Lipid-based nutrient supplements do not decrease breast milk intake of Malawian infants

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ABSTRACT

**Background:** The potential for small-quantity lipid-based nutrient supplements (LNS) to promote growth and development after 6 mo of age is currently being investigated. Because infants self-regulate energy intake, consumption of LNS may reduce breast milk intake and potentially decrease the beneficial effects of breast milk.

**Objective:** The objective was to test the hypothesis that the breast milk intake of 9- to 10-mo-old rural Malawian infants receiving LNS would not be lower than that of infants receiving no supplementation.

**Design:** This was a substudy of the International Lipid-based Nutrient Supplements (iLiNS) DOSE trial, in which 6-mo-old infants were randomly assigned to receive 10, 20, or 40 g LNS/d containing 56, 117, or 241 kcal/d, respectively, or no LNS until 18 mo of age. A subset was randomly selected to estimate breast milk intake at 9–10 mo of age with the dose-to-mother deuterium oxide dilution method. The noninferiority margin was <10% of total energy requirements.

**Results:** Baseline characteristics (n = 376) were similar across groups. The mean (±SD) daily breast milk intake of un-supplemented infants was 730 ± 226 g. The differences (95% CIs) in mean intake of infants provided with 10, 20, or 40 g LNS/d, compared with controls, were +62 (−18, +143), +30 (−40, +99), and +2 (−68, +72) g/d, respectively. Non–breast milk oral water intake did not differ by group (P = 0.39) and was inversely (r = −0.22, P < 0.01) associated with breast milk intake.

**Conclusion:** In this rural Malawian population, breast milk intake at 9–10 mo of age was not reduced by supplementation with complementary foods with 10–40 g LNS/d. This study was a substudy within the iLiNS DOSE trial, which was registered at clinicaltrials.gov as NCT00945698.

INTRODUCTION

The WHO recommends that infants receive breast milk exclusively until they reach 6 mo of age, with continued breastfeeding along with safe and nutritious complementary foods thereafter to 2 y of age or beyond (1). In rural Malawi, although initiation of breastfeeding is nearly universal, infants usually begin receiving maize porridge at ~3–4 mo of age (2), and the complementary food diet is usually very low in nutrient and energy densities (3). To address nutrient gaps, lipid-based nutrient supplements (LNS)4 have been designed to enrich the local diet with micronutrients, macrominerals, essential fatty acids, and high-quality protein beginning at 6 mo of age (4). Preliminary studies in Ghana and Malawi suggest that the addition of small (~20 g/d) quantities of LNS to complementary foods that are prepared in the home daily may help to prevent growth faltering in infancy (5, 6). However, there is concern that additional energy from LNS may displace breast milk intake, thereby reducing the benefits of breast milk for infant health. Breastfed infants self-regulate their energy intake (7), and some studies have shown an inverse relation between the energy density of complementary foods and breast milk intake (8, 9). Two studies have assessed breast milk intake after LNS supplementation: one at 7 mo of age (10) and the other at 9–10 mo of age (11); however, neither study included an un-supplemented control group.

We therefore designed the current study to measure breast milk intake in a subsample of infants 9–10 mo of age participating in a randomized clinical trial to assess the effect of consumption of different daily quantities and formulations (with and without milk powder) of LNS on child growth and development in rural Malawi. Specifically, we assessed the effect of 10, 20, or 40 g LNS provided for daily use between 6 and 18 mo of age; a comparison group did not receive any study supplement until after 18 mo of age (when they received a fortified maize-soy blend). The target age for this substudy was chosen so that infants in the intervention groups would have received LNS for ≥3 mo before the measurement of breast milk intake.

SUBJECTS AND METHODS

**Study site and subjects**

The International Lipid-based Nutrient Supplements (iLiNS) DOSE trial was carried out in southern Malawi in areas surrounding the Mangochi District Hospital and Namwera Health Centre. Healthy infants were eligible for enrollment into the main...
trial if they were 5.50–6.49 mo of age, resided in the 2 study catchment areas, would be available during the 12-mo study period, and were not concurrently participating in any other clinical trial. Participants in the main trial were randomly assigned to 6 groups: 3 groups receiving milk-containing LNS (10, 20, or 40 g/d), 2 groups receiving LNS without milk (20 or 40 g/d), and the control group, which did not receive LNS between 6 and 18 mo of age (the iLiNS-DOSE trial). All mothers were encouraged to breastfeed their infants on demand during the 12-mo intervention period and to offer a variety of locally available complementary foods.

In the current substudy, the 2 intervention groups receiving 20 g LNS/d (with or without milk) were combined, and the 2 intervention groups receiving 40 g LNS/d were combined, making 4 groups varying only in the energy received from LNS (0, 56, 117, or 241 kcal/d). Initially, infants were randomly assigned concurrently to the breast milk intake study during enrollment into the main trial by using a predetermined randomization scheme. However, as the substudy progressed, we noted higher than anticipated participant attrition; thus, additional mother-infant pairs were randomly selected from the main trial participants.

Mother-infant pairs were eligible for the breast milk intake substudy if the infant was enrolled in the main iLiNS-DOSE trial, infant age was between 9.0 and 10.0 mo, the mother was breast-feeding the infant on demand, and the mother and infant would be available for the full study period of 2 wk. Exclusion criteria were as follows: 1) the mother was breastfeeding more than one infant and 2) the mother and/or infant had a severe illness warranting hospital referral. Informed consent from the mother (for mother and infant participation) was obtained at enrollment, for both the main iLiNS-DOSE trial and the breast milk intake substudy. Both the main trial and the substudy protocols were approved by the Institutional Review Boards of the College of Medicine, University of Malawi, and the Pirkanmaa Hospital District, Finland.

Study protocol

Breast milk intake was estimated by using the dose-to-mother 2H2O dilution method developed by Coward et al (12) and later modified by Haisma et al (13, 14). The method is suitable for estimating average daily breast milk intake in community settings (12) and also provides estimates of water intake from sources other than breast milk (13). Maternal and infant saliva samples were collected for analysis of deuterium enrichment, following a standard protocol (14). On study day 0 (baseline), mother-infant pairs came to the study clinic, where maternal and infant morbidity during the previous 7 d was assessed by using a questionnaire. If the mother reported that she or her infant experienced fever or symptoms of diarrhea or vomiting within the past 7 d, the pair was requested to report back to the clinic 1 wk later. For healthy mother-infant pairs, maternal and infant weights were measured, followed by saliva sample collection from both the mother (two 2-mL samples) and infant (one 2-mL sample). Then an oral dose of 30 g 2H2O (99.8% purity; Cambridge Isotopes Laboratories) was administered to mothers soon after the baseline saliva sample was collected. The 2H2O doses were weighed to the nearest 0.0001 g into a sterile Nalgene bottle (60 mL) by using an analytic scale (Adventurer Pro Balances-AV64 Pine Brook).

After 2H2O was consumed, 50 g drinking water was added to the bottle without removing the straw, and the mother was asked to drink all of the water to ensure that all the 2H2O was ingested. Subsequent saliva samples were collected from the mother-infant dyad in their home on study days 1, 2, 3, 4, and 13. On study day 14, mother-infant pairs came to the study clinic for final saliva sample collection and weight measurement. Fieldworkers also collected weekly information on maternal and infant morbidity during the study period by administering questionnaires to the mother.

Anthropometric measurements

Anthropometric measurements were taken by trained fieldworkers, who were supervised and retrained every 3 mo; all measurements were done in triplicate. Mothers were weighed in light clothing to the nearest 0.01 kg with an electronic scale (SECA 846; Chasmors Ltd), and their height was measured to the nearest 0.1 cm with a stadiometer (Harpenden; Holtain Ltd). Infants were weighed nude to the nearest 0.01 kg with an electronic scale (SECA 735; Chasmors Ltd). The study scales were calibrated every morning in compliance with the main trial’s standard operating procedures for anthropometric measurements.

Saliva collection

Maternal saliva was collected by carefully placing a small piece of cotton wool in the mother’s mouth for about 2 min until it was fully soaked with saliva. The mother transferred the soaked cotton wool directly to the empty barrel of a 20-mL disposable syringe (to prevent contamination of the cotton). Saliva was squeezed out of the soaked cotton wool into a vial labeled with participant number, date, and time of sample collection. The procedure was repeated by using a new piece of cotton wool, until a total of 4 mL saliva was collected. Infant saliva was collected by tightly wrapping a piece of cotton wool around the tip of a wooden stick and placing the stick in the infant’s mouth, between the lower gum and cheek for ∼1–2 min until the cotton wool was soaked with saliva. Cotton wool was separated from the stick and placed into a 20-mL disposable syringe for collection of saliva as described for mothers. In infants the procedure was repeated until a total of ∼2 mL saliva was collected.

Saliva samples from the field were carried back to the study clinic in soft cooler boxes on frozen ice packs. For both mothers and infants, the baseline and postdose saliva samples were stored separately in labeled plastic sealed bags to prevent cross-contamination of samples and to protect samples from evaporation or exposure to environmental moisture. All saliva samples were stored at −20°C until analyzed for deuterium enrichment. Infant breast milk intake (g/d), non–breast milk oral water intake, and total water intake were calculated by fitting the deuterium enrichment data to a 2-compartment steady state model of water turnover in the mother–infant dyad by using the solver function in Microsoft Excel (12, 13).

Deuterium enrichment analysis

Deuterium enrichment in saliva was measured by Fourier transform infrared spectroscopy (FTIR 8400 Series; Shimadzu Corporation) at the College of Medicine, Mangochi Laboratory, following standard protocols (14). Before analysis, frozen saliva was thawed at room temperature. Calibration curves were prepared by using a set of standards with known deuterium enrichment and comparing the calculated (known) concentration with the measured concentration. Each day, before proceeding
with the saliva analysis, the accuracy of the FTIR measurements was assessed by measuring a standard that contained 1000 ppm deuterium. Saliva samples were analyzed if the measured deuterium of the standard by FTIR was within 1% (990–1010 ppm) of the known enrichment. The within- and between-day CVs for the deuterium standard were 0.59%.

LNS used in iLiNS-DOSE trial

The LNS that was used in the iLiNS-DOSE trial was produced and packaged by Nutriset S.A.S. (each package weighed 140 g). Raw ingredients included vegetable oil, peanut paste, dried skimmed milk, maltodextrin, sugar, and a mineral and vitamin mix (see Supplemental Table 1 under “Supplemental data” in the online issue). LNS was delivered to caregivers at 2-wk intervals by the study team for the main trial. The infants’ guardians were provided with small spoons (5 g) and advised to mix one spoonful (5 g) of LNS with 2 tablespoons of porridge prepared in the home. Participants in the 10-, 20-, and 40-g groups were told to provide 2, 4, or 8 spoonfuls of LNS/d, respectively. Every 2 wk, the study team collected empty LNS cups and leftover LNS, and a new supply was provided to the mother. For a subsample of infants also enrolled in a substudy of dietary intake (n = 568), the intake of LNS was estimated by using the interactive 24-h dietary recall method (15) on 2 different days. During the dietary intake assessment visits, the data collectors carried additional packages of LNS as models so that caregivers could demonstrate how much LNS they added to the infant’s porridge. The purpose of collecting dietary data was to estimate energy intake from all non–breast milk sources of energy (LNS + complementary foods) and to test whether there was a difference in energy intake between the LNS and control groups. The dietary data will be published separately.

Sample size calculation and statistical analysis

The original sample size calculation was based on an assumed average breast milk intake at 9–11 mo of age of 616 ± 172 g/d (16); using this assumption, a sample size of 89 mother-infant pairs per group was needed to detect a group difference in milk intake of...
RESULTS

The study was conducted between March 2010 and November 2011. In total, 595 iLiNS-DOSE trial mother-infant pairs were approached for enrollment into this substudy. The flow of participants is shown in Figure 1. No clinically significant differences in participant characteristics were found at baseline between the study groups (Table 1). No significant differences were found between groups in the proportion of participants not included in the analysis for the reasons shown in Figure 1 (P = 0.17). In addition, no statistically significant differences in maternal or infant baseline characteristics were found between those whose data were and were not included in the analyses (P > 0.06). Breast milk intake was measured in mother-infant dyads with 7 time point saliva samples for both the mother and the infant. Incomplete saliva collection (n = 27–36 per group) was a result of missed clinic visits by the mothers or inability to complete home visits because of the unavailability of the mother-infant pairs. One infant excluded from the breast milk intake measurement because of insufficient breastfeeding was included in the final analysis, with an assumed zero breast milk intake (0 g/d). The infant stopped breastfeeding 2 wk after starting the intervention at 6 mo. Because the reason for stopping breastfeeding is not known, we could not rule out an effect of the intervention.

Among the unsupplemented control infants, the mean (±SD) intakes of breast milk and other fluids were 730 ± 226 and 378 ± 234 g/d, respectively. The range and distribution of breast milk intakes were similar between the control and the intervention groups (Figure 2). Compared with the controls, the mean intake of breast milk was 62, 30, and 2 g/d higher among infants supplemented with 10, 20, or 40 g LNS/d, respectively (Table 2). In all breast milk intake comparisons between the

TABLE 1
Baseline infant and maternal characteristics

<table>
<thead>
<tr>
<th>Study group</th>
<th>Control ( n = 79)</th>
<th>LNS-10 g/d ( n = 75)</th>
<th>LNS-20 g/d ( n = 98)</th>
<th>LNS 40 g/d ( n = 107)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of males [n/N (%)]</td>
<td>39/82 (48)</td>
<td>39/75 (52)</td>
<td>49/105 (47)</td>
<td>49/112 (44)</td>
<td>0.81</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>8.0 ± 1.1</td>
<td>8.1 ± 1.0</td>
<td>8.1 ± 1.1</td>
<td>8.0 ± 1.0</td>
<td>0.85</td>
</tr>
<tr>
<td>Age (mo)</td>
<td>9.9 ± 0.5</td>
<td>9.9 ± 0.5</td>
<td>9.8 ± 0.5</td>
<td>9.8 ± 0.5</td>
<td>0.66</td>
</tr>
<tr>
<td>Maternal characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height (cm)²</td>
<td>154.1 ± 4.9</td>
<td>155.2 ± 5.8</td>
<td>155.4 ± 5.7</td>
<td>155.2 ± 5.2</td>
<td>0.34</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>52.1 ± 6.7</td>
<td>52.4 ± 9.0</td>
<td>52.7 ± 7.8</td>
<td>53.3 ± 8.6</td>
<td>0.78</td>
</tr>
<tr>
<td>Age (y)</td>
<td>26.0 ± 6.2</td>
<td>26.3 ± 7.7</td>
<td>26.0 ± 6.1</td>
<td>27.2 ± 6.2</td>
<td>0.86</td>
</tr>
<tr>
<td>Education (y)³</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>3.5</td>
<td>0.77</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.9 ± 2.8</td>
<td>21.8 ± 3.3</td>
<td>21.8 ± 2.8</td>
<td>22.1 ± 3.2</td>
<td>0.90</td>
</tr>
</tbody>
</table>

1 Continuous values are means ± SDs and were compared by ANOVA; the categorical variable was compared by chi-square test. LNS, lipid-based nutrient supplements.
2 Height was measured at enrollment into the main trial.
3 Values are medians.

≥86 g/d (α = 0.05, β = 0.80, effect size = 0.5); the number was increased to 100 per group to account for attrition, which was estimated as 12%. A difference in breast milk intake of ≥86 g/d represents <10% of total daily energy needs of infants at 9–11 mo of age [86 g of breast milk intake represents ~55–60 kcal, which is 8–9% of the total energy needs of 686 kcal/d at that age (16) and was therefore chosen as the noninferiority margin]. We assumed that a reduction in breast milk intake of this magnitude would not result in negative health consequences to the infant.

Data analyses were done by using Stata software (version 12.1; StataCorp). Variables were first assessed for normality to determine whether any transformations were necessary. Baseline characteristics were compared between groups by using ANOVA for continuous variables and a chi-square test for proportions. The noninferiority of differences in breast milk intake of each of the LNS groups compared with the control group was assessed by using 2-sided 95% CIs. Noninferiority was deemed established if the lower bound of the 2-sided 95% CIs of the LNS group was above the set noninferiority margin, a difference in breast milk intake of 86 g between the LNS and control groups. Non–breast milk oral water intake and total water intake in each of the intervention groups were compared with the intakes of the control group by using a 2-sample t test and by using Holm’s method to adjust for multiple comparisons (17). The primary analysis was conducted on the basis of intention to treat. The interaction between baseline anthropometric indexes (weight-for-length, weight-for-age, and length-for-age z scores) and intervention group was assessed by using a likelihood ratio test. A secondary, per-protocol analysis was conducted by using data on actual LNS intake, as described above.

FIGURE 2. Box-whisker plots of breast milk intakes by group. The outer bounds for the control group are 161 and 1512 g/d. For the LNS-10 g/d, LNS-20 g/d, and LNS-40 g/d groups, the outer bounds are 225 and 1895 g/d, 125 and 1580 g/d, and 0 and 1679 g/d, respectively. LNS, lipid-based nutrient supplements.
The percentage of infants whose breast milk intake was below the global reported average intake of 616 g/d at this age (16) was 26% and did not differ by group (P = 0.79). No interaction effect on breast milk intake was observed between group assignment and baseline weight-for-age z score (P = 0.95), length-for-age z score (P = 0.73), or weight-for-length z score (P = 0.69).

The mean non–breast milk oral water and total fluid intakes were similar between the groups (Table 2). For all groups combined, an inverse relation was found between the infants’ daily intake of breast milk and non–breast milk oral water (r = −0.22, P < 0.01).

The per-protocol analysis supported noninferiority in breast milk intake among those who received 1–10 or 11–20 g LNS/d compared with those who received 0 g LNS/d (Table 3). For the comparison between infants who consumed >20 g LNS/d and those with no LNS intake, the CI included both the preset noninferiority margin and zero, which made the finding inconclusive. The differences in sample sizes in the intention-to-treat and per-protocol analyses are a result of the fact that the latter categorized infants based on reported LNS intakes rather than group assignment.

**DISCUSSION**

Our objective was to test the hypothesis that mean breast milk intake (g/d) at 9–10 mo of age would not be reduced by providing LNS at a daily dose of 10, 20, or 40 g/d among rural Malawian infants. The intention-to-treat results are consistent with this hypothesis, i.e., breast milk intake was not lower among infants receiving LNS compared with the group not receiving LNS. Furthermore, on the basis of the per-protocol analysis, no difference in breast milk intake was observed between infants reportedly consuming no LNS and those reportedly consuming 1–10, 11–20, or >20 g LNS/d, although, for the latter group, we could not conclusively reject the possibility of a difference based on the 95% CI. The intention-to-treat analysis is a stronger test of our hypothesis than is the per-protocol analyses, given that the latter could be affected by reverse causation (i.e., women with lower milk volume feed more LNS to their infants).

Our results are consistent with those of 2 previous studies showing no differences in breast milk intake between infants provided with LNS and those given traditional corn-soy blends. The first study was conducted in rural Malawi in 7-mo-old infants (10) who were supplemented with LNS at doses of 25 and 50 g/d with an energy density of 5 kcal/g for 1 mo. In the other study, conducted in the Democratic Republic of Congo (11), infants were supplemented with 50 g ready-to-use lipid-based complementary food with an energy density of 5.5 kcal/g. In our study, LNS had a similar energy density, 5.5 kcal/g. Two studies that evaluated the effect of the overall energy density of the complementary food diet have reported an effect on breast milk intakes. In India, increasing the energy density of cereal-legume–based complementary foods by adding vegetable oil reduced...
breast milk intake in 6- to 10-mo-old infants (18). In Bangladesh, increasing the dietary energy density from 0.5 to 1.5 kcal/g significantly reduced breast milk intake by ~11% in infants 9–18 mo of age (9). However, in our study, LNS were only one part of the complementary food diet, and even though LNS themselves are energy-dense foods, their addition to home-prepared foods results in an overall diet that is not necessarily high in energy density. Thus, our findings are not inconsistent with the available evidence and indicate that home fortification of complementary foods with LNS does not negatively affect breast milk intake among 9- to 10-mo-old infants.

The overall mean breast milk intake (752 g/d) in our study participants exceeded the global estimate of average infant breast milk intake of 616 g/d (16) in developing countries at this age. Breast milk intakes higher than the reported global average have also been reported among 9- to 10-mo-old Congolese infants (705 g/d) receiving ready-to-use complementary food (11) and Zambian infants 9 mo of age (635 g/d), whose cereal-legume complementary foods were treated with α-amylase to increase energy density (19). The higher average breast milk intake among our study infants, compared with those from Zambia and the Democratic Republic of Congo, may be partly attributable to rural compared with urban differences (11). In all 3 studies, breast milk intake was measured by using deuterium dilution methods, whereas the global average intake estimates are based on data obtained by using the test-weighing method, which has been shown to underestimate breast milk intake (20). Another possible explanation for higher-than-expected breast milk intakes is that national and community breastfeeding promotion campaigns and programs may have resulted in increased breastfeeding in sub-Saharan countries (20, 21). Last, it is possible that the provision of LNS or improved complementary foods increases overall appetite, including appetite for breast milk. In Zimbabwe, breastfeeding frequency increased significantly from 9.9 ± 0.7 to 10.8 ± 0.7 breastfeeding/24-h period in infants 6–12 mo of age who received 20 g LNS/d for 2 wk (21).

The mean non–breast milk oral water intake in this study was 389 g/d, which is within the range of what has been reported in the sub-Saharan region. In the Democratic Republic of Congo (11) and Zambia (19), infants consumed 333 and 451 g/d, respectively, of non–breast milk oral water. Our results also confirm that none of the participating infants was still exclusively breastfed, because all had positive values for non–breast milk oral water intake, which is a proxy for complementary food intake (22). Exclusive breastfeeding beyond 6 mo is associated with poor nutritional outcomes in infants (23).

Our study had many strengths. Unlike similar studies (10, 11), ours had a large sample size and was therefore appropriately powered to test a noninferiority hypothesis. We also included a true control group that did not receive any study supplements, which allowed us to assess the independent effect of LNS on breast milk intake. Furthermore, we obtained dietary intake data (data not reported) from all study groups to ascertain the amounts of complementary food and LNS intake, which allowed us to perform the per-protocol analysis to confirm the intention-to-treat findings. In addition, our study used an objective method to measure breast milk intake and thus increased the validity of the findings. The analytic error was minimized by calibrating the FTIR machine every day before using it and measuring its precision on a daily basis. The study team had access to facilities for maintaining a cold chain in the field, which minimized the potential for error due to differences in sample handling.

One limitation of our study was that we did not directly observe the supplement intake of our study participants. However, the per-protocol analysis of the data agrees with the intention-to-treat results, although the sample size was smaller for the former than for the latter because dietary data were not collected for all of the infants in this substudy. Because of the higher attrition than anticipated, we implemented a second phase of recruitment, which could have introduced selection bias. However, the chance of bias was minimized by randomly selecting participants from all treatment groups and keeping the study implementation team blind to group assignment. The attrition rate was higher than estimated because the mother-infant dyads were not always available to provide saliva samples at their assigned time points during the 14-d sampling period, and/or they were not available for body weight measurements. Because their saliva and/or body weight data were incomplete, breast milk intake could not be measured reliably and they were not included in the final analysis.

### TABLE 3

<table>
<thead>
<tr>
<th>LNS intake (n)</th>
<th>Actual daily intake of LNS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 g/d (n = 107)</td>
</tr>
<tr>
<td>Breast milk intake (g/d)</td>
<td>751 ± 222.4±</td>
</tr>
<tr>
<td>Difference (95% CI) in means between each group and the infants with zero LNS intake</td>
<td>36 (−36.8, 108.2)</td>
</tr>
<tr>
<td>Non–breast milk oral water intake (g/d)</td>
<td>387.3 ± 256.2</td>
</tr>
<tr>
<td>Raw P value for intervention compared with control</td>
<td>0.33</td>
</tr>
<tr>
<td>Difference (95% CI) in means between each group and the infants with zero LNS intake</td>
<td>48.2 (−48.2, 144.6)</td>
</tr>
<tr>
<td>Total water intake (g/d)</td>
<td>1180.6 ± 316.6</td>
</tr>
<tr>
<td>Raw P value for intervention compared with control</td>
<td>0.17</td>
</tr>
<tr>
<td>Difference (95% CI) in means between each group and the infants with zero LNS intake</td>
<td>86.9 (−36.5, 210.4)</td>
</tr>
</tbody>
</table>

1 The data for the per-protocol analysis are from infants (n = 285) for whom dietary-assessment data were available; thus, n is not equal to 359. LNS, lipid-based nutrient supplements.
2 Mean ± SD (all such values).
3 Values were compared by 2-sample t test.
These results contribute to the knowledge base demonstrating that complementary foods in rural settings of developing countries can be fortified with LNS without negatively affecting breast milk intake.

We thank Christine Slater (Division of Human Health, International Atomic Energy Agency) for sharing the laboratory standard operating procedures for the preparation of standards and analysis of deuterium oxide enrichment in the saliva samples. We are also grateful to the iLiNS-DOSE participants, data collection team, and site supervisors in Mangochi and Namwera for their support and help during the implementation of the study; Mary Arimond (iLiNS Project Manager) for her guidance and leadership; Mark J Manary for his advice on the collection of biospecimens; and the iLiNS Project Steering Committee for oversight and guidance.

The authors’ responsibilities were as follows—KGD, MJH, PA, and KM: designed the substudy, supervised the research, and contributed to the manuscript; CK: conducted the research, analyzed the data, and wrote the draft manuscript; and JH: supervised the dietary intake assessment. All authors read and approved the final manuscript. None of the authors had a conflict of interest.

REFERENCES