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The Health of HIV-exposed Children after Early Weaning

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Abstract

There are potential health risks associated with the use of early weaning to prevent mother-to-child transmission of HIV in resource-poor settings. Our objective was to examine growth and nutrient inadequacies among a cohort of children weaned early. Children participating in the Breastfeeding Antiretrovirals and Nutrition (BAN) Study in Lilongwe, Malawi, had HIV-infected mothers, were weaned at 6 months and fed LNS until 12 months. 40 HIV-negative, BAN-exited children were compared to 40 HIV-negative, community children matched on age, gender and local health clinic. Nutrient intake was calculated from 24-hour dietary recalls collected from

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BAN-exited children. Anthropometric measurements were collected from BAN-exited and matched community children at 15-16 months, and 2 months later. Longitudinal random effects sex-stratified models were used to evaluate anthropometric differences between the 2 groups. BAN-exited children consumed adequate energy, protein, and carbohydrates but inadequate amounts of fat. The prevalence of inadequate micronutrient intakes were: 46% for vitamin A; 20% for vitamin B6; 69% for folate; 13% for vitamin C; 19% for iron; 23% for zinc. Regarding growth, BAN-exited girls gained weight at a significantly lower rate (0.02g/kg/day [95%CI: 0.01, 0.03] than their matched comparison (0.05g/kg/day [95%CI: 0.03, 0.07]); BAN girls grew significantly slower (0.73cm/month [95%CI: 0.40,1.06]) than their matched comparison (1.55cm/month [95%CI: 0.98, 2.12]). Among this sample of BAN-exited children, early weaning was associated with dietary deficiencies and girls experienced reduced growth velocity. In resource-poor settings, HIV prevention programs must ensure that breastfeeding stop only once a nutritionally adequate and safe diet without breastmilk can be provided.

Keywords

LNS; early breastfeeding cessation; HIV; Malawi; child growth

Introduction

HIV-infected mothers living in resource-poor settings are advised to exclusively breastfeed (EBF) from 0-6 months, take antiretroviral drugs during pregnancy and breastfeeding, introduce complementary foods at 6 months, and stop breastfeeding once a nutritionally adequate, affordable, feasible, acceptable, sustainable and safe (AFASS) replacement diet can be provided (WHO 2006; WHO 2009). The most recent WHO guidelines state “mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first six months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life. Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast-milk can be provided” (WHO 2009). Since breastfeeding is the most cost effective infant feeding strategy for food insecure families and supplies optimal nutrition and protection against common childhood infections (e.g. diarrhea, pneumonia), early cessation is potentially dangerous for infants living in resource-poor settings (Habicht et al. 1986; Victora et al. 1987). The WHO's global strategy on infant and young child feeding recommends the infants of HIV-negative mothers be EBF for the first six months of life and continue breastfeeding for up to 2 years of age or beyond (WHO 2002).

Malawian infants are traditionally fed a complementary diet based on maize porridge in addition to breastmilk (Corneli et al. 2007; National Statistical Office 2005; Hotz & Gibson 2001). This combination often cannot meet infant nutrient needs thus the traditional diet alone increases the risk of malnutrition (Dewey et al. 2004; Adu-Afarwuah et al. 2007; Dewey & Brown 2003). Among low-income families in Malawi, the addition of nutrient-dense foods to the child diet is essential but is often limited by seasonality and cost (Chirwa 2009). Children are most susceptible to growth faltering during the first 2 years of life (Victora et al. 2010), and nutritional insult during this critical developmental window can have lifelong health consequences including increased risk of child mortality, short adult stature, reduced intellectual development and economic productivity, and low offspring birth weight (Grantham-McGregor et al. 2007; Black et al. 2008; Victora et al. 2008). Considering the potential health risks associated with early breastfeeding cessation, we aimed to evaluate the effects of using early breastfeeding cessation as an HIV prevention strategy in a resource-poor setting by investigating dietary adequacy and growth after early weaning.

We evaluated dietary intakes among a sample of 15 to 18 month old children after exiting the Breastfeeding Antiretrovirals and Nutrition (BAN) Study to determine the prevalence of nutrient inadequacies. To determine if BAN-exited children exhibited significantly greater growth faltering, we also compared the anthropometric status of BAN-exits (non-breastfeeding) to a sample of self-reported HIV-negative, community controls matched on age, gender, and local health clinic. This study was conducted to inform policy regarding best infant feeding practices where concerns over breastfeeding increasing the risk of HIV transmission must be balanced by the risks of malnutrition.

Materials and Methods

The BAN Study

The BAN study was a randomized controlled clinical trial conducted in Malawi between 2004 and 2010. 2,369 HIV-infected mothers were assigned to two main study interventions: a 2-arm maternal nutritional intervention to promote maternal health, and a 3-arm antiretroviral intervention—with drugs given for up to 28 weeks to the mother, the infant, or neither—to prevent HIV transmission during breastfeeding (Chasela et al. 2010; van der Horst et al. 2009). All mothers were counseled to EBF to age 24 weeks, and then rapidly transition to a replacement diet, achieving early breastfeeding cessation by 28 weeks. To reduce the risk of malnutrition following early breastfeeding cessation, mothers were provided with a lipid-based nutrient supplement (LNS) made locally from full-cream powdered milk, peanut butter, sugar, oil, and micronutrients (Briend 2001). This breastmilk substitute (LNS) was designed to fulfill infant micronutrient requirements and replace the energy (400 kcal) and protein (9.5 g) that would have been provided by breastmilk (12mo) (van der Horst et al. 2009). This product was based on the ‘Plumpynut’ standard recipe intended for short term use among children with severe acute malnutrition but was used by the BAN Study due to the current paucity of alternative LNS formulations for long-term use (WHO/WFP/UNICEF, 2007). Lipid-based nutrient supplements are bacteria resistant, do not require water for preparation, and can be consumed directly from the container without cooking, making its use safe even in poor hygienic conditions (Briend 2002). LNS was provided after weaning until infants exited the study at 48 weeks (12 months).

Between 24 and 48 weeks, mothers were taught how to feed their children an adequate diet without breastmilk using a *Complementary Feeding Counseling Script* that emphasized the appropriate age for each food introduction, serving sizes, nutrient density and variety, feeding frequency, food safety, feeding during illness, and responsive feeding (Bentley et al. 2011; Ferguson et al. 2009). Specifically, mothers were instructed to practice responsive feeding; feed frequently with patience to ensure a maximum amount was consumed; prepare soft, thick porridge; enrich porridge with cooking oil, groundnut flour, sugar, honey, groundnuts, milk, soybeans, meat, or fish; ensure diet diversity to prevent micronutrient deficiencies; avoid sweets and soft drinks; feed 4 - 5 meals and 2 - 3 snacks per day.

Follow-up Study

The data for this Feasibility Study were collected by observing a sub-sample of HIV-infected mothers and their infants after exiting the BAN Study using a cohort design. When infants exited the BAN Study they no longer received LNS. Of concern were the dietary intakes and nutritional status of non-breastfed children after LNS supplementation ceased, and this formed the basis of the current study. In particular, nutrients of concern for the non-breastfed child in urban Malawi include energy, protein, fat, vitamin A, vitamin B6, folate, vitamin C, calcium, iron, and zinc (Dewey et al. 2004; National Statistical Office 2005).

The Feasibility Study was conducted at Bwaila Hospital in central Lilongwe, Malawi between April 2008 and March 2009. This study evaluated the dietary intakes of a sample of children after exiting the BAN Study (BAN-exits) when they were between 15 and 18 months of age to determine the prevalence of nutrient inadequacies and anthropometric status among non-breastfed children in comparison to a matched sample of non-participants from the community. BAN-exited children were EBF to 6 months with no breastmilk thereafter; received intensive face to face nutrition counseling and close medical attention to 12 months; received the local standard of care after 12 months. The matched community children were EBF for less than 6 months but continued breastfeeding to 18 months; received the local standard of care regarding nutrition counseling and medical care up to 18 months.

BAN-exited children were eligible to participate in this follow-up study if they: were singletons at birth, carried to term (>36 weeks), completed the BAN Study to 12 months, HIV-negative, available at 15-16 months of age for their first study visit, and willing to return 2 months later for a follow-up visit. For each child in the BAN-exited group, a non-participant child from the community was recruited into a comparison group matched on age, gender, and local health center. If a matched non-participant child did not return for their second visit they were withdrawn from the sample and another child was chosen from the community, matched on age, gender, and local health clinic to the already enrolled BAN-exited child. The mothers of all matched community children reported themselves and their children to be HIV-negative. Reports of HIV-negative status were most likely correct since all mothers would have been informed about their status during the HIV counseling and testing procedures conducted at all urban antenatal clinics; mothers also submitted to two confidential interviews, each approximately one hour in length, and answered in depth questions regarding the child's medical history and food practices thus making dishonesty difficult to sustain.

The sample size of 40 children per group was determined from power calculations described in the anthropometrics section, below. Recruitment occurred at the same 3 urban health clinics as the BAN Study and continued until a minimum of 80 children completed the study. Mother-child pairs were recruited in one of the following ways: at the BAN clinic following the exit interview, at a catchment clinic following HIV+ support group meetings, at a catchment clinic following healthy baby clinic visits, or using home locator maps. Compensation to participants included 600MK (US \$4) for transport and 1kg fortified corn-soya blended flour for both study visits.

Dietary intake

Dietary intake data were collected from BAN-exited children because they had stopped breastfeeding and total intake could be easily calculated; dietary intake data was not collected from the matched community children because they were still breastfeeding and funding was not available to quantify breastmilk intake using precise estimates (i.e. doubly labeled water). Two 24-hour diet recalls were collected from each child within one week between 15 and 16 months of age, and again between 17 and 18 months of age, for a total of 4 recalls from each of the BAN-exited children. Diet recalls were conducted by BAN nutrition officers. Mothers were prompted to recall what their child had eaten over the past 24 hours using food models, standard household dishes and utensils, and recording recipes. Nutrient consumption was calculated using a Malawi food composition table (FCT) developed by Rosalind Gibson (Ferguson et al. 1995). Additional information was added from a Tanzanian FCT (Lukmanji et al. 2008), the USDA nutrient database (USDA 2010), or directly from the manufacturer. The resulting database had the nutritional value of individual food items as well as mixed dishes based on standard recipes (e.g. nsima).

Anthropometrics

Anthropometrics were obtained from each child, once between 15 and 16 months and again between 17 and 18 months. The sample size was calculated using Malawi's 2004 demographic and health survey and the mean height-for-age Z-score (and respective standard deviation) for infants 15 to 18 months. A convenience sample size of 40 per group was feasible to recruit within our time frame and allowed us to be able to detect a 0.92 difference in mean Z-scores between samples, with 80% power and significance set at 10% (National Statistics Office and ORC Macro, 2005). If significance had been set at 5% while keeping sample size and power parameters constant, we could have only detected a difference greater than 1.03 in mean Z-scores.

Two trained Malawian research assistants recorded recumbent length following standardized protocol using a Pediatric Length board (to the nearest 1 mm) made locally based on UNICEF model specifications and a calibrated Tanita infant scale (to the nearest 10 g) (MCHB 2000). All measurements were made in triplicate and averaged. Length-for-age Z scores (LAZ), weight-for-age Z scores (WAZ), and weight-for-length Z scores (WLZ) were calculated in Microsoft Excel using the LMS method (Box-Cox power, $L(t)$; median, $M(t)$; and coefficient of variation, $S(t)$) and the WHO 2006 standards for breastfed children (Cole & Green 1992). Stunting, underweight, and wasting were respectively defined as having an LAZ, WAZ or WLZ score less than 2SD below the WHO median.

Background questionnaire

A background survey was administered to obtain data from each mother on age, marital status, education and occupation of both parents, number of household members, household socio-economic indicators, and food availability. Ethical approval for this study was obtained from the institutional review boards at the U.S. Centers for Disease Control and Prevention, UNC-Chapel Hill, and the National Health Sciences Research Committee in Malawi. Participants in the original BAN Study had signed a consent form to be contacted after the study was completed.

Seasonality

The Malawian climate is characterized by 4 seasons: rainy (November to April), post-rainy (April to May), cool (May to mid-August), and hot (mid-August to November). The rainy season is known locally as the 'hungry season' because food is limited during this time. For each BAN-exited child, a matched child was measured within the same month; however, high attrition among the matched comparison extended their enrollment period and reduced seasonal overlap between the samples. Since a child's growth velocity is affected by season, a variable was created to measure percent exposure to the hungry season during the 2 months prior to each study visit. All regression models comparing growth outcomes controlled for exposure to the hungry season. Diet recalls were collected from BAN-exited infants between April 2008 and December 2008 and did not greatly overlap the hungry season.

Data analysis

Nutrient intake was analyzed only within the BAN-exited sample, since the comparison group was still receiving breastmilk. Nutrient intake distributions were calculated from the 24-hour dietary recalls. The prevalence of inadequacy for each nutrient, approximated from the proportion of children consuming less than the Estimated Average Requirement (EAR) cut-point (IOM 1997; IOM 1998; IOM 2000; IOM 2001; IOM 2002/2005), was estimated using C-SIDE (C-SIDE, version 1.0, 1996; Department of Statistics, Iowa State University) (Carriquiry 2003; Dodd 1996; Guenther et al. 1997). C-SIDE requires multiple dietary

recalls per individual to reduce within-individual day-to-day variation and enable an estimation of within-and between-individual variation (Dodd et al. 2006; Dodd 1996). The EAR equivalent for energy is EER (expected energy requirement) and can be calculated for each individual (15-18mo) based on body weight [EER = (89 × weight [kg] – 100) + 20kcal]. For calcium, only an adequate intake (AI) level exists preventing the calculation of inadequacy prevalence. Total protein, carbohydrate, and fat intakes were compared to the Acceptable Macronutrient Distribution Ranges (AMDR) (IOM 2002/2005). Typical foods consumed and sources of certain vitamins were also examined using the dietary recalls.

We used Stata 10, longitudinal random effects sex-stratified models to evaluate group differences in WAZ, LAZ, and WLZ. The linear regression models accounted for exposure to the hungry season, maternal age, parity, visit (at 15 vs. 17 months), and an interaction variable between visit number and group. Child's age was not included because the age range was small and groups were age-matched. The models were selected using a priori variable selection, checks for collinearity, and sequential removal of variables that did not statistically confound the association of interest; final models were checked using residual analysis. Parity was dropped because of its collinearity with maternal age. Based on the findings from the longitudinal models, we did further group comparisons of weight and length velocity between the 2 visits using one-way ANOVA (Lepage et al. 1996). The prevalence of stunting, underweight, and wasting were calculated for each child sample in each age group; a chi-square test was used to determine if the differences in proportions were significant between the two groups using Stata 10.

Results

Subjects

A total of 99 children were recruited into the study, 81 children completed the study, and 78 were included in the analysis (Figure 1). Thirteen of the matched community children were lost to follow up between the first and second visit; a comparison of socioeconomic characteristics revealed no differences of practical importance between the final sample and those lost to follow up. Three children were excluded due to suspected measurement error because they had anthropometric Z-Scores more than 4 standard deviations above or below the WHO median. A sensitivity analysis found their exclusion did not change the direction of the relationships but attenuated the growth velocity differences between groups in girls as well as boys. The BAN-exited group and the matched community group each contained 39 children. Of the 39 matched community children, 37 (95%) were still breastfeeding at 15 months. None of the 39 BAN-exited children were breastfed past 7 months.

Socio-demographic characteristics

In both samples, most households were headed by males and had more than 1 child younger than 5 years. Selected socioeconomic and demographic characteristics of the sample are shown in Table 1. Three notable differences between groups were that the matched community mothers were younger, more likely to be married, and more were primiparous.

Nutrient adequacy

On average, the diet of the non-breastfeeding BAN-exited sample exceeded protein and carbohydrate requirements but was deficient in energy and fat (Table 2). Nutrient intakes at 15-16 months were similar to intakes at 17-18 months. Overall, energy intake was composed of carbohydrate (66%), protein (11%), and fat (22%). Approximately 65% of BAN-exited children consumed energy-deficient diets and 81% consumed an inadequate amount of fat (Table 2). Micronutrient intakes were not normally distributed (skewed right) and are

therefore summarized by medians. Median intakes of vitamin B6, vitamin C, iron, and zinc were above their respective EAR but median vitamin A and folate intake fell below. The prevalence of inadequacy was: 46% for vitamin A, 20% for vitamin B6, 69% for folate, 13% for vitamin C, 19% for iron, 23% for zinc (Table 2). Mean calcium intake (172 mg) was below the AI and thus there is a reasonable likelihood that dietary intakes were inadequate (Table 2).

In addition to the general diet description above, we further explored if dietary differences existed between genders. The only difference was that girls consumed significantly less fat and more carbohydrate as a proportion of their total energy intake than boys (Student's t-test, $p < 0.05$). Boys consumed 24% of total calories from fat and 64% from carbohydrate sources; girls consumed only 20% from fat calories and 69% from carbohydrate.

Typical Food Consumption

Diets were based primarily on maize flour and consumed in the form of porridge and nsima. Nsima is a stiff porridge made from maize flour and eaten with a relish, an accompanying vegetable, bean, fish, or meat side dish. Together porridge and nsima provided 60% of total energy. On average, children received 2.25 servings of porridge (200g) per day providing 350kcal (53g carbohydrate; 12g protein; 10g fat). The typical recipe included maize flour, water, sugar, and salt but the frequent addition of soya (26%) and groundnut flour (33%) increased protein and fat consumption. Child intakes were deficient in fat but surpassed the protein recommendation (Table 2). Protein was mainly consumed from porridge (10.5g/day) due to the presence of soya flour, groundnut flour, and large quantity of maize flour.

Food choices differed by gender. Boys were 3.9 times as likely to receive fresh or powdered milk, 1.2 times as likely to receive animal products, 1.2 times as likely to consume vegetable oil in their mixed dishes. Girls were 1.44 times as likely to consume fruits. The frequency of groundnut and soya flour consumption was similar between genders. Overall, boys were fed slightly more frequently and slightly larger portion sizes.

Sources of vitamin A, folate, fat

Dietary intakes were deficient in fat, vitamin A, and folate. Primary sources of vitamin A in the diet were leafy green vegetables and tomatoes (vitamin A precursors). Less frequent were animal products (e.g. liver, eggs, and milk) and sweet potatoes. Folate was mostly consumed from groundnut flour and soya flour in porridge. Additional sources included fruits, other vegetables, beans, and leafy green vegetables but small portion sizes limited intake. Fat was largely consumed from groundnut flour and soya flour.

Growth Comparison

Both BAN-exited and matched comparison children were below the WHO reference median but still of moderately healthy weight. Table 3 lists the mean WAZ scores of each sub-group adjusted for exposure to the hungry season, maternal age, visit number, and an interaction variable between visit number and BAN status; when the matching criteria were included as covariates in the model (e.g. child age, sex) the results were unchanged. The interaction term was significant ($p = 0.076$) implying that BAN-exited girls had a different pattern of change in their WAZ scores over time. Weight velocity significantly differed between the groups among girls; BAN-exited girls ($N = 16$) gained an average of 0.02g/kg/day and the matched community girls ($N = 18$) gained an average of 0.05g/kg/day ($p < 0.05$) (Table 3). The WAZ scores of BAN-exited boys ($N = 23$) and community boys ($N = 21$) did not significantly differ; velocity of weight gain among BAN-exited boys was 0.02g/kg/day and community boys was 0.03g/kg/day (Table 3).

Both groups were on average shorter than the WHO 2006 reference median. Table 3 lists the mean LAZ scores of each sub-group adjusted for exposure to the hungry season, maternal age, visit number, and an interaction variable between visit number and BAN status; when the matching criteria were included as covariates in the model (e.g. child age, sex) the results were unchanged. Overall, the LAZ and length velocity scores of BAN-exited (N=23) and matched community (N=21) boys did not differ (Table 3). The LAZ scores of BAN-exited (N=16) and matched community (N=18) girls did not differ, but the group by visit interaction variable was significant, suggesting BAN-exited girls did worse over time ($p=0.076$). This was further illustrated by the lower length velocity of BAN-exited girls ($p<0.05$) (Table 3).

The combination of short stature and moderately healthy weight status resulted in WLZ scores above the WHO median. Adjusted mean WLZ scores are listed in Table 3. WLZ scores did not significantly differ between girl samples or boy samples.

Malnutrition

At 15 -16 months, 36% (14/39) of BAN-exits and 49% (19/39) of community children were stunted; at 17-18 months, 31% (12/39) of BAN-exits were stunted and 31% (12/39) of community children were stunted. At 15-16 months, 5% (2/39) of BAN-exits and 13% (5/39) of the community comparison were underweight; at 17-18 months, 5% (2/39) and 3% (1/39) of BAN-exited and community children were underweight, respectively. While none of the BAN-exited children were wasted, 5% (2/39) of community children were wasted at 15-16 months and 5% (2/39) were wasted at 17-18 months. Table 4 illustrates these differences were not significant.

Discussion

This study provides insight into the diets of 15-18 month old children, living in a resource-poor setting within Malawi, who were weaned from the breast at 6 months and who received LNS through 12 months as a breastmilk substitute. After children stopped receiving LNS, their diet was maize-based but enriched with purchased ingredients, such as groundnuts and soya. Overall, the diet without breastmilk was rich in carbohydrate and protein but deficient in energy, fat and micronutrients. Among this sample, early breastfeeding cessation was associated with low growth velocity scores between 15 and 18 months when no substitute was provided after 12 months. In comparison to the matched community sample of breastfed girls, BAN-exited girls had significantly reduced growth velocity outcomes over the 2-month follow-up.

The results of the present study are consistent with dietary modeling studies that reported difficulties constructing affordable child diets from traditional food sources to provide sufficient energy, 30% of calories from fat, and adequate amounts of vitamin A, thiamine, riboflavin, vitamin B6, folate, vitamin C, calcium, iron, and zinc (i.e. 'problem nutrients') (Dewey et al. 2004). A previous complementary diet study in Malawi found that young children were fed mainly maize flour, few animal-source foods, and inadequate amounts of energy, calcium, iron and zinc (Hotz & Gibson 2001; Ferguson et al. 1993). The Malawi DHS reported that at least one serving of meat, fish, shellfish, poultry, or eggs was consumed by children 16-19 months old less than once a day, whether the child was breastfeeding or not, but small servings of fruits and vegetables were eaten 3 to 4 times a day. Also consistently reported were high rates of childhood anemia and sub-clinical vitamin A deficiency, thus our findings of inadequate intakes of iron, vitamin C, folate, and vitamin A are not surprising (National Statistical Office 2005; MOHP 2003).

BAN-exited children received intensive nutrition counseling and medical care to 12 months which may have given them an advantage over the matched community comparison. Stunting is an indicator of chronic malnutrition and our data suggest that this sample of BAN-exited children was less stunted at 15-16 months than the community comparison sample. Wasting is indicative of acute malnutrition and a greater proportion of the community comparison was measured during the hungry season, which may explain their greater wasting prevalence. While the prevalence rates of stunting and underweight improved by 18% and 10% among the matched comparison, respectively, little to no improvement was observed among the BAN-exited sample. Although the difference between study groups was not statistically significant, these data could suggest that BAN-exited children may have less ability to recover from malnutrition and thus may have greater prevalence malnutrition as they progress through childhood. The prevalence of stunting, wasting, and underweight within these 2 child samples was lower than national average for this age group in Malawi (National Statistical Office, 2005). Previous studies in Malawi found height and weight velocity vary according to a seasonal pattern after 12 months of age (Maleta et al. 2003) possibly due to greater dependence on the external environment. Children typically experience negative weight velocity during the hungry season (Dec-Jan), peak weight gains following the harvest (May, June, and July), and greatest height gains 3 months after the harvest (August-October).

In this region of the world, there is little evidence of gender preference; the anthropometric Z-scores of boys and girls under 5 years are similar within the Malawi Demographic and Health Survey (National Statistical Office 2005). Both the length and weight velocity of BAN-exited girls fell significantly below that of community girls, and the same difference was not observed between boy samples. We suspect the growth of BAN-exited girls was negatively impacted by social factors such as traditional differences in diet quality (Ferguson et al. 1995). Families were 4 times as likely to purchase milk products for male children as for female children; suggesting households with boys allocated their resources to ensure boys continued receiving milk in the absence of breastmilk; this finding may be restricted to low-income, non-breastfeeding, HIV-infected populations. Girls consumed significantly less fat and more carbohydrate. While neither gender achieved the AMDR for fat, girls fell further from the 30-40% recommendation which may have contributed to their reduced growth outcomes (Lifschitz & Moses 1989).

There is limited prior evidence of son preference in sub-Saharan Africa (Basu & de Jong 2006; Klasen & Wink 2003; Kabeer 2003), especially Malawi, where vaccination coverage is equal, the percent of sick children receiving adequate health care does not differ by gender, and the under-5 child mortality rate is greater among boys than girls (166 vs. 149 per 1,000) (National Statistical Office 2005). Thus our findings could be the consequence of a small sample size, indicate differences between HIV infected families and the general population, or more likely be attributable to factors currently unknown. Poor growth outcomes among girls weaned early are particularly problematic because the deleterious effects of malnutrition can be passed on to their future offspring (Victora et al. 2008).

In Malawi, families place great value on complementary foods and believe they are essential for weight gain and growth (Parker et al. 2011) even when the staple food is not energy or nutrient dense. If families preferentially fed male children a greater ratio of complementary foods to breast milk, male growth would be impeded if the complementary foods were inadequate. While BAN-exited children received enriched home-made complementary foods between 12-15 months, matched community children likely received standard complementary foods in addition to breastmilk. Since the growth rate of community comparison boys was similar to that of non-breastfeeding boys, it is possible the matched community boys were primarily fed complementary foods.

All BAN-exited children included in this study were HIV-negative therefore we cannot attribute their lack of growth to HIV infection. We hypothesize that the community comparison had better growth outcomes because most were still breastfeeding between 15 to 18 months (mean intended duration = 28 months) and were buffered against seasonal changes. Non-breastfeeding children are more vulnerable to dietary deficiencies and are not protected against infections by maternal antibodies thus their recovery from infection is impaired and could negatively impact their growth and recovery from growth faltering.

Breastmilk provides a superior diet, contains anti-infective properties, promotes gastrointestinal track development, a healthy immune system, and lower morbidity incidence (Goldman 1993; Hanson 1998; Duncan et al. 1993; Dewey et al. 1995; Cushing et al. 1998; Bachrach et al. 2003). Early breastfeeding cessation as an HIV-prevention method has been associated with increased risk of serious gastroenteritis (Onyango-Makumbi et al. 2009), gastroenteritis-associated mortality (Kafulafula et al. 2010), growth faltering (Arpadi et al. 2009), nutrient deficiencies (Lunney et al. 2008) and failed to improve the rate of HIV-free survival (Kuhn et al. 2008). Infants who participated in the BAN Study were all indirectly exposed to antiretroviral medicines during labor, delivery and the first 2 weeks of life, a third received ARVs directly during the 6-month breastfeeding period, and a third ingested their mother's ARVs indirectly through breastmilk to 6 months (van der Horst et al. 2009). While maternal HIV infection is documented to impair prenatal growth (Bulterys et al. 1994) there is conflicting evidence on whether or not it negatively impacts postnatal growth (Hankin et al. 2005; Paul et al. 2005). Exposure to ARVs during pregnancy and delivery does not affect postnatal growth (Briand et al. 2006) and research to date has not evaluated if postnatal ARVs impact infant growth. It is possible that HIV-exposed infants do not develop sufficient nutrient stores due to the combination of inadequate maternal intake or bodily stores and the increased energy and nutrient needs of HIV infection (Grinspoon et al. 1998; Friis et al. 2001; Friis et al. 2001a). Such inadequate infant stores would be quickly depleted after birth if breastmilk was only consumed for a short time and replaced by inadequate complementary foods, resulting in growth faltering.

The greatest limitation to our study was the accuracy and comparability of recumbent length measurements. Children consistently prove difficult to measure using a length board and we were forced to omit 3 due to suspected measurement error in an attempt to improve validity. Although the rapid decline in stunting prevalence among matched community children could suggest error, the measuring assistants were not changed over the course of the study thus any measurement error would have been random and thus could only have mitigated the differences between samples. While we recognize thirteen of the matched community sample were lost to follow up, no socioeconomic differences were found between those lost and those retained and thus it is unlikely that such attrition introduced bias. Differences in the timing of participation between the 2 groups did create a systematic bias and limited the conclusions we could draw by comparing the growth of BAN-exited children to community children. However, we do suspect that the difference in growth velocities documented here would have been further amplified if the entire matched community sample been measured during the harvest season rather than the hungry season. In retrospect, this study would have benefited from measuring morbidity incidence among both samples to examine if BAN-exited children experienced more illness and if this difference impacted growth outcomes. While the lack of dietary information from the matched community comparison group and confirmed HIV-negative status are also limitations, we must still recognize the possibility that other biases and unknown confounders may exist between the groups.

Previous studies among Malawian children found mean intakes derived from the 24-hour recall were within $\pm 10\%$ of values calculated from weighed food records (Ferguson et al. 1989). The 24-hour recall underestimates actual intake due to memory error reporting snack

consumption, the use of average recipes, and underestimations of the quantity consumed from the main meal (Ferguson et al. 1989; Ferguson et al. 1995). In comparison, the present study was less affected by such errors because BAN Study mothers had 12 months experience reporting 24-hour dietary recalls, we did not use standard recipes for dishes with varying ingredients, and mothers were prompted to remember accurate intakes using standard household measures and food models.

To our knowledge, this is the first study to investigate growth outcomes one year after performing early breastfeeding cessation as an HIV prevention method, and in comparison to a matched community sample. By conducting this assessment, we were able to investigate the dietary deficits of non-breastfeeding children and confirm that the traditional child diet was in fact deficient in macronutrients and micronutrients, the most concerning of which were fat, vitamin A, and folate. This information will help tailor future complementary feeding guides used to counsel HIV-infected mothers choosing to not breastfeed in resource-poor settings.

This study has raised concerns about the safety of breastfeeding cessation as an HIV prevention method. The most recent revisions to the WHO HIV and infant feeding guidelines now advise mothers to continue breastfeeding for the first 12 months of life, with receipt of maternal or infant antiretroviral medications, and perform breastfeeding cessation only once a nutritionally adequate and safe diet without breast-milk can be provided (WHO 2009). Since early breastfeeding cessation appears to have trade-offs in resource-poor settings, we believe it is essential that HIV prevention programs provide dietary counseling to participating families to ensure they understand what components are necessary to provide an adequate child diet and help them evaluate if they are capable of providing those components. This information will help families to make an informed decision regarding whether or not they should stop breastfeeding at 12 months.

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Key Messages

1. Non-breastfed children consumed inadequate amounts of fat and the prevalence of inadequate micronutrient intakes was: 46% for vitamin A; 20% for vitamin B6; 69% for folate; 13% for vitamin C; 19% for iron; 23% for zinc.
2. The dietary intakes of non-breastfeeding children differed significantly by gender. Boys consumed 24% of total calories from fat and 64% from carbohydrate sources; girls consumed only 20% from fat calories and 69% from carbohydrate. Boys were 4 times as likely to receive milk products.
3. The matched community comparison sample of girls (95% breastfeeding) had significantly greater weight velocity and length velocity scores than the sample of BAN-exited girls who stopped breastfeeding at 6 months.
4. Early breastfeeding cessation as an HIV prevention method may have trade-offs in resource-poor settings such as inadequate dietary intakes and reduced infant growth.

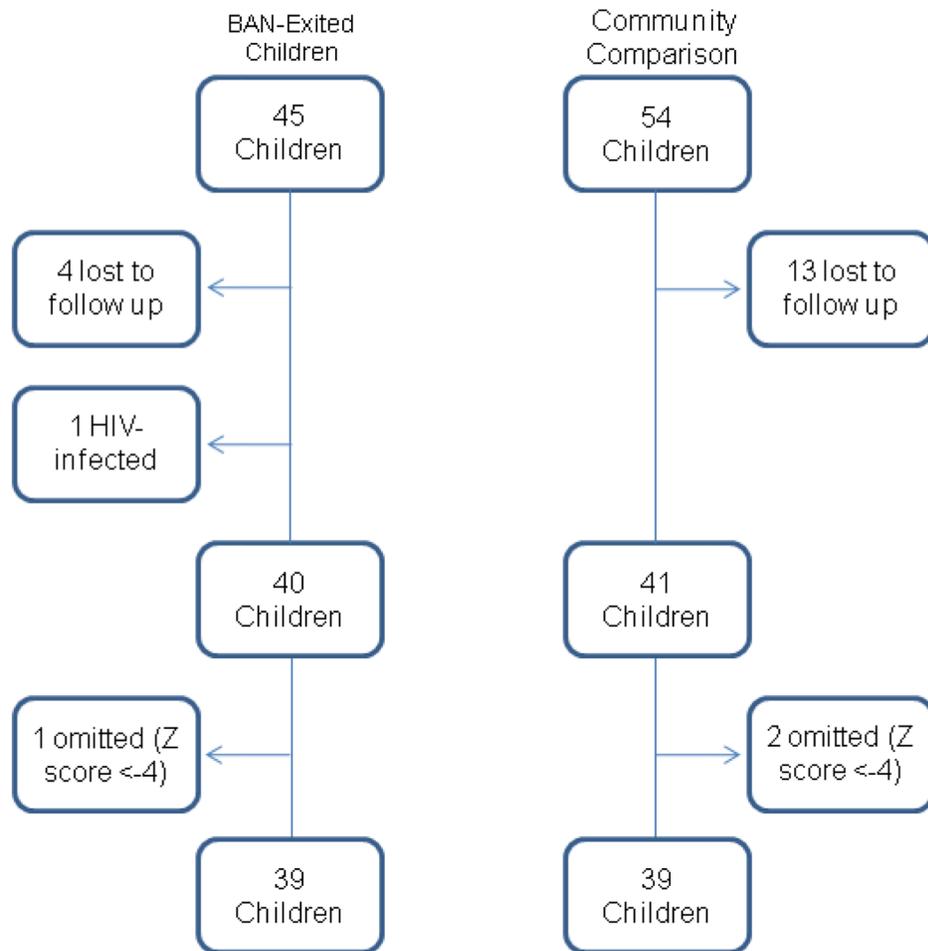


Figure 1. A flow chart illustrating subject enrollment during the Feasibility Study in Lilongwe, Malawi, April 2008 to March 2009.

Table 1

Demographic and socioeconomic characteristics of mothers participating in the Feasibility Study in Lilongwe, Malawi, 2008.

	BAN-exited sample N=39	Matched community sample N=39
Age in years (\pmSD)	28.8 (\pm 5.9)	23.6 (\pm 3.8)
Marital Status		
Married	75.6%	93%
Separated	17%	7%
Divorced	5%	0
Widowed	2%	0
Education		
0	2%	0
< 8 yrs	39%	46%
8 yrs	27%	27%
8-12 yrs	15%	10%
12 yrs	17%	17%
Occupation		
Currently working	45%	39%
Self-employed (non-farming)	30%	24%
Husband's Occupation		
Salaried employment	58%	58%
Self-employed (non-farming)	30%	37%
Other (military, landlord)	6%	2.5%
Unemployed	3%	2.5%
Fertility		
Proportion primiparous	17%	46%
Parity	3.4 (\pm 1.9)	2.1 (\pm 1.4)
Total number of Living Children	2.9 (+1.4)	2.0 (+1.3)
Number of Children < 5 yrs in Household	1.7 (\pm 0.9)	1.5 (\pm 0.6)
Socio-economic Status		
Refrigerator	7%	5%
Electricity	22%	12%
Personal water source	29%	17%
Traditional latrine with roof	66%	75%
Cement floor	66%	78%
Iron sheet roofing	83%	80%

Table 2

Macronutrient and select micronutrient intakes from BAN-exited child participants in the Feasibility Study in Lilongwe, Malawi, 2008.

Nutrient	Expected total intake *	Median intake	Mean (SD) intake	Inadequacy prevalence (adjusted)
Energy	$EER = (89 \times \text{weight}[\text{kg}] - 100) + 20\text{kcal}$	91.5%	92% ($\pm 40\%$)	65%
Protein	EAR = 0.87g/kg/day	250%	221% ($\pm 105\%$)	0.5%
Protein AMDR	5 - 20% of Energy	11.2%	11.5% ($\pm 2\%$)	2.3%
Fat AMDR	30 - 40% of Energy	21.7%	22% ($\pm 6\%$)	80.8%
Carbohydrate AMDR	45 - 65% of Energy	66.7%	66% ($\pm 7\%$)	6.6%
Vitamin A	EAR = 210 μg /day	143 μg	235 μg (± 228)	46%
Vitamin B6	EAR = 0.4mg/day	0.58mg	0.7mg (± 0.58)	20%
Folate	EAR = 120 μg /day	113 μg	104 μg (± 67)	69%
Vitamin C	EAR = 13mg/day	25mg	38mg (± 39)	13%
Iron	EAR = 3.0mg/day	4.7mg	4.4mg (± 2.4)	19%
Zinc	EAR = 2.5mg/day	3.5mg	3.5mg (± 1.7)	23%
Calcium	AI = 500mg/day	137mg	172mg (± 150)	--

* Expected total nutrient intake, derived from the IOM, was used as the comparison referent. Expected intakes of energy, protein, fat, and carbohydrate were obtained from IOM 2002/2005; Expected intakes of vitamin A, zinc, and iron were obtained from IOM 2001; Expected intake of vitamin C was obtained from IOM, 2000; Expected intakes of vitamin B₆ and folate were obtained from IOM 1998; Expected intake of calcium was obtained from IOM 1997.

Table 3

Adjusted anthropometric means for BAN-exited and matched community children in the Feasibility Study in Lilongwe, Malawi, April 2008 to March 2009.

Group	Sample size (N)	Weight for age Z-score ¹	Length for age Z-score ²	Weight for length Z-score ³
15-16 Months				
BAN-exited girls	N=16	-0.41 [-0.98, 0.17]	-1.34 [-1.88, -0.79]	0.30 [-0.36, 0.95]
Matched girls	N=18	-0.41 [-0.95, 0.13]	-1.52 [-2.03, -1.01]	0.36 [-0.25, 0.97]
BAN-exited boys	N=23	-0.10 [-0.58, 0.38]	-1.49 [-2.02, -0.95]	0.80 [0.20, 1.39]
Matched boys	N=21	-0.56 [-1.1, -0.05]	-2.03 [-2.60, -1.47]	0.50 [-0.12, 1.12]
17-18 Months				
BAN-exited girls	N=16	-0.41 [-0.99, 0.16]	-1.53 [-2.07, -0.98]	0.43 [-0.22, 1.08]
Matched girls	N=18	0.07 [-0.48, 0.61]	-1.30 [-1.82, -0.79]	0.90 [0.28, 1.52]
BAN-exited boys	N=23	-0.01 [-0.50, 0.48]	-1.34 [-1.89, -0.80]	0.83 [0.22, 1.44]
Matched boys	N=21	-0.53 [-1.05, 0.00]	-1.73 [-2.32, -1.15]	0.36 [-0.29, 1.02]
Velocity		Weight gain⁴ (g/kg/day)	Height gain⁵ (cm/month)	
BAN-exited girls	N=16	0.02 [0.01, 0.03] †	0.73 [0.40, 1.06] †	
Matched girls	N=18	0.05 [0.03, 0.07] †	1.55 [0.98, 2.12] †	
BAN-exited boys	N=23	0.02 [0.01, 0.04]	1.19 [0.79, 1.58]	
Matched boys	N=21	0.03 [0.02, 0.04]	1.47 [0.97, 1.98]	

† Significant difference (p<0.05);

¹WAZ,

²LAZ,

³WLZ scores were adjusted on exposure to the hungry season, maternal age, visit number, and the interaction between visit number and BAN status.

⁴Weight gain and

⁵height gain were adjusted to the number of days the child was followed.

Table 4

The prevalence of malnutrition among BAN-exited and matched community children in the Feasibility Study in Lilongwe, Malawi, April 2008 to March 2009.

	BAN-exited children	Matched children	p-value
% Stunted (15-16m)	36	49	0.25
% Stunted (17-18m)	31	31	1.00
% Underweight (15-16m)	5	13	0.24
% Underweight (17-18m)	5	3	0.56
% Wasted (15-16m)	0	5	0.15
% Wasted (17-18m)	0	5	0.15