)	62
Copper (mg)	0.15
Calcium (mg)	294
Vitamin B-1, thiamine (mg)	0.8
Vitamin B-2, riboflavin (mg)	0.9
Vitamin B-3, niacin (mg)	10
Vitamin B-6, pyridoxine (mg)	1.1
Vitamin B-12, cyanocobalamine (μg)	1.3
Vitamin C, ascorbic acid (mg)	50
Vitamin E, α-tocopherol (mg)	6
Folic acid (μg)	150
Iodine (μg)	200

[1] The supplement was manufactured by Nutriset in France (www.nutriset.fr) from peanut paste, vegetable fat, dry skimmed milk, dry whey, dextrin-maltose, sugar, and a mineral and vitamin complex. BAN, Breastfeeding, Antiretroviral, and Nutrition.

Mother-infant pairs were randomly assigned to 1 of 3 antiretroviral intervention arms with drugs given to the infant, mother, or neither. The infant nevirapine regimen consisted of an age-adjusted daily dose of 10–30 mg nevirapine. The maternal antiretroviral regimen included zidovudine and lamivudine plus either nevirapine (until January 2005), nelfinavir (from January 2005 to February 2006), or lopinavir and ritonavir (Kaletra; Abbott) (from February 2006 until study completion). Most women who were randomly assigned to the maternal antiretroviral arm received the Kaletra-containing regimen ($n = 664$). On 26 March 2008, the National Institute of Allergy and Infectious Diseases Vaccine and Prevention Data and Safety Monitoring Board recommended stopping enrollment to the antiretroviral control arm after 668 of the planned 806 mother-infant pairs received their treatment assignment. The BAN Study halted random assignment to the control arm and offered mothers on that arm and who were <21 wk postpartum the choice to initiate the maternal or infant antiretroviral intervention or to remain on the control arm (11).

At all study visits, maternal weight was measured by using a regularly calibrated electronic scale, and height was measured by using a wall-mounted stadiometer. Some women with $\geq$5% weight loss between visits occurring $\geq$4 wk postpartum or a BMI (in kg/m^2) <17 ($n = 25$) were offered the LNS if not already receiving it ($n = 13$ and 12 in the maternal antiretroviral and no-maternal-antiretroviral arms, respectively).

With the use of a standardized protocol derived from the WHO Breastfeeding Counseling Training Manual (14), all mothers were individually counseled to breastfeed exclusively for 24 wk then to rapidly wean to breastfeeding cessation by 28 wk (15). In addition, BAN Study nurses conducted weekly breastfeeding support groups. To minimize concern for infant malnutrition during breastfeeding cessation, the study provided a locally produced ready-to-use therapeutic food for the infants (16). Breastfeeding practices and timing of breastfeeding cessation were captured by trained staff by using standardized questionnaires.

Ethics

The BAN protocol and study forms were approved by the Malawi National Health Science Research Commission, the institutional review boards at the University of North Carolina at Chapel Hill, and the CDC (clinicaltrials.gov; NCT00164762). The trial was monitored for safety and efficacy by the National Institute of Allergy and Infectious Diseases Vaccine and Prevention Data and Safety Monitoring Board.

Statistical analyses

The dependent variable for the primary analysis was maternal weight loss between delivery and 28 wk postpartum. Complete data to calculate this variable were available for 848 and 853 mothers receiving the LNS intervention and control arms who had both a delivery weight and a 28-wk weight. For the analysis, we focused on 4 groups defined by maternal antiretroviral and LNS assignment. Mothers whose infants were assigned to receive antiretroviral drugs were included with the no-maternal-antiretroviral arms, resulting in groups defined as LNS with ($n = 424$) and without ($n = 760$) antiretroviral drugs and no LNS with ($n = 425$) and without ($n = 760$) antiretroviral drugs (Figure 1). Differences between mean weights of mothers randomly assigned to the LNS intervention arm and mothers randomly assigned to the LNS control arm, overall, and within groups stratified by maternal antiretroviral assignment were evaluated by using 2-factor ANOVA procedures with $\alpha = 0.05$.

Women with at least one weight measurement at any time point were included in a secondary repeated-measures longitudinal analysis (1182 and 1181 mothers in the LNS intervention and control arms, respectively). Linear mixed-effects models with an autoregressive covariance structure were used to evaluate weight from 0 to 28 wk, with adjustment for initial BMI at delivery to account for the expected dependence of weight change on starting weight. Potential interactions of the LNS with study visit, the maternal antiretroviral intervention with study visit, and of the LNS with the maternal antiretroviral intervention were evaluated. Predicted values were calculated by adding the appropriate fixed-effects variables for study visit, LNS, and maternal antiretroviral intervention with mean initial BMI and used to create predicted weight-change curves for each intervention. All data analysis used SAS 9.2 software (SAS Institute Inc).

RESULTS

Women in the LNS arm ($n = 1184$) were no different from those in the control arm ($n = 1185$) with respect to sociodemographic characteristics and anthropometric and laboratory measures collected at random assignment (**Table 2**). The majority (72%) of women were exposed to the famine season (August to March) within 4 wk before giving birth, and yet their mean baseline BMI was 23.6. Of the women on the maternal antiretroviral arm, 77.4% took Kaletra, and there was no difference in drug regimens between the LNS intervention (77.4%) and control (77.4%) arms. A similar analysis restricted to the

TABLE 2
Mean baseline characteristics of the BAN Study participants in the primary analysis of the effects of an LNS provided to HIV-infected Malawian women during lactation[1]

	LNS (n = 1184)	No LNS (n = 1185)
Age (y)	25.8 ± 5.0[2]	25.7 ± 5.0
Postprimary education (%)	36.4	32.9
Parity (n)	3.1 ± 1.6	3.0 ± 1.5
Cesarean delivery (%)	5.1	6.0
Married (%)	93.6	91.9
Electricity in home (%)	20.0	18.8
Exposed to famine season[3] (%)	72.2	72.1
Anthropometric measurements		
Height (cm)	156.8 ± 5.5	156.9 ± 5.6
Weight (kg)	57.7 ± 8.4	58.4 ± 8.6
BMI (kg/m^2)	23.4 ± 3.0	23.7 ± 3.0
Laboratory measures		
Hemoglobin (g/dL)	11.7 ± 1.6	11.8 ± 1.7
Albumin (g/L)	2.6 ± 0.3	2.6 ± 0.5
CD4 count (cells/μL)	482.0 ± 205.2	472.9 ± 188.5
Antiretroviral intervention arm (%)		
Infant nevirapine arm	36.0	35.9
Maternal anti-retroviral intervention arm[4]	35.8	35.9
No-antiretroviral-drugs arm (%)	28.2	28.2

[1] There were no significant ($P < 0.05$) differences between the LNS and the no-LNS arms. BAN, Breastfeeding, Antiretroviral, and Nutrition; LNS, lipid-based nutrient supplement.

[2] Mean ± SD (all such values).

[3] Women were defined as exposed to the famine season (August–March) if it occurred within 4 wk before delivery.

[4] The BAN Study changed the maternal antiretroviral therapy regimen twice during the course of the study for reasons of availability, safety, and potency. The majority (77.4%) of women in the maternal antiretroviral therapy arm used lopinavir/ritonavir (Kaletra; Abbott) for both the nutrient-rich supplement arm (77.4%) and the family maize–only arm (77.4%).

848 and 853 mothers receiving the LNS intervention and control arms who had both a delivery weight and a 28-wk weight also found no significant differences with respect to baseline characteristics. A comparison of women included in the primary analysis with those in the secondary analysis (those with at least one weight measurement) showed that the former had a higher mean age (26.1 compared with 24.9 y; $P < 0.001$) and parity (3.2 compared with 2.8; $P < 0.001$).

Adherence to the LNS was high, and the supplement was well tolerated. Overall, women reported taking the prescribed amount of supplement on the day before the visit an average of 92.4% of the time (over adherence assessments collected at 6 visits between 0 and 28 wk). Women reported taking none of the supplement on the prior day <5% of the time. There was no significant difference in adherence to the LNS across the 3 antiretroviral intervention arms (P = 0.421). The self-reported frequency of exclusive breastfeeding was high in both the LNS intervention and control groups (97% and 96%, respectively, at 21 wk).

Between delivery and 28-wk postpartum, women in the LNS control arm (n = 853) lost an average of 2.56 kg and those in the LNS intervention arm (n = 848) lost an average of 1.97 kg (P = 0.003) (**Figure 2**, **Table 3**). These numbers remained relatively unchanged in sensitivity analyses that excluded the 25 women who were given LNS because of weight loss (−2.54 and −1.97 kg, P = 0.004). The benefit of the LNS for reduced weight loss was observed in the first 12 wk postpartum: between 0 and 2 wk, −1.27 compared with −1.50 kg (P = 0.018); between 2 and 4 wk, −0.06 compared with −0.31 kg ($P < 0.001$); and between 4 and 12 wk, −0.08 compared with −0.35 kg (P = 0.007). Between 12 and 28 wk, there was no significant difference in weight loss between the LNS intervention and control arms (P = 0.939) (Table 3).

Women in the antiretroviral arm lost more weight from 0 to 28 wk than did those not provided with antiretroviral drugs (−2.93 compared with −1.90 kg, respectively; $P < 0.001$). Within both the maternal antiretroviral arm and the no-maternal-antiretroviral arms, women receiving LNS lost less weight from 0 to 28 wk than did those not receiving the LNS (−2.56 compared with −3.32 kg in the maternal antiretroviral arms, P = 0.019; −1.63 compared with −2.16 kg in the no-maternal-antiretroviral arms, P = 0.034).

In a linear mixed-effects model with adjustment for BMI at delivery, significant interactions were observed between study

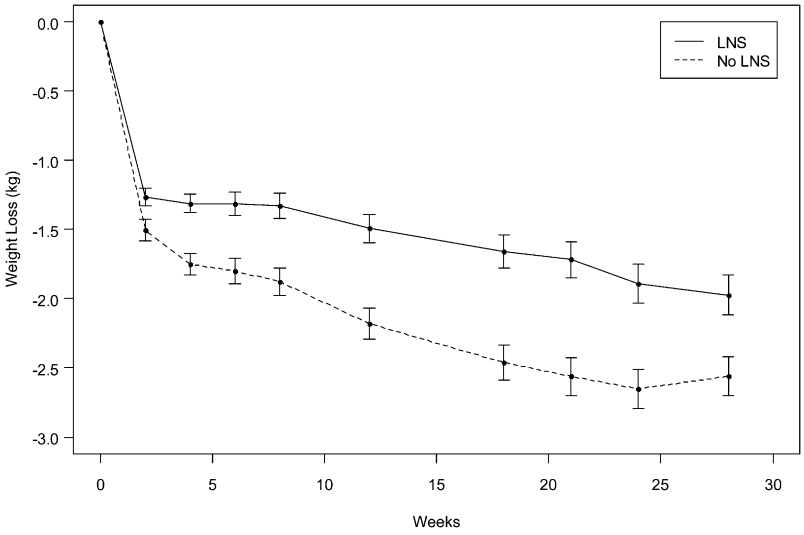

FIGURE 2. Mean (±SE) cumulative maternal weight loss by random assignment to the LNS and weeks since delivery among BAN Study participants. The mean (±SE) weight loss was calculated from delivery cumulatively at each visit and includes data for all women with at least one weight measurement (n = 1182 in the LNS intervention arm, n = 1181 in the control arm). BAN, Breastfeeding, Antiretroviral, and Nutrition; LNS, lipid-based nutrient supplement.

TABLE 3
Weight at delivery and postpartum weight change in BAN Study participants in the primary analysis of the effects of an LNS provided to HIV-infected Malawian women during lactation[1]

	LNS		No LNS		
Outcome	*n*	Mean ± SD	*n*	Mean ± SD	*P* value
Weight (kg)					
Delivery		57.90 ± 8.51		58.51 ± 8.63	
28 wk		55.94 ± 9.24		55.95 ± 8.48	
Difference					
0–28 wk	848	−1.97 ± 4.17	853	−2.56 ± 4.09	0.003
0–2 wk	997	−1.27 ± 1.99	970	−1.50 ± 2.37	0.018
2–4 wk	892	−0.06 ± 1.19	882	−0.31 ± 1.17	<0.001
4–12 wk	872	−0.08 ± 2.10	873	−0.35 ± 2.03	0.007
12–28 wk	821	−0.44 ± 2.59	828	−0.43 ± 2.50	0.939

[1] Differences were adjusted for maternal antiretroviral group; *P* values represent results from a 2-factor ANOVA. BAN, Breastfeeding, Antiretroviral, and Nutrition; LNS, lipid-based nutrient supplement.

visit and the antiretroviral intervention ($P < 0.001$), and between study visit and the LNS intervention ($P < 0.001$). The interaction between the LNS and the antiretroviral intervention was not significant ($P = 0.16$), and neither was the 3-way interaction between the LNS, antiretroviral intervention, and study visit ($P = 0.81$). On the basis of predicted curves from the model, weight loss was the lowest among mothers who received the LNS without the maternal antiretroviral intervention and greatest among women who received the maternal antiretroviral intervention without the LNS (**Figure 3**).

DISCUSSION

HIV-infected, breastfeeding women in the BAN Study who received a LNS in addition to a family maize provision had significantly less weight loss from delivery to 28 wk postpartum compared with those who received the family maize alone. The benefit of the LNS for prevention of weight loss was greatest in the earlier postpartum period. The significant reduction in weight loss associated with the LNS was observed in women randomly assigned to the maternal antiretroviral intervention for prevention of postnatal HIV transmission to the infant and in those randomly assigned to not receive antiretroviral drugs. Whereas the observed benefit of the LNS was greater in those women who were randomly assigned to receive antiretroviral drugs (a 0.76 kg difference between the LNS and control groups in women receiving antiretroviral drugs, and a 0.53 kg difference between the LNS and control groups in those not receiving antiretroviral drugs), this was not supported by a significant interaction between the LNS and antiretroviral drugs in a longitudinal mixed-effects model. Although the LNS was significantly associated with less weight loss, the difference in average weight loss between the LNS intervention and control arms was small. Furthermore, the average percentage weight loss from 0 to 28 wk in the LNS intervention (3.4%) and control (4.4%) arms was not in excess of what is expected during this postpartum period for physiologic reasons, including changes in body water, uterine size, and mobilization of fat stores to support milk production (17). This finding is somewhat surprising given the high exposure to the famine season and food insecurity during the study period, and the generally poor quality of diets of Malawian women. The dietary intake of 577 potential BAN participants during pregnancy showed that their mean daily energy intake was low (1378 kcal), and the most frequent dietary pattern was characterized by a low intake of fruits, vegetables, and meats (18). World Food Programme distributions occurred during the study period, but neither a variable indicating receipt of food from the World Food Programme nor a variable for study year was significant in the multivariable model. Alternatively, the BAN Study provision of

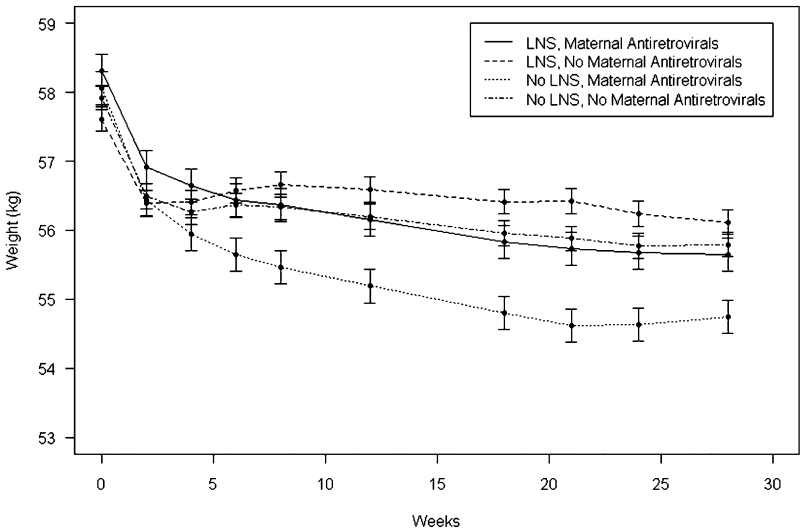

FIGURE 3. Predicted maternal weight change over weeks since delivery by random assignment to the LNS and maternal antiretroviral interventions in the BAN Study. Predicted curves from a mixed-effects model containing study visit ($P < 0.001$), nutritional supplement ($P = 0.009$), maternal antiretroviral drugs ($P = 0.025$), BMI at delivery ($P < 0.001$), and 2-way interactions between study visit and nutritional supplement ($P < 0.001$), between study visit and maternal antiretroviral drugs ($P < 0.001$), and between nutritional supplement and maternal antiretroviral drugs ($P = 0.16$). The 3-way interaction between study visit, maternal antiretroviral drugs, and nutritional supplement was not significant ($P = 0.81$) and was not included in the final model. Data from all women with at least one weight measurement were included (LNS, maternal antiretroviral drugs: $n = 423$; LNS, no maternal antiretroviral drugs: $n = 759$; no LNS, maternal antiretroviral drugs: $n = 424$; and no LNS, no maternal antiretroviral drugs: $n = 757$). BAN, Breastfeeding, Antiretroviral, and Nutrition; LNS, lipid-based nutrient supplement.

a family maize supplement to all participants may have partially met the energy needs of breastfeeding and reduced the potential effect of the LNS intervention.

For ethical reasons, women with ≥5% weight loss between visits and who were not already in the LNS intervention arm were given LNS as a therapeutic intervention. However, the number of women who received LNS because of weight loss was small (n = 25); a sensitivity analysis with these women removed did not alter the significance of study results, so this practice is not likely to have biased our results.

Prior literature provides conflicting reports on whether breastfeeding leads to nutritional depletion and even mortality among HIV-infected women (7–9, 19–21). A trial conducted in Kenya reported that breastfeeding mothers lost more weight than did women who were randomly assigned to formula feed, and that each kilogram of weight loss per month was associated with a 3.4-times higher risk of dying in the first 24 mo postpartum (8). More recent studies that looked at prolonged breastfeeding reported no increased mortality or faster HIV disease progression among HIV-infected, breastfeeding women (19–21). These studies speculated that the Kenyan results may be a chance finding due in part to differences across the study arms in viral load at randomization and the duration of follow-up for accrual of deaths. In contrast, the Zvitambo study in Zambia found that >10% weight loss among HIV-infected, lactating women increased subsequent mortality >7-fold (7).

The lower postpartum weight loss with the LNS observed in the BAN Study may not be generalizable to all HIV-infected women in resource-limited settings. On average, women enrolled in the BAN Study were likely healthier than HIV-infected mothers in Malawi due to the study inclusion criteria and high-quality health care provided in the postpartum period. As such, the benefit of the LNS among breastfeeding women with poorer nutritional status or more advanced HIV disease is unknown.

Random assignment to the LNS and antiretroviral intervention arms occurred within 36 h of delivery. To conduct an appropriate intent-to-treat analysis, the interval for weight change included the early postpartum period, when normal physiologic changes are expected. The inclusion of the early postpartum period and the lack of complete information on prepregnancy weight and weight gain during pregnancy may complicate the interpretation of postpartum weight loss. But, in the absence of differences between treatment arms in maternal weight at delivery, it is unlikely that results would differ even if we could account for the prenatal changes. We adjusted for BMI at delivery to reduce the error variance in the estimation of weight change.

As is the case with all food-based nutrition supplementation trials, blinding was not possible. Lack of blinding is very unlikely to have biased weight measurements. However, it is possible that women who knew they were getting an energy- and nutrient-rich supplement adjusted their home intake or their intake of the study-provided family maize supplement so that the difference in total energy intake between the LNS and no-LNS groups was not as high as intended. Unfortunately, the absence of dietary intake data on the full sample of BAN participants does not allow us to determine whether the LNS was substituted for a portion of usual intake. We do not know whether the LNS resulted in a net increase in energy intake in the LNS intervention group compared with the no-LNS group. Nevertheless, the comparison of weight loss across the 2 LNS intervention arms should remain valid. We have no reason to believe that the loss to follow-up observed in the BAN Study differentially affected the study outcomes, because participants with a 28-wk visit remained equally balanced and representative of the total population who were randomly assigned according to sociodemographic, anthropometric, and laboratory values at baseline.

In conclusion, HIV-infected women randomly assigned to receive an LNS and family maize provision during 28 wk of breastfeeding had less weight loss than did women receiving only the family maize. The benefit of the LNS for prevention of weight loss was observed in the earlier postpartum period and among both women randomly assigned to the maternal antiretroviral intervention and those randomly assigned to not receive the maternal antiretroviral intervention. Although the difference in weight loss between the nutritional arms over the breastfeeding period reached statistical significance, the actual difference was small and may be of limited clinical significance. However, we cannot rule out the potential value of maternal LNS for HIV-infected breastfeeding women in the early postpartum period, particularly for those who are initiating triple-drug antiretroviral regimens, because the effect noted in this study was likely mitigated by the provision of a family maize supplement to all participants.

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