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Decreased consumption of common weaning foods is associated with poor linear growth among HIV-exposed infants participating in the Kigali Antiretroviral and Breastfeeding Assessment for the Elimination of HIV (Kabeho) Study

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Abstract

Objective: The World Health Organization recommends that complementary foods that are adequate, safe, and appropriate be introduced to infants at age six months. Using an innovative modeling technique, we examine patterns of nutrient intake in HIV-exposed and -uninfected (HEU) infants and establish their relationship with growth.

Methods: Single-day dietary recalls and anthropometrics were collected every two to three months from 543 infants living in Kigali, Rwanda and attending clinics for the prevention of mother-to-child HIV transmission. A common weaning food index (CWFI) was calculated in grams and nutrient density for infants to reflect the extent to which the infants consumed the weaning foods typical of this population at ages 6-10, 11-15, and 16-20 months. Regressions among the CWFI, length-for-age z-scores (LAZ), and weight-for-length z-scores (WLZ) were conducted to estimate the relationship between the dietary patterns and growth.

Results: Mean absolute intake of zinc and calcium from complementary foods was insufficient. Increasing CWFI was related to increasing cow milk consumption. The density CWFI showed a decrease in the density of iron and folate as infants consume more of the weaning foods typical of this population. Density CWFI, breastfeeding, and caloric intake act on early LAZ and WLZ and interact with one another. Among breastfed infants, those who consume little of the common weaning foods and have a high caloric intake develop deficits in LAZ and have an elevated WLZ.

Conclusions: A diet that is more dominated by the typical weaning foods of this population may support a healthy growth pattern.

Authors contributions:
Charlotte Lane conducted analysis and wrote the body of the paper
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Keywords

HIV; infant; breastfeeding; Option B+; HIV-exposed and uninfected infants; HEU

Introduction

The World Health Organization (WHO) recommends that safe, adequate, and appropriate complementary foods be introduced to infants at six months of age. Current WHO guidelines for feeding HIV-exposed and -uninfected (HEU) infants recommend exclusive breastfeeding until age six months at which time complementary foods should be introduced and breastfeeding should continue along with appropriate antiretroviral (ARV) treatment of the mothers (World Health Organization, 2016). Dietary patterns from six to 24 months are expected to have a significant impact on infant growth outcomes (Arpadi et al., 2009; Prendergast, Humphrey, Prendergast, & Humphrey, 2017). Many infants develop linear growth deficits at this time (Prendergast et al., 2017; Stewart, Iannottie, Dewey, Michaelsen, & Onyango, 2013). The weaning diet may affect weight immediately and later in life (Ong, Emmett, Noble, Ness, & Dunger, 2006; Pearce & Langley-evans, 2013; Scaglioni et al., 2000; Tang & Krebs, 2014). Early stunting (low length-for-age) predicts increased morbidity and mortality, reduced cognitive and behavioral skills, and poor long-term health (Black et al., 2013; Dewey & Begum, 2011; Goldberg & Short, 2016; Onis & Branca, 2016; Prendergast et al., 2017). Individuals with faster linear growth and weight gain in the first two years of life tend to complete more years of schooling and have a lower risk of school failure in low- and middle-income countries (Martorell et al., 2010). Among HEU infants, stunting and wasting are associated with decreased psychomotor and mental development (McDonald et al., 2013). Some populations of HEU infants in sub-Saharan Africa show a growth pattern characterized by low average length-for-age z-scores (LAZ) but slightly elevated weight-for-length z-scores (WLZ) (Flax et al., 2013; Jumare et al., 2019; Lane, Bobrow, Ndatimana, Nadyisaba, & Adair, 2019).

HEU infants may be particularly vulnerable to poor developmental outcomes due to a unique set of harmful exposures. They experience increased risk of maternal illness and death, deleterious socioeconomic factors that co-vary with HIV infection, and exposure to HIV and antiretroviral drugs (Brennan et al., 2016; Evans, Jones, & Prendergast, 2016; Filteau, 2009; Goldberg & Short, 2016; Pierre et al., 2016; Slogrove, 2016). There is some indication that HEU infants may have metabolic differences from their unexposed counterparts, thereby modifying the relationship between diet and growth in this unique population (Jao & Abrams, 2014; Jao et al., 2017).

A number of specific nutrients have been identified as important for infant health and adequate growth in the general population. Some nutrients have specific metabolic functions and a deficiency produces a specific set of clinical symptoms. For example, iron deficiency results in anemia, and iodine deficiency causes goiter. Deficits in nutrients such as protein and zinc may result in growth retardation before producing clinical symptoms (Golden 1995). The relationship between these nutrients and growth in length and weight is now well established (Berger et al., 2006; Black et al., 2013; Koletzko et al., 2009; Lind et al., 2004;

Pearce & Langley-evans, 2013; Salgueiro et al., 2002; Scaglioni et al., 2000; Tang & Krebs, 2014; Umeta, West, Haidar, Deurenberg, & Hautvast, 2000).

In the last decade, work has shifted from focusing on specific nutrients to analyzing diets as a whole using a variety of novel approaches (Hu, 2002; Tucker, 2010). Analytic methods focusing on dietary or nutrient *patterns* are an improvement over methods focusing on single nutrients or foods because nutrients are derived from foods which are typically consumed in combinations that together determine the overall adequacy or quality of a diet. Any underlying patterns in adequate/inadequate nutrient intake that arise within a population are the result of these nutrients being found in adequate or inadequate amounts in the foods typically consumed within the population. For example, a healthy dietary pattern, high in vegetables, fruit, meat, and fish at age six months is related to better child cognitive outcomes because these foods provide the nutrients needed to support healthy brain development (Gale et al., 2009). However, very few studies have looked longitudinally at how nutrient intake patterns during complementary feeding relate to growth (Agostoni et al., 2008).

Much of the reason for the lack of research on this topic is the technical difficulty related to analyzing an infant's diet over time. Diet tends to change rapidly over the first two years of life. Therefore, diet must be considered as an evolving trait with distinct features and potentially different consequences at different times. Effects of diet may be age-specific, but may also reflect persistence of an underlying pattern, with important long-term consequences for child health. Our goal is to use a structural equation modeling technique borrowed from behavioral research to examine the common weaning diet in this population of HEU infants and establish the relationship of this pattern to growth. Similar structural equation models are used in behavioral research to quantify latent (not directly measured) traits which are measured by a set of observed factors that change over time. This approach is often used in quantifying persistent traits such as behavior problems, academic skills, and measures of wellbeing (Breslau, Breslau, Miller, & Raykov, 2011; Tremblay, Masse, Leblanc, Schwartzman, & Ledingham, 2005; Wiesner, 2003). Like diet, these are abstract concepts that are the aggregate of a set of underlying factors and develop over time.

Through structural equation modeling, we first employ a data-driven approach to characterize the nutrient pattern represented in the complementary foods commonly consumed by a sample of HEU infants from the Kabeho study of the prevention of mother-to-child transmission of HIV in Kigali, Rwanda. We focus on nutrients known to be associated with growth. This approach uses data on the diet actually consumed within this population to characterize the local diet rather than applying an external metric. We then assess how adherence to this common pattern is related to growth. The analysis allows us to determine whether consumption of the usual 6 weaning diet is an explanation for the pattern of linear growth faltering and elevated relative weight observed in Kabeho infants.

Previous work has characterized the Rwandan weaning diet as high in sorghum, maize, potatoes, beans, and green leafy vegetables (National Institute of statistics, Ministry of Health, ICF International, National Institute of statistics, & ICF International, 2015; Uwiringiyimana, Ocké, Amer, & Veldkamp, 2019). Often, these foods are consumed in the form of porridges, which do not supply sufficient fiber, vitamin A, vitamin E, calcium, and zinc (Grosshagauer et al., 2019). The consumption of commercially produced infant formulas and complementary foods is rare in Rwanda; however, during the early phase of weaning, animal milk consumption is common (National Institute of statistics, et al., 2015). Egg consumption is limited (National Institute of statistics, et al., 2015). At about one year of age, only 16% of infants received both the minimum dietary diversity and meal frequency recommended by the WHO (National Institute of statistics, et al., 2015). This work, while invaluable from a descriptive standpoint, is unable to quantify the extent to which infants follow this characteristic pattern or link that pattern to relevant health outcomes. Our data-driven approach creates a latent variable which scores infants on the extent to which they follow the characteristic pattern of nutrient intake from complementary foods observed within this population and relates it to growth.

Methods

Participants

The Kigali Antiretroviral and Breastfeeding Assessment for the Elimination of HIV (Kabeho) Study enrolled HIV-positive, pregnant and postpartum women participating in prevention of mother-to-child transmission programs in selected high-volume health facilities in Kigali, Rwanda. The women were required to have documented HIV infection, plan on remaining in the Kigali area following delivery, and provide consent. Women received lifelong antiretroviral therapy under Option B+ (World Health Organization, 2012). During infant clinic visits at six, eight, 11, 14, 17, 21, and 24 months, the women were asked to report all foods the infant had consumed in the last 24 hours. This dietary assessment protocol required 20-25 minutes to administer. Standard size utensils and visual aids were used to assist mothers in estimating portion sizes. Energy and nutrient intakes from complementary foods were estimated using the Uganda food composition table (FCT) (Hotz, Lubowa, Sison, Moursi, & Loechl, 2012), updated to include foods consumed by Kabeho infants but missing from the FCT. In the absence of a Rwandan FCT, we chose the Ugandan FCT because weaning foods fed to infants are very similar in these two settings, and because of the high quality of the Ugandan FCT which was recently produced by Harvest Plus. Similar to Rwanda and our sample, cow milk, beans, fish, potatoes, maize, soy, leafy vegetables, and banana are common early weaning foods in Uganda (Bekele & Turyashemererwa, 2019; Ekesa, Nabuuma, & Kennedy, 2019; Kikafunda, Walker, & Tumwine, 2003; Ssemukasa & Kearney, 2014). Breastfeeding was defined as a binary variable (yes/no) based on maternal report. During each visit, trained nurses took duplicate measures of infant length to the nearest 0.1 centimeter using Shorr boards, and weight to the nearest 10 grams using UNICEF scales. If mothers did not present at a study visit, attempts were made to contact them and data were collected during the next possible opportunity. Only data from infants ages six months to 25 months were included in the analysis. The repeat measurements within visits for infant length and weight were averaged at each time point. Z-scores were calculated using the WHO standard (World Health Organization, 2011). Stunting was defined as a LAZ less than −2, and wasting was defined as a WLZ less than −2.

Recruitment took place from April 2013 to January 2014. Initially, 608 women were recruited for the study; however, 34 mothers left the study before the six-week visit. In addition, there were seven sets of twins, resulting in a total of 577 mother-infant pairs enrolled in the study at six weeks of age (Figure 1). Dietary data are available on 543 infants. Mean nutrient intake from complementary foods was calculated for infants ages six to seven months, nine to ten months, 13 to 15 months, 16 to 18 months, and 23 to 25 months. These values were compared with recommended nutrient intakes from complementary foods for breastfeeding infants compiled in 2003 by Dewey and Brown from WHO, UNICEF, and the United States Institute of Medicine. (Dewey & Brown, 2003).

Ethical approvals were obtained from the Rwandan National Ethics Committee, the Rwanda National Health Research Committee, and the George Washington University Institutional Review Board. The protocol is registered with the United States National Institutes of Health at https://clinicaltrials.gov (NCT02295800).

Data analysis

Given our objective of learning how dietary patterns characterized by different nutrient profiles over time relate to growth, we need to take several key issues into consideration. First, with the introduction of complementary foods, infant diets change rapidly in the relative contribution of breastfeeding and in the amounts and types of foods consumed. Second, we want to focus on the nutrient profiles that characterized the usual weaning diet over time *in this population,* with a focus on nutrients deemed most relevant for growth. The nutrients we consider (zinc, protein, calcium, thiamin, riboflavin, retinol, and folate) are important for healthy growth and development and have recommendations for intake levels to support healthy growth and development (Dewey & Brown, 2003; Golden, 1995). Finally, because diet can have long term effects on growth, our measure of diet must allow for some persistence, with previous measures of diet affecting later values. This allows us to quantify diet *up to* a given age rather than simply *at* that age.

To address the set of challenges outlined above, we use a data-driven method, thereby preventing the introduction of biases related to cultural differences or scientific preconceptions regarding these nutrients. We develop a structural equation model with latent variables measured by nutrient intake and representing a data-derived quantification of the common weaning nutrient profile (Figure 2). We posit that any underlying (latent) patterns in nutrient intake that are observed in this population must arise from these nutrients being present in a certain pattern in the common weaning foods of this culture. Therefore, a latent variable defined by nutrients represents the extent to which an infant's weaning diet is dominated by this set of common weaning foods. We refer to this latent variable as the common weaning foods index (CWFI). A high CWFI value represents consuming even more of these common foods than typical; whereas, a low value represents consuming less of these foods than is typical. The estimated weights between the CWFI and the nutrients it is measured by reflect the extent to which intake of that nutrient is determined by intake of these common weaning foods or other foods. A high weight means that most of the intake of that nutrient is determined by intake of the set of common weaning foods. To allow for the CWFI to have a persistence component, we specify that the CWFI at one period influences the CWFI at the subsequent period. Therefore, the CWFI does not simply represent the extent to which an infant's weaning diet is currently dominated by the common weaning foods; it also reflects the extent to which the infant's weaning diet has been dominated by these common foods up to the specified time point. CWFI values were estimated for each infant at ages six to ten months, 11 to 15 months, and 16 to 20 months. CWFI values were not estimated at 23-25 months because diet at this time was overly co-linear with diet at 16 to 20 months.

Separate CWFI values were estimated using nutrient intake in grams, termed absolute CWFI, and nutrient density per 1,000 kilocalories, termed density CWFI. These two measures were used because larger infants are expected to eat more, introducing the possibility of reverse causation in the relationship between absolute intake and growth. However, higher nutrient density does not mean sufficient intake if energy intake is insufficient, so nutrient density may not directly relate to growth. As such, these two measures capture different aspects of diet, both of which may be relevant to our outcome of interest. Data were standardized to be normal with a mean of zero and a standard deviation (SD) of one so that all data were on the same scale and coefficients were comparable. CWFI values were also defined to have a mean of zero and a standard deviation of one. Calculations were conducted in Mplus using random analysis (Muthen & Muthen, n.d.).

After estimating CWFI values for each infant, multilevel models were used to establish the relationship of the CWFI to growth outcomes, defined as LAZ and WLZ. The average number of observations per infant per period was 1.5±0.55. Regressions were specified using CWFI values and growth outcomes at the same period and alternately as CWFI values at one period and growth at the following period to account for reverse causation. Breastfeeding was represented as a binary variable. Nutrient intake from breastfeeding was not available. As a result, this model is only appropriate for estimating the association of the complementary diet patterns with growth. It does not reflect the relationship between total nutrient intake and growth. Infant baseline characteristics (infant sex, maternal education, parity, and maternal age) were included as additional controls.

Three interactions were built into the models: CWFI by energy intake, CWFI by breastfeeding, and breastfeeding by energy intake. The first was included because the effect of diet is modulated by the amount of food consumed, especially for the density model. Similarly, the effect of diet depends on the amount of nutrients consumed through breastmilk, necessitating the second interaction. The third interaction is a proxy for nutrients received through breastfeeding. As infants are weaned, they receive more energy from complementary foods and the importance of breastfeeding diminishes.

Results

The average LAZ at age six months was −1.02 and it declined steadily over most of the study period, reaching −1.52 by age 24 months (Table 1). By contrast, the average WLZ at age six months was 0.62 and declined to 0.42 by age 24 months. At age 24 months, 28 (29%) infants were stunted and no infants were wasted. At three to four months of age, 80%

of infants were exclusively breastfed, and this was reduced to 22% by six months. Only 5% of infants continued to receive breastmilk at 24 months.

The most frequently consumed complementary foods were ingredients in porridges and stews ("imvanges" or mixtures made from what is on hand in the household each day). Porridges were typically made from sorghum, maize, wheat, and/or soy flours using single grains, home-made mixtures of these flours or a commercial product called "SOSOMA" (a fortified mixture of soy, sorghum, and maize flours) to which sugar is added. Imvanges are usually a mixture of cassava or other flours, kidney or other beans, tubers, other vegetables, oil, and sometimes dried fish. Infants were frequently given cow milk from local dairies. Other than milk, fish was by far the most common animal source food consumed, with other meats being very rare.

At the first recall, when infants were approximately five months of age, the most frequently reported food was cow milk, followed by different types of porridge. By approximately seven months and thereafter, nearly all infants were fed porridges and imvanges. As infants aged, other foods, mostly porridges, surpassed cow milk as the most frequently consumed. Variation in the quality of the infant diet largely reflects the type of grain included in the porridges and ingredients in the imvange recipes, including, for example, what vegetables, legumes, and animal source foods are included.

Mean nutrient intake and nutrient density often fell well below recommended intake for infants engaged in a moderate amount of breastfeeding (Table 2) (Dewey & Brown, 2003). Mean zinc, retinol, and calcium intake and zinc density were generally below the recommended values. Protein intake and density were above the recommended intake at all time periods.

CWFI development – patterns in nutrient and food intake

All nutrients except riboflavin weighted heavily onto to the CWFIs at all time points (Table 3). Therefore, the same underlying factor which represents the set of common weaning foods used in this culture, is driving consumption of all these nutrients. Higher absolute CWFI is associated with higher nutrient intake across all nutrients (Table 4). Infants with larger absolute CWFIs simply eat more, so they have larger nutrient intakes. However, higher density CWFI is associated with lower density of folate and iron. Eating more of the common weaning foods is, therefore, associated with lower folate and iron per 1,000 kilocalories. The common weaning foods must therefore have less folate and iron per 1,000 kilocalories than other, less commonly consumed foods. CWFI at one time period significantly influenced scores at the next period. Absolute and density CWFI had a correlation of 0.48, 0.42, and 0.29 at six to ten months, 11 to 15 months, and 16 to 20 months respectively.

To establish the relationship between the CWFI and actual foods consumed, we considered the intake in grams of food groups consumed across thirds of the distribution of CWFI. Figure 3 (Supp 1) shows a striking pattern in increasing consumption of cow milk and cow milk products across tertiles of CWFI at all time points, indicating that milk and milk products are likely the dominant factor driving the underlying pattern in nutrient intake.

While cow milk was a ubiquitous weaning food, infants with a high CWFI consumed more milk than those with lower scores. Although the amount of cow milk consumed by the upper tertile of absolute and density CWFI were similar, the amount of cow milk consumed by the lowest tertile of density CWFI was much lower than that consumed by the lowest tertile of absolute CWFI.

The association of the common diet with growth

Breastfed infants were slightly shorter than non-breastfed infants at six to 10 months and became heavier by 11 to 15 months (Table 5). A higher density CWFI was associated with an elevated WLZ from six to 15 months. Over this period, there was a significant interaction between the CWFI and caloric intake on linear growth. As a result, among breastfed infants with low density CWFI, a high caloric intake is related to 0.40 SD lower LAZ and a 0.51 SD higher WLZ compared to a low caloric intake at 11 months (Figure 4). Similarly, among breastfed infants with high caloric intake, those with a high density CWFI had a 0.40 SD higher LAZ and but 0.17 SD lower in WLZ at 11 months. There was no significant effect of absolute CWIF on growth outcomes (Table 6). When diet at one time period is regressed on growth at the subsequent period, these results become non-significant.

Discussion

A variety of dietary indicators, such as breastfeeding and dietary diversity metrics, are already established as predictors of infant growth (Jones et al., 2014). Among HEU infants, poor diet patterns have been shown to increase the risk of low length and weight-for-age (Becquet et al., 2006). However, such external metrics that quantify *dietary quality* make assumptions about which aspects of diet influence health outcomes. These assumptions may not hold across contexts. For example, the health consequences of added sugar provided to an infant in the form of a cookie in a calorie rich environment are likely to be different than those of added sugar in fortified, soy-based porridge given to an infant living in a low resource setting. In addition, external metrics created for a Western population may not be designed to score non-Western foods. In contrast to approaches that quantify diet relative to an external metric, our approach to the characterization of the weaning diet is unique in that it uses the available data to objectively identify the pattern of nutrient intake actually observed in the population. We make no *a priori* assumption about the health effects of this pattern; rather, we use the identified pattern to determine how the nutrient profile of the usual weaning diet relates to infant growth. This is useful as it allows us to determine the extent to which common weaning practices are meeting the nutritional needs of these HEU infants, who are believed to be at increased risk of early morbidity and mortality. Our CWFI reflects the extent to which infants consume the common weaning foods used within this population. The scores are largely driven by the consumption of cow milk, with higher scores indicating the consumption of more milk products. Although cow milk is not the most commonly consumed food, the more commonly consumed foods do not provide our nutrients of interest. Cow milk is the most commonly consumed food that contains our nutrients of interest and is therefore driving our score. As such, this approach reflects both nutrient intake and real foods consumed without making any assumptions about patterns of consumption or which factors will be most important for health outcomes.

Many of the infants participating in the Kabeho study did not achieve the recommended nutrient intake for zinc, retinol, or calcium yet they exceeded the recommended intake of protein. This is consistent with a cow milk-based weaning diet. One cup of whole milk contains 7.6 g of protein and 1 mg of zinc. As such, while protein and zinc tend to be consumed together, two cups of milk a day would result in excess protein intake but insufficient zinc intake. Both the WHO and the American Academy of Pediatrics recommend against feeding infants under the age of one year whole cow milk (American Academy of Pediatrics, 1992; Martin, Ling, & Blackburn, 2016; Saadeh, Prinzo, Gegout, & Kunal, 2014). Much of the reason for these recommendations is that whole cow milk does not provide the necessary amount of iron, folate and other nutrients to support healthy infant development (Leung & Sauve, 2003; Seper et al., 2015). High protein density of early food is related to increased weight status in infants and young children, but the relationship between absolute protein intake and future body mass index remains unclear (Gunther, Buyken, & Kroke, 2007; Koletzko et al., 2009; Scaglioni et al., 2000).

Intake of nearly all nutrients considered weighted heavily onto the absolute CWFI. This is as expected because infants eating larger quantities of nutrients are expected to eat more of all nutrients. However, it is surprising that this quantification of diet was not related to growth. One possible explanation for this is that the absolute CWFI is less related to cow milk consumption than is the density CWFI. The difference in cow milk consumed by the highest and lowest tertile of CWFI is much less than the difference in the amount consumed by the highest and lowest tertile of density CWFI. The absolute CWFI therefore reflects different aspects of the weaning diet than the density CWFI, and these are influential in determining growth outcomes. This is one of the major drawbacks of our data driven approach: we identify dietary patterns that are observed in the population, but we do not know a *priori* if these patterns are related to health outcomes.

In contrast, the density CWFI shows that the common weaning foods have more zinc, protein, calcium, thiamine, and retinol per 1,000 kilocalories than less common foods but less folate and iron. This too is consistent with the use of milk as a common weaning food. The inverse relationship between the density CWFI and iron reflects the concern of the WHO and the American Academy of Pediatrics that cow milk may not meet infants' nutritional needs.

However, among breastfed infants, those with a low density CWFI, i.e. those consuming less cow milk, and high caloric intake develop the most severe growth deficits by 11 months. Although LAZ among the other three combinations of density CWFI and caloric intake levels are similar, WLZ is close to the WHO standard for those who have low caloric intake, regardless of CWFI at this time.

We must acknowledge one major limitation to this study; there is no comparator with unexposed infants. Mothers in the Kabeho study began weaning their infants about a month earlier than the Rwandan average (Lane et al., 2019). Similarly, in Uganda, HIV-positive women breastfed their infants less than HIV-negative women (Okong et al., 2010). This likely reflects concern regarding HIV transmission via breastmilk; however, there is no reason to believe that there were any other differences in the weaning diet of these infants relative to other Rwandan infants. The foods consumed by Kabeho infants are similar to those which characterize the Rwandan weaning diet as reported in the DHS (National Institute of statistics, et al., 2015). In other east African populations, beans and porridge are also common weaning foods (Ekesa et al., 2019; Poggensee et al., 2004). Therefore, we believe that patterns of nutrient intake and CWFI scores identified here could likely be replicated in an unexposed, Rwandan population. Nonetheless, there is considerable variation in the weaning diet across much of east Africa with 59% of Kenyan infants at six to eight months but only 26% of Tanzanian infants consuming dairy (Gewa & Leslie, 2015). Cereal and tuber consumption is also highly variable being only 55% in Kenya and 83% in Tanzania at this time (Gewa & Leslie, 2015). Uganda fell in between these extremes for both values.

This study has some additional limitations. First, we compare the mean nutrient intake in this population to the recommendations in Dewey and Brown REF). Their recommendations are for a population with a moderate level of breastfeeding and we do not measure breast milk consumption. However, the main purpose of this paper is not to compare intake relative to an external reference and these values are never used in any formal tests. This comparison is simply used for descriptive purposes. As such, we consider it to be acceptable. Second, the model assumes that measurement error is constant over time. Mothers may have learned that reporting more foods increased their burden when participating in 24-hour recalls.

Consequently, they may have decreased their reporting accuracy over time. Third, this data-driven approach to identifying patterns of nutrient intake only reflects what is observed in the population. It does not necessarily highlight all of the nutrients that are most closely related to growth outcomes. Nevertheless, we believe that the identification of the true pattern of nutrient intake seen in this population and the determination of its relationship to growth is of value. We show that infants who follow the standard diet may have worse growth outcomes early in life, whereas those who continue to rely on breastmilk may have better outcomes. Finally, our dietary measures may be related with other prenatal or postnatal factors that could also be influencing growth outcomes.

In the future, policy makers should continue supporting the use of healthy, culturally appropriate weaning foods that are related to improved infant growth outcomes. Research should continue to identify culturally acceptable weaning foods that support healthy growth and development. Efforts to understand the effects of the dietary patterns consumed by real individuals, rather than dietary patterns developed by nutrition researchers, need to be strengthened.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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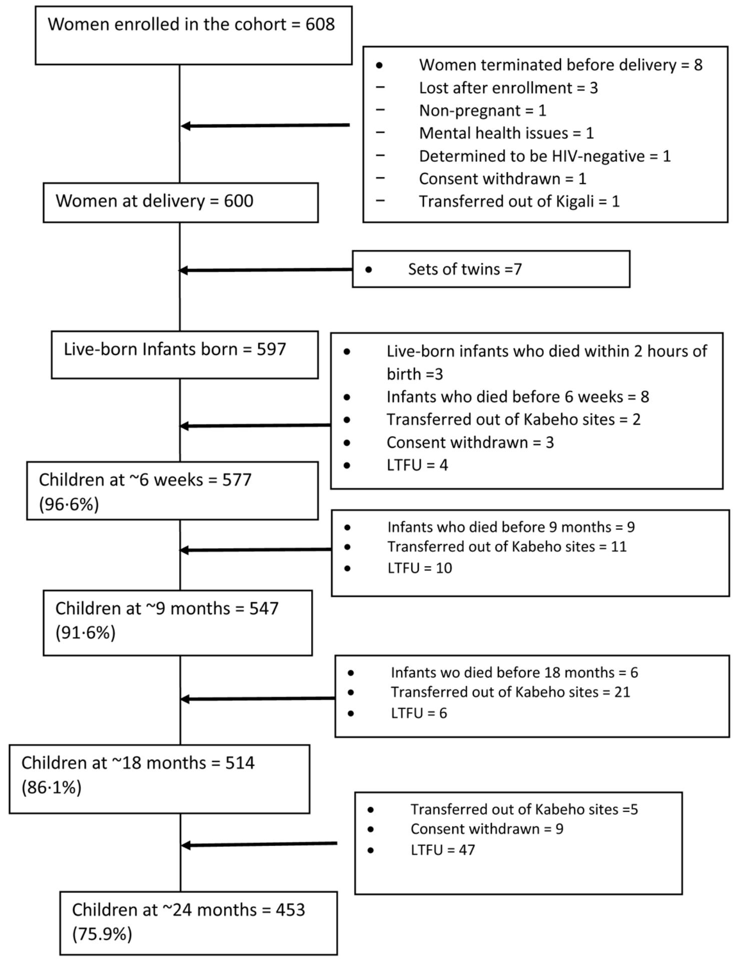

Figure 1:
CONSORT diagram of participant recruitment and follow-up.

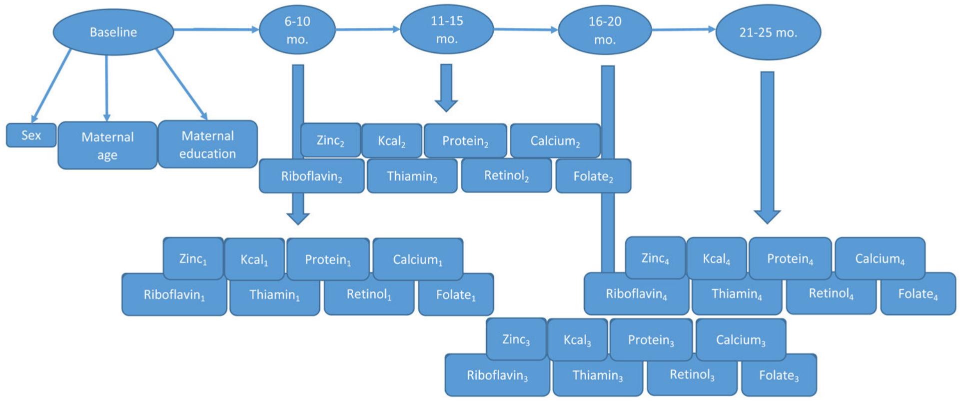

Figure 2:
Model for latent variable construction

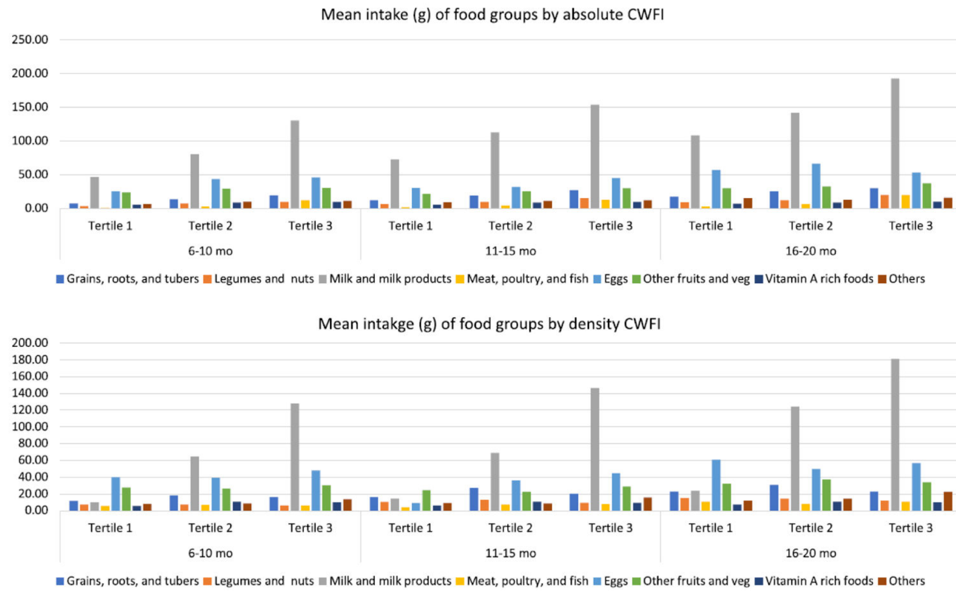

Figure 3.

Description of the foods consumed by tertile of CWFI.

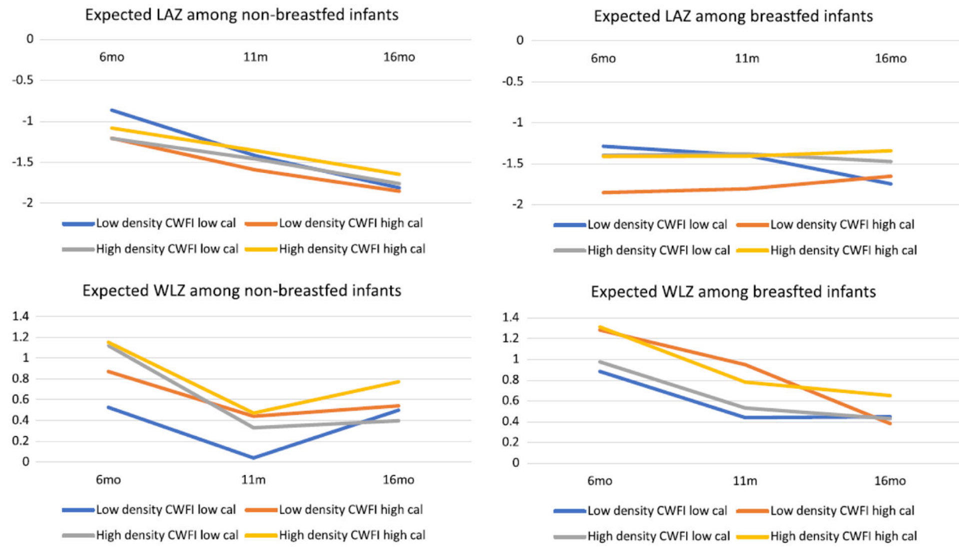

Figure 4.

Patterns in growth by density CWFI, breastfeeding, and caloric intake. Estimated values are for a male infant whose mother was 29 years old, had 2.4 children, and completed primary school. High values were defined as the 90th percentile while low values were the 10th.

TABLE 1

Demographic characteristics of study participants

Characteristic	No. (%) or mean (sd)
No. of infants	543
No. of female infants	282 (52%)
Maternal education	
Did not complete primary school	169 (16%)
Completed primary school	653 (61%)
Completed secondary school	253 (24%)
Parity	2.41 (1.45)
Maternal age (years)	29.5 (6.1)
LAZ at 6 mo.	−1.02 (1.1)
LAZ at 24 mo.	−1.52 1(1.0)
WLZ at 6 mo.	0.62 (1.2)
WLZ at 24 mo.	0.42 (1.02)

TABLE 2:

Mean nutrient intake of infants engaging in a moderate amount of breastfeeding relative to recommendation made in Dewey & Brown.

Absolute intake	6,7 mo.			9,10 mo.			13, 14, 15 mo.[#]			16, 17, 18 mo.			23, 24, 25 mo.		
	Dewey & Brown	Mean	Std. Dev.	Dewey & Brown	Mean	Std. Dev.	Dewey & Brown	Mean	Std. Dev.	Dewey & Brown	Mean	Std. Dev.	Dewey & Brown	Mean	Std. Dev.
Protein (g)	9.1	10.28	10.74	9.60	14.27	10.85	10.90	19.52	12.98	10.90	24.66	15.06	10.90	27.76	14.28
Calcium (mg)	400	274.15	359.62	400.00	250.66	318.72	500.00	291.66	318.49	500.00	337.93	352.95	500.00	324.27	311.11
Zinc (mg)	4.1	1.50	2.38	4.10	1.94	1.69	4.10	2.56	1.75	4.10	3.24	2.10	4.10	3.78	2.08
Thiamin (mg)	0.3	0.17	0.20	0.30	0.25	0.22	0.50	0.37	0.29	0.50	0.44	0.30	0.50	0.52	0.34
Riboflavin (mg)	0.4	0.09	0.35	0.40	0.07	0.19	0.50	0.20	0.93	0.50	0.20	0.71	0.50	0.27	0.90
Folate (mcg)	80	44.46	63.02	80.00	89.81	81.65	160.00	144.00	117.96	160.00	171.24	127.47	160.00	215.41	143.77
Retinol (mcg)	400	69.36	125.16	400.00	48.48	84.02	400.00	46.53	80.83	400.00	53.51	85.89	400.00	37.16	72.48
Calories (kcal)[*]	343.15	291.55	271.19	473.80	449.32	279.84	825.60	653.70	357.37	825.60	821.40	388.23	825.60	977.71	396.27
Density															
Protein	1.00	3.35	1.46	1.00	3.06	1.04	0.90	2.93	1.02	0.90	2.95	1.05	0.90	2.80	0.87
Calcium	105.00	77.54	69.30	74.00	49.44	46.12	63.00	42.95	38.46	63.00	40.06	37.23	63.00	32.01	29.76
Zinc	1.60	0.45	0.30	1.10	0.42	0.19	0.60	0.39	0.14	0.60	0.39	0.15	0.60	0.39	0.14
Thiamin	0.08	0.06	0.03	0.06	0.05	0.03	0.07	0.06	0.03	0.07	0.05	0.03	0.07	0.05	0.02
Riboflavin	0.08	0.03	0.12	0.06	0.01	0.03	0.06	0.04	0.16	0.06	0.03	0.16	0.06	0.03	0.17
Folate	11.00	14.53	11.75	9.00	19.49	11.85	21.00	21.10	11.20	21.00	19.99	10.22	21.00	21.35	10.02
Retinol	31.00	175.12	197.17	30.00	8.82	12.76	23.00	6.83	11.06	23.00	6.19	9.64	23.00	3.41	6.41

[#]Dewey & Brown 2003 report recommended intake for 12-23 months. Here they are broken down further, but the recommended intake is over the entire time period.

[*]Calories reported are mean intake of breastfed US children, not recommendations. Calories were reported monthly from 0-11 months and then together for 12-23 months.

Table 3:

Nearly all nutrients weight heavily and positively onto the absolute CWFI, but folate and iron weight negatively onto the density CWFI.

	6-10 mo		11-15 mo		16-20 mo	
	Est.	P-value	Est.	P-value	Est.	P-value
absolute CWFI						
Zinc	0.757	<0.001	0.918	<0.001	0.931	<0.001
Protein	0.937	<0.001	0.975	<0.001	1.000	<0.001
Calcium	0.875	<0.001	0.771	<0.001	0.640	<0.001
Thiamine	0.892	<0.001	0.775	<0.001	0.701	<0.001
Riboflavin	0.253	0.001	0.104	0.013	−0.021	0.623
Retinol	0.790	<0.001	0.629	<0.001	0.544	<0.001
Folate	0.656	<0.001	0.722	<0.001	0.683	<0.001
Iron	0.510	<0.001	0.702	<0.001	0.675	<0.001
		CFI 1 on CFI 2: 0.519 P<0.001		CFI 2 on CFI 3: 0.254 P<0.001		
densiy CWFI						
Zinc	0.538	<0.001	0.502	<0.001	0.359	<0.001
Protein	0.705	<0.001	0.579	<0.001	0.447	<0.001
Calcium	0.999	<0.001	0.960	<0.001	1.000	<0.001
Thiamine	0.440	<0.001	0.358	<0.001	0.550	<0.001
Riboflavin	0.017	0.677	0.233	<0.001	0.413	<0.001
Retinol	0.893	<0.001	0.871	<0.001	0.771	<0.001
Folate	−0.165	<0.001	−0.128	<0.001	−0.137	<0.001
Iron	−0.369	<0.001	−0.365	<0.001	−0.405	<0.001
		CFI 1 on CFI 2: 0.353 P<0.001		CFI 2 on CFI 3: 0.440 P<0.001		

Table 4:

Mean nutrient intake tends to increase across tertile of CWFI.

	6-10 mo						11-15 mo						16-20 mo					
	Tertile 1		Tertile 2		Tertile 3		Tertile 1		Tertile 2		Tertile 3		Tertile 1		Tertile 2		Tertile 3	
	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.
Absolute Intake																		
Zinc	0.43	0.32	1.31	0.48	3.37	2.46	0.98	0.69	2.03	0.46	4.13	1.73	1.64	0.93	2.95	0.43	4.96	1.81
Protein	3.27	1.91	10.26	2.58	23.92	9.57	7.16	4.99	15.49	7.88	31.35	10.70	12.09	6.53	23.02	11.63	38.15	11.43
Thiamine	0.06	0.04	0.17	0.08	0.41	0.21	0.15	0.15	0.32	0.16	0.56	0.28	0.24	0.21	0.45	0.18	0.65	0.29
Retinol	4.66	12.25	31.86	36.26	140.45	140.20	6.77	32.08	29.46	42.00	96.20	107.30	15.12	47.73	60.92	62.42	97.37	107.49
Folate	20.53	18.26	62.39	40.41	117.66	89.61	54.89	58.51	119.90	62.97	218.31	118.26	89.38	72.37	169.61	81.62	254.79	135.27
Calcium	35.65	43.04	166.34	115.08	583.46	379.00	139.06	131.48	218.15	145.39	514.66	361.06	246.15	211.19	346.92	204.72	552.53	401.39
Riboflavin	0.03	0.10	0.08	0.27	0.13	0.35	0.10	0.42	0.12	0.35	0.17	0.36	0.23	1.16	0.17	0.60	0.20	0.50
Iron	1.04	0.88	2.69	2.67	4.15	4.90	2.18	1.81	4.26	2.96	7.27	4.11	3.44	2.29	5.65	4.18	8.73	4.36
LAZ	−1.15	1.11	−1.05	1.22	−0.94	1.23	−1.36	1.16	−1.36	1.07	−1.24	1.21	−1.67	1.11	−1.55	1.21	−1.32	1.17
WLZ	0.58	1.18	0.45	1.21	0.65	1.24	0.37	1.22	0.31	1.09	0.50	1.18	0.25	1.12	0.54	1.00	0.51	1.09
Nutrient Density																		
Zinc	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Protein	0.02	0.01	0.03	0.01	0.04	0.01	0.02	0.01	0.03	0.01	0.04	0.01	0.03	0.01	0.03	0.01	0.04	0.01
Thiamine	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Retinol	0.00	0.01	0.02	0.03	0.10	0.04	0.00	0.01	0.00	0.01	0.06	0.04	0.00	0.01	0.01	0.02	0.05	0.03
Folate	0.16	0.11	0.24	0.16	0.14	0.07	0.18	0.13	0.30	0.13	0.19	0.10	0.19	0.11	0.28	0.11	0.18	0.09
Calcium	0.13	0.06	0.46	0.15	1.34	0.39	0.30	0.10	0.30	0.08	0.86	0.34	0.31	0.09	0.33	0.04	0.83	0.37
Riboflavin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Iron	0.01	0.01	0.01	0.00	0.00	0.01	0.01	0.00	0.01	0.00	0.01	0.00	0.01	0.00	0.01	0.00	0.01	0.00
LAZ	−1.12	1.18	−1.20	1.21	−0.89	1.16	−1.44	1.09	−1.21	1.18	−1.26	1.20	−1.68	1.12	−1.59	1.16	−1.24	1.15
WLZ	0.51	1.18	0.45	1.25	0.71	1.21	0.29	1.18	0.46	1.15	0.47	1.18	0.25	1.08	0.46	1.04	0.58	1.15

TABLE 5:

There is a complex interaction between breastfeeding, density CWFI, and caloric intake when predicting infant growth

	Simultaneous regression						Lagged regression ℑ			
	6-10 mo		11-15 mo		16-20 mo		11-15 mo		16-20 mo	
	Est.	**p-value**	**Est.**	**p-value**	**Est.**	**p-value**	**Est.**	**p-value**	**Est.**	**p-value**
LAZ										
CWFI	−0.315	0.092	−0.109	0.315	0.004	0.985	0.053	0.787	0.211	0.507
Breastfed	**−0.364**	**0.024**	−0.067	0.547	0.272	0.163	0.057	0.741	0.047	0.875
Calories	−0.255	0.191	−0.087	0.392	0.024	0.852	0.032	0.880	0.166	0.597
CWFI*breastfed	0.151	0.322	−0.171	0.073	0.341	0.160	−0.035	0.826	−0.53	0.073
CWFI*calories	**0.580**	**0.026**	**0.323**	**0.024**	0.255	0.278	0.230	0.376	0.445	0.285
Breastfed*calories	0.186	0.441	0.081	0.543	−0.38	0.155	0.027	0.925	0.072	0.853
Age#	−0.001	0.719	**−0.013**	**<0.001**	−0.01	0.354	**−0.012**	**0.002**	0.003	0.818
Female	**0.397**	**0.001**	**0.409**	**<0.001**	**0.48**	**<0.001**	**0.392**	**0.001**	**0.437**	**<0.001**
Parity	0.05	0.289	0.027	0.557	0.025	0.607	0.009	0.860	0.012	0.819
Maternal age	**−0.027**	**0.024**	**−0.029**	**0.015**	−0.02	0.185	**−0.033**	**0.007**	−0.02	0.206
Maternal education: referent is did not complete primary school										
Completed primary	0.123	0.458	0.128	0.430	0.183	0.273	0.189	0.292	0.214	0.239
Completed secondary	**0.483**	**0.014**	**0.625**	**0.001**	**0.683**	**<0.001**	**0.586**	**0.005**	**0.575**	**0.007**
Marginal R^2	0.066		0.082		0.103		0.080		0.097	
WLZ										
CWFI	**0.498**	**0.027**	**0.342**	**0.040**	−0.334	0.172	0.214	0.416	0.135	0.698
Breastfed	0.232	0.220	**0.395**	**0.015**	−0.023	0.917	−0.119	0.598	0.388	0.235
Calories	0.353	0.136	**0.377**	**0.016**	0.182	0.216	−0.362	0.210	0.411	0.251
CWFI*breastfed	−0.329	0.072	−0.164	0.254	0.335	0.225	−0.225	0.292	−0.430	0.141
CWFI*calories	−0.388	0.215	−0.306	0.156	0.544	0.052	−0.041	0.907	0.289	0.526
Breastfed*calories	−0.461	0.115	−0.279	0.169	0.187	0.525	0.211	0.574	−0.655	0.160
Age#	**−0.013**	**0.008**	**−0.012**	**0.002**	0.002	0.763	−0.003	0.543	−0.004	0.745
Female	−0.230	0.054	−0.054	0.635	−0.038	0.742	−0.135	0.281	−0.083	0.493
Parity	−0.088	0.069	−0.076	0.108	−0.075	0.125	−0.071	0.162	−0.076	0.121

	Simultaneous regression						Lagged regression[ℑ]			
	6-10 mo		11-15 mo		16-20 mo		11-15 mo		16-20 mo	
	Est.	p-value	Est.	p-value	Est.	p-value	Est.	p-value	Est.	p-value
Maternal age	−0.005	0.711	0.002	0.884	0.010	0.392	0.002	0.881	0.011	0.370
Maternal education: referent is did not complete primary school										
Completed primary	−0.15	0.377	0.092	0.574	−0.3	0.069	0.102	0.583	−0.17	0.327
Completed secondary	−0.009	0.963	0.335	0.083	−0.06	0.773	0.375	0.083	0.018	0.929
Marginal R^2	0.036		0.032		0.034		0.023		0.041	

[#] Age in weeks

[ℨ] Per 1,000 kcal

[ℑ] Regression of diet values at one period on growth at the subsequent period

TABLE 6:

There is no relationship between absolute CWFI and growth in this population.

	Simultaneous regression						Lagged regression[ℱ]			
	6-10 mo		11-15 mo		16-20 mo		11-15 mo		16-20 mo	
	Est.	**p-value**	**Est.**	**p-value**	**Est.**	**p-value**	**Est.**	**p-value**	**Est.**	**p-value**
LAZ										
CWFI	0.031	0.832	0.056	0.525	0.039	0.769	0.113	0.497	0.161	0.473
Breastfed	−0.265	0.257	−0.365	0.068	0.530	0.153	0.052	0.826	−0.508	0.352
Calories	−0.392	0.335	−0.350	0.097	−0.045	0.823	−0.306	0.459	−0.608	0.320
CWFI*breastfed	0.091	0.580	−0.213	0.060	0.166	0.396	0.069	0.681	−0.258	0.395
CWFI*calories	0.066	0.514	0.061	0.258	0.004	0.966	0.033	0.788	0.128	0.475
Breastfed*calories	−0.056	0.906	0.589	0.055	−0.707	0.123	−0.044	0.925	0.901	0.314
Age#	0.000	0.922	**−0.014**	**<0.001**	−0.005	0.464	**−0.013**	**0.001**	0.005	0.669
Female	**0.388**	**0.001**	**0.416**	**<0.001**	0.484	**<0.001**	**0.393**	**0.001**	**0.440**	**0.001**
Parity	0.050	0.293	0.025	0.590	0.028	0.579	0.010	0.835	0.015	0.774
Maternal age	**−0.028**	**0.021**	−0.029	0.014	−0.015	0.222	−0.034	0.007	−0.016	0.210
Maternal education: referent is did not complete primary school										
Completed primary	0.109	0.507	0.130	0.423	0.198	0.241	0.184	0.303	0.178	0.331
Completed secondary	**0.475**	**0.015**	**0.627**	**0.001**	**0.737**	**<0.001**	**0.585**	**0.005**	**0.553**	**0.010**
Marginal R^2	0.065		0.080		0.096		0.080		0.077	
WLZ										
CWFI	0.242	0.174	0.162	0.213	0.130	0.391	0.125	0.566	0.168	0.514
Breastfed	0.096	0.730	0.291	0.318	0.509	0.217	−0.258	0.413	−0.318	0.560
Calories	0.003	0.996	0.103	0.741	0.136	0.552	−0.822	0.146	−0.057	0.926
CWFI*breastfed	−0.133	0.505	−0.050	0.765	0.274	0.219	−0.051	0.822	−0.476	0.145
CWFI*calories	−0.115	0.344	−0.069	0.390	−0.078	0.481	0.042	0.789	0.019	0.922
Breasfted*calories	−0.159	0.781	−0.132	0.772	−0.451	0.371	0.495	0.442	0.470	0.597
Age[#]	**−0.015**	**0.002**	**−0.011**	**0.004**	0.005	0.521	−0.002	0.666	−0.003	0.821
Female	−0.220	0.066	−0.059	0.605	−0.042	0.717	−0.134	0.282	−0.070	0.563
Parity	−0.085	0.080	−0.075	0.111	−0.070	0.152	−0.072	0.156	−0.077	0.120
Maternal age	−0.005	0.712	0.002	0.855	0.010	0.389	0.002	0.879	0.011	0.382

	Simultaneous regression						Lagged regression[ℑ]			
	6-10 mo		11-15 mo		16-20 mo		11-15 mo		16-20 mo	
	Est.	**p-value**	**Est.**	**p-value**	**Est.**	**p-value**	**Est.**	**p-value**	**Est.**	**p-value**
Maternal education: referent is did not complete primary school										
Completed primary	−0.142	0.402	0.087	0.592	−0.299	0.071	0.093	0.616	−0.193	0.267
Completed seconday	−0.014	0.944	0.334	0.084	−0.036	0.853	0.356	0.099	0.007	0.972
Marginal R^2	0.032		0.030		0.034		0.023		0.034	

[#]Age in weeks

[ʒ]Per 1,000 kcal

[ℑ]Regression of diet values at one period on growth at the subsequent period