Effect of locally produced complementary foods on fat-free mass, linear growth and iron status among Kenyan infants: a randomized controlled trial[1-17]

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[13]Abbreviations used: ASF, animal-source food; CSB, corn-soy blend; WFC, WinFood Classic; WFL, WinFood Lite; CSB+, corn-soy blend plus; CSB++, corn-soy blend plus plus; FFM, fat-free mass; FM, fat mass; LAZ, length-for-age z score; MUAC, mid-upper arm circumference; WAZ, weight-for-age z score; WFP, World Food Programme; WLZ, weight-for-length z score.

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[16]**Author contributions:** The authors' responsibilities were as follows: NR, HF and KFM conceived the idea and designed the study. BBE, SMF, JKHS and VOO reviewed the study design. SOK, SAO, JNK and BOO, trained field workers and implemented all aspects of data collection and quality assurance under supervison by BBE and VOO. SOK, SAO, JNK, BOO, BBE, NR and VOO,: developed the WinFood products; SOK, ,HR and NR analyzed and interpreted the data; SOK: drafted the manuscript. NR, HF and VOO offered overall editorial oversight. All authors contributed to manuscript development and read and approved the final version prior to submission.

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ABSTRACT

The impact of quality complementary food products on infant growth and body composition has not been adequately investigated. This study evaluated the effect on fat-free mass (FFM) accrual, linear growth and iron status of locally produced complementary food products comparing to a standard product. In a randomized, double-blind trial, 499 infants at 6 mo received 9 monthly rations of: 1) WinFood Classic (WFC) comprising germinated amaranth (71%), maize (10.4%), small fish (3%) and edible termites (10%); 2) WinFood Lite (WFL) comprising germinated amaranth (82.5%), maize (10.2%) and multi-micronutrient premix; or 3) fortified Corn-soy blend plus (CSB+). Primary outcomes were changes in FFM, length, and plasma ferritin and transferrin receptors (TfR). FFM was determined using deuterium dilution. Analysis was by intention-to-treat, based on available cases. Compared to CSB+, there were no differences in change from 6 to 15 mo in FFM for WFC 0.0 kg, (95% CI:-0.30, 0.29) and WFL 0.03kg, (95% CI:-0.25, 0.32) and length change for WFC -0.3cm (95% CI:-0.9, 0.4) and WFL -0.3cm (95% CI:-0.9, 0.3). TfR increased in WFC group 3.3mg/L (95% CI: 1.7, 4.9) and WFL group 1.7mg/L (95% CI: 0.1, 3.4) compared to CSB+.. Compared to the increase in Hb in CSB+ group, there was a reduction in Hb in WFC of -0.9 g/dl (95 %CI:-1.3,-0.5) and a lower increase in WFL -0.4 g/dl (95 %CI:-0.8, 0.0).In conclusion, the tested WinFoods had the same effect on FFM and length as CSB+, while Hb and iron status decreased, suggesting inhibited iron bioavailability from the amaranth-based WinFoods.

Keywords: body composition, deuterium dilution technique, animal-source foods, complementary feeding, iron status, edible termites.

INTRODUCTION

Growth faltering begins and rapidly accelerates in the first 1000 days of life with lifelong consequences (UNICEF -WHO-The World Bank Group, 2017). Linear growth failure is a strong marker of a complex of pathological disorders that in sum lead to increased morbidity and mortality, loss of physical growth potential, reduced neurodevelopment and cognitive functions and decreased human potential (UNICEF -WHO-The World Bank Group, 2017). Attempts to address linear growth faltering through a number of interventions including high-energy plant-based foods fortified with a mix of multiple micronutrients, improved water, hygiene and sanitation, behavior change communication to improve infant and young child feeding practices have had limited effects on linear growth (Byrd et al., 2018; Lin et al., 2018; Null et al., 2018; Nair et al., 2017).

However, a number of studies have shown that animal-source foods (ASFs) are beneficial to child growth, cognitive functions and reduced morbidity and mortality as they provide high quality protein and micronutrients that are difficult to obtain in adequate quantities from a diet based on plant-source foods alone (Dror & Allen, 2011; Allen, 2008). ASFs are not easily accessible and often unaffordable to many poor households, and therefore lacking or scarce in the diets of children in low- and middle-income countries (LMICs) (Dror & Allen, 2011). However, communities in LMICs may have access to other sources of relatively affordable ASFs such as small fish species with low market value (Roos et al.,2007) and edible insects (or other arthropods such as spiders) collected from the wild (FAO,2013).

The WinFoods study aimed to develop nutritionally improved foods for infants in LMIC based on improved utilization of locally available foods, together with improved traditional food technologies (e.g. fermentation, malting etc). These foods were dubbed “WinFoods”. The WinFood project was carried out in parallel in Kenya and Cambodia from 2009 to 2012. In each site, processed complementary food products were formulated and produced based on locally available foods and optimized for nutrient composition with emphasis on iron and zinc (Skau et al., 2015, Kinyuru et al., 2012, Kinyuru et al., 2015). Prior to the final decision on formulations, the acceptability of the products was assessed among mothers and infants (Konyole et al., 2012). The efficacy of the developed complementary food products was then tested in randomized trials to assess the impacts of a daily supplement over a 9 month period on growth, nutritional status and development. A Cambodian study found no difference in the primary outcomes of increment in fat-free mass (FFM) and iron status after 9 months intervention, between either of the two versions of WinFood products tested (one fortified and one not fortified with micronutrients) in comparison with either of two corn-soy blend (CSB+ and CSB++) products (Skau et al., 2015). It was concluded that micronutrient fortification may be necessary, and small fish may be an affordable alternative to milk to improve complementary foods. The Cambodian trial also showed that, despite the daily complementary food supplement, the children became increasingly stunted over the intervention period (Skau et al., 2015).

The aim of the current study was to evaluate the effect on FFM accrual, linear growth and iron status of improved cereal-legume-based WinFood products, one product prepared with ASFs (small fish and white-winged termites) and one product prepared without ASFs but fortified with a multi-micronutrient premix. The products were compared with the fortified standard product CSB+.

KEY MESSAGES

- To develop effective interventions targeting linear growth, it is important to explore possibilities of using locally available food resources particularly the ASFs to enhance the intake of the same in infants and young children diet

- It is important to understand the body composition in terms of fat free mass in complementary feeding interventions to be able to link them to growth outcomes later in life
- Engaging local food resources, such as grain amaranth, edible termites and small fish has a potential to the utilization and sustainability of stunting and anaemia reduction interventions.
- Germinated amaranth with ASFs or fortificant need optimizing to improve nutritional status compared to CSB+ in resource limited settings.

METHODS

Study setting

The study was conducted in a malaria-prone and food-insecure rural area of Mumias Sub-county in Kakamega County, Western Kenya (Desai et al., 2005) from January 2012 to January 2013. It was based at Makunga, Khaunga and Lusheya health centres. About 26 % of children aged below five years in the region are stunted (Kenya National Bureau of Statistics et al., 2015).

Study participant recruitment, inclusion and exclusion criteria

Mothers and infants pairs were invited to the study at 5 months of age and randomized at 6 to receive one of the three study foods from the health facilities they visited for routine monthly growth monitoring. Trained health workers screened the infants for severe acute malnutrition [<-3 weight-for-length Z score (WLZ)], pitting edema, clinical signs of vitamin A deficiency, severe anemia (hemoglobin < 80 g/L) and mid-upper arm circumference (MUAC) <11.5 cm. If any of these symptoms were detected, the infant was excluded and referred for treatment as per the Kenya Ministry of Health guidelines. An additional inclusion criterion was that caregivers had to consent to participate and accept to prepare and feed their infants with the assigned complementary foods. Exclusion criteria were lack of consent, severe malnutrition or anemia as defined above or chronic illness requiring medication or genetic disorders interfering with normal growth. Twins were recruited into the study if both were healthy and met the inclusion criteria and randomized to receive the same intervention to avoid cross-contamination due to confusing the foods or sharing during feeding.

Study design

This was a randomized, double blind, controlled trial in which infants aged 6 months received a monthly ration for 9 months of one of the three study foods: 1) WinFood Classic (WFC), 2) WinFood Lite (WFL) or 3) CSB+ as the comparison group. Changes in FFM, length, plasma ferritin, plasma transferrin receptors, and hemoglobin from 6 to 15 months of age were the main outcomes. Secondary outcomes were change in weight, MUAC, head circumference, skinfolds and weight.

Intervention foods

Food ingredients used for the complementary foods are already widely available and consumed in the locality (Kinyuru et al., 2012). Details of recipe formulation, nutrient composition, processing technology and safety are described elsewhere (Kinyuru et al., 2015) and the foods were found to be acceptable prior to the intervention in the study population (Konyole et al., 2012).

All the foods were centrally processed by extrusion cooking at AllGrain Co. Limited in Nairobi Kenya and packed in opaque food grade white plastic containers, weighed at 500 g, and labelled with computer-generated random numbers corresponding to WFL, WFC and CSB+ under close supervision of the study team. Two complementary foods WFC and WFL based on germinated grain amaranth (*Amaranthus cruentus*) and maize (*Zea mays*) had been developed. WFC had (as % dry w/w) 71 % grain amaranth,10.4 % maize, 0.6 % soybean oil, 5 % sugar, 10 % edible termites *(Macrotermes subhylanus)* and 3 % small fish *(Rastrineobola argentea*). These fish are the silver cyprinid, a species of ray-finned fish in the family Cyprinidae found in Lake Victoria and locally called *omena* (Kenya), *dagaa* (Tanzania), and *mukene* (Uganda). *Omena* is a rich source of iron and zinc (FAO, 2013; Kinyuru et al., 2013; Capinera et al., 2008; Rumpold & Schlüter, 2013). The grain amaranth was germinated to reduce phytates and potentially enhance micronutrient bioavailability (Kinyuru et al., 2015), especially the bioavailability of iron and zinc. WFL had 82.5 % grain amaranth, 10.2 % maize, 0.6 % soybean oil, 5 % sugar, no ASFs but fortified with micronutrients (vitamins and minerals premix) at 0.2 % of mineral/vitamin premix and 1.56 % mono-calcium phosphate and sodium chloride which are the same rate as CSB+ (World Food Program, 2015). According to World Food Program(2015), CSB+ also called a supercereal plus is made of corn (74 %) and soya (19 %), sugar (5 %), oil (0.5 %),Premix (1.5 %) and contains no other ASF not even milk powder and is meant for children 6-23 months. The micronutrients were added to the blends (where applicable) after extrusion cooking to avoid vitamin losses at high processing temperatures (World Food Program, 2015). WFC provided, per 100 g dry weight, 423.6 kcal, 19 g protein, 12.2 mg Fe and 6.3 mg Zn; and WFL provided 407.2 kcal, 14.6 g protein, 12.5 mg Fe and 5.5 mg Zn; and CSB+ provided 391.7 kcal, 15.1 g protein, 7.7 mg Fe and 5.1 mg Zn. All the study foods were given in daily rations adjusted to the age of the child with children in the age-group 6-8 months, 9-11 months and 12-15 months receiving 50 g/day, 75 g/day and 125 g/day of flour, respectively, based on the WHO recommendations for complementary feeding of breastfed infants to supply 200, 300, or 550 kcal/d (Pan American Health Organization, 2001; Dewey & Brown, 2003).

The food ration was a complement to breast milk and other foods. The daily rations were delivered in monthly rations packages with instructions to caregivers not to share the food with other young children not in the study and how to correctly measure quantities for daily use. Compliance was assessed by asking the caregivers how much of the study foods the child consumed while checking for any spoilage, spillages and the frequency of feeding (results not shown). A regimen compliance study was also done once mid-way through the intervention in a sub-sample of 254 participants to confirm compliance with the prescribed feeding regime; adequate compliance, defined as consuming at least 60 % of the amount provided, was achieved by 65 % of the group (results not shown). The degree of sharing with other household members was also assessed by occasional home visits and caregiver's recall at the health facility during the monthly visits. The caregivers were to keep all the distributed packets, including those used, to be counted on a monthly basis.

Randomization and blinding

Individual randomization stratified by sex was done by labels generated using Microsoft Excel^{TM} for the infants to receive WFC, WFL or CSB+ at 6 months old. Packaging was similar for all three foods. Barcodes were assigned to the foods for complete blinding with 2 different codes for each food, resulting in a total of 6 codes. The randomization key was kept in a sealed envelope, not available to the study team or participants, until preliminary analyses were completed.

Participant visits

Health personnel then examined the child for different symptoms which could be related to diseases and malnutrition. Additional data was collected on breastfeeding, introduction of complementary foods (dietary assessment using the 24 hr recall), morbidity, and socio-demographic and economic variables at baseline. Defaulting participants were followed up and accommodated during the next session.

Body composition measurement

Fat free mass (FFM) and fat mass (FM) were assessed at 6 months and 15 months using the deuterium dilution technique. Briefly, a predose sample of about 2 ml of saliva was taken from the child's mouth using a cotton ball. Each child was given a standardized oral dose of deuterium labelled water (15 ml of ^2H_2O solution comprising 3 g deuterium [99.8 % ^2H_2O -Cambridge Isotope

Laboratories Inc.] and 12 ml of mineral water) which had been accurately weighed at the Kenya Medical Research Institute (KEMRI) laboratories in Nairobi, Kenya and transported refrigerated at 4 ^{o}C to the field following guidelines from the International Atomic Energy Agency (IAEA) (IAEA, 2011). Post-dose saliva samples were taken at 2 hours and 3 hours. Saliva samples were collected into a tightly capped 1.5 mL cryogenic tube by squeezing the saliva from the wet cotton ball removed from the child's mouth, using a syringe. Samples were kept in a cooler box with ice packs and were transported the same day to a central collection point at Lusheya health centre where they were stored in a chest freezer at -20 ^{0}C pending transfer in dry ice package to KEMRI in Nairobi for analysis. Enrichment of deuterium in saliva samples was determined using Fourier Transform Infrared (FTIR) spectrophotometer (Shimadzu model 8400s, Shimadzu Corporation, Kyoto, Japan). Enrichment of the pre-dose sample from the child was used for background correction of post-dose samples. Our study was based on a previous protocol assuming that deuterium equilibration takes less than 3 hours in infants and children when saliva is the primary specimen (Colley, Byrne & Hills 2007). Using the mean of deuterium enrichment based on the two post-dose samples (Colley, Byrne & Hills 2007) as per the protocol at the time (IAEA, 2011), the dilution space and Total Body Water (TBW) were calculated accordingly. FFM was calculated by dividing TBW by an age specific hydration factor as: TBW/0.79 for both sexes. FM was calculated as body weight minus FFM (IAEA, 2011).

Iron status

Three (3)-mL blood samples were drawn by venepucture from non-fasting subjects both at 6 months and 15 months. Haemoglobin concentration was measured on blood drop aliquots using a HemoCue HB301 photometer (HemoCue Sheffield, United Kingdom). Blood left in the syringe was put into a plain Vacutainer (Becton Dickinson), kept chilled at 4 ^{o}C, and separated within 4 hours by centrifugation (1300 x g, 10 min at 4 ^{o}C). Plasma samples were kept frozen at -20 ^{o}C for 3 months at Lusheya health centre until they were sent to the University of Nairobi Institute of Tropical and Infectious Diseases, Nairobi, Kenya for further storage at -80 ^{o}C. Plasma samples were subsequently transported by air to the VitMin Lab (Willstaett, Germany) for analysis of plasma ferritin, plasma transferrin receptors, alpha-1-acid glycoprotein (AGP) and C-reactive protein (CRP) concentrations using enzyme immunoassays using commercial ELISA test kits (Ramco Laboratories) as described by Erhardt et al. (2004).

Anthropometry

Measurements were carried out monthly by trained assistants who had previous experience in growth monitoring at the clinics' maternal and child health department. Measurements (nude weight, recumbent length, subscapular skinfolds, head circumference, MUAC) were made in triplicate using standardized anthropometric techniques and calibrated equipment (Lohman, Roche & Martorell, 1988). Length was measured to the nearest 0.1 cm using calibrated length board. Weight was measured to the nearest 0.01 kg, using a hanging Seca scale (UniScale). Triceps, biceps, subscapular and suprailiac skinfolds were measured to the nearest 0.1 mm using Harpenden skinfold calipers (Crymych, United Kingdom) while the head circumference and MUAC were measured to the nearest 0.1 cm using non-stretchable measuring tape (Harlow Printing Limited). To minimize inter-observer variation in measurements, each assistant took daily measurements of weight, height, MUAC and skinfolds (triceps, biceps, subscapular and suprailiac) of the same volunteer until these agreed within the allowable error margin during the training period (Lohman, Roche & Martorell, 1988).

Morbidity

Morbidity data were collected based on caregivers' recall about specific symptoms and clinic visits in the past seven days especially for the upper respiratory tract infection (URTI) and diarrhoea as defined by WHO respectively (WHO, 2001; WHO, 2017). General assessment of overall morbidity in the last month (scored as healthy; mild, self-limited illness; moderate illness requiring symptomatic treatment at the clinic; severe illness requiring antibiotics or other medical intervention) for the child during their monthly visits to clinic using questionnaires was also done. Caregivers were encouraged to bring their children to the clinic in the event of severe illness prior to the next visit.

Sample size consideration

Sample size was based on expected increase length-for-age of at least 0.1±1.2 standard deviations (Lartey et al., 1999; Ashworth, 2006), a standard deviation (SD) of 4.6 (Faber et al., 2005; Eichler et al., 2012) and change in FFM. Based on the expected increase length-for-age , a sample size of at least 165 children per group (total of 499) was needed at 80 % power and 5 % level of significance allowing for 10 % loss to follow up as observed in previous studies (Admassu et al., 2017; Owino et al., 2007; Bauserman et al., 2017).

Data analysis

Primary outcomes were changes in FFM, length, plasma ferritin and plasma transferrin receptors. Analysis was by intention-to-treat, based on available cases. Case record forms were checked daily and entered within 2 weeks. Quantitative data was double entered in Microsoft Excel ™ with length and weight measurements converted to Z-scores using WHO Anthro™ v3.2.2 based on the WHO's 2006 Child Growth Standards (WHO, 2014). Frequencies, means and median values were calculated using STATA® version 12 (A Stata Press Publication, 2011). Analysis of variance (ANOVA) was used to determine differences between groups in change in parameters from 6 to15 months. Plasma ferritin concentrations were log-transformed after correction for inflammation using CRP and AGP concentrations and the correction factors as published elsewhere (Thurnham et al., 2010). The means from the log-transformed plasma ferritin values were then back-transformed to get a geometric mean. The same was done for the differences and back-transformed to give a ratio. Selected pair-wise comparisons were considered with CSB+ used as the reference group. Stunting, underweight and wasting were defined as length-for-age, weight-for-age and weight-for-length, respectively, < -2 standard deviations of the WHO reference standards while moderate-to-severe and severe acute malnutrition in infants were defined as MUAC < 12.5 cm and MUAC < 11.5 cm, respectively (WHO, 2014). Before the study was unblinded, all infants with negative % FM were considered implausible and removed because negative values occur when the deuterium dose has not had sufficient time to fully equilibrate with body water, or the dose was not completely consumed (IAEA, 2011). We also reviewed and checked with field notes regarding problems administering the ^2H_2O to the child. Any uncertainty of how much ^2H_2O the child consumed led to his or her exclusion from the deuterium analyses. Furthermore, in cases of poor agreement between pairs of enrichment values, we discarded all of those where the two values differed by >50 ppm based on expert opinion of what is plausible but these variations could be due to spillages of deuterium during dosing. We also rejected outliers which fitted very poorly with the general association of body water with weight and height as described by other workers (IAEA, 2011; Colley, Byrne & Hills, 2007). More samples were removed at 15 months than 6 months because more had poor agreement due to longer equilibration times in older children as observed previously by Colley, Byrne & Hills, (2007).

Ethical considerations

Mothers and caretakers gave written informed consent after explanations in the local language and Kiswahili with an option to discontinue from the study at anytime while still receiving the monthly food ration and other health facility services. All data obtained in the study were kept anonymous.

The study was approved by the Kenyatta National Hospital-University of Nairobi Ethics Review Committee (KNH-UON ERC-P436/12/2010) with a consultative approval also obtained from the Danish National Committee on Biomedical Research Ethics. Permission to implement the study was obtained from relevant government line ministries and local authorities.

The trial was registered at Controlled-trials.com. No: ISRCTN30012997.

RESULTS

We screened 527 infants of whom 499 (94.6 %) met the inclusion criteria and were randomized to one of the three food groups (**Figure 1**). Four hundred and twenty-eight children (86 %) completed the study. Of the 71 (14 %) children lost to follow-up, 63 (89 %) relocated from the study area while 8 (11 %) died. The dropout rate did not differ between groups. Of the 499 included, we obtained body composition data from 442 (89 %) at 6 months and 288 (58 %) at 15 months. The numbers at 15 months being lower compared to 6 months due to longer equilibration time as explained by Colley, Byrne & Hills, (2007).

Randomization resulted in baseline equivalence with respect to breastfeeding status, means age of introduction of complementary foods, weight at 6 months and household characteristics, although the LAZ scores at baseline was slightly higher among children receiving WFC (**Table 1**). Infants lost to follow up did not differ from those who remained in the study during the 9 months intervention. All caregivers reported the intervention foods were not shared. Breastfeeding at end line was 87 %.

No differences in body composition were observed among the three intervention groups over the 9 month intervention (**Table 2**). There were no differences in FFM gain in WFC 0.0 kg (95 % CI:-0.30, 0.29) or WFL 0.03 kg (95 % CI:-0.25, 0.32), compared with the CSB+ group. Similarly, length gain in either WFC 0.3 cm (95 % CI:-0.9, 0.4) or WFL -0.3cm (95 % CI:-0.9, 0.3) groups was not different compared to CSB+. The weight gained in all three groups was mainly FFM, while FM remained unchanged.

There was a decrease in plasma ferritin in the WFC group ratio of geometric means: 0.6 µg/L (95 % CI: 0.4, 0.8) and the WFL group 0.6 µg/L (95 % CI: 0.5, 0.9) compared to CSB+ (**Table 3**). There was also an increase in plasma transferrin receptor in the WFC group 3.3 mg/L (95 % CI: 1.7, 4.9) and the WFL group 1.7 mg/L (95 % CI: 0.1, 3.4). As seen in Table 3, compared to the increase in hemoglobin over time in the CSB+ group, there was a reduction in hemoglobin in the WFC group -0.9 g/dl (95 %CI:-1.3,-0.5) and a lower increase in the WFL group -0.4 g/dl (95 %CI:-0.8, 0.0).Despite all these findings, the low follow-up was a limitation.

As defined by WHO cut offs (WHO, 2001), 67 % of all children were anemic at 6 months while 73 %, 64 % and 63 % respectively were anemic at 15 months for WFC, WFL and CSB+, respectively; the WFC group was different from the CSB+ group (p=0.01). A similar trend was observed for mild anaemia (Hb between 10-10.9g/dl) where a greater proportion (p=0.04) of children (41.8 %) in the WFC group had mild anaemia at 15 months compared to children in the CSB+ group (22.4 %). CRP was slightly elevated at 6 months 6.9 (SD 12.4) mg/L and at 15 months 6.2 (SD 11.3) mg/L but did not differ among the study groups. AGP was 1.1 (SD 0.4) g/L at 6 months and 1.2 (SD 0.5) g/L at 15 months.

There were no differences between the WinFoods and the CSB+ in the relative changes in MUAC and biceps triceps, subscapular and supra-iliac skinfolds. In contrast, there was a slight positive change in head circumference for WFC 0.2 cm (95 % CI:-0.3, 0.8) and WFL 0.5 cm (95 % CI:-0.0, 1.1) relative to CSB+ (**Table 4**).

DISCUSSION

The current study compared with CSB+ the effects of two locally-produced, centrally- processed complementary food products, one made with germinated grain amaranth, maize and small fish and edible termites and the other without the ASFs but fortified with micronutrients. The results show no differences in 9-month changes in FFM, length gain and weight gain in the WFC and WFL groups, compared to infants receiving CSB+. Weight gained in all three groups over the 9 months was mainly FFM, while FM remained unchanged. Plasma ferritin decreased while plasma transferrin receptors increased in all three groups over the 9 months indicating an overall deterioration in iron status. However, the deterioration in the indicators of iron status was more pronounced among children in the ASF-fortified food (WFC) compared to children in the two groups (WFL and CSB+) fortified with multi-micronutrient premix. Hemoglobin concentration also dropped in the WFC group relative to CSB+.

The inclusion of ASFs (small fish and termites) in the non-fortified WFC product did not promote growth or impact body composition differently than the fortified products without ASFs. This is similar to the findings in the WinFood trial in Cambodia in which the two WinFoods tested both contained ASFs while one of the products was fortified with micronutrients and the other product was non-fortified (Skau et al., 2015). The CSB products used as references in the Cambodia study included the milk-enriched CSB++. The results in Cambodia supported a tendency for better linear growth and gain of FFM in children receiving foods which were both fortified and contained ASFs (fish or milk) (Skau et al., 2015). Since the present study did not include foods which contained ASFs and were also fortified with micronutrients, it is not possible to make similar comparison, but the findings are consistent with the Cambodian trial. The present study supports that adding ASFs to a non-fortified food supplement may not be sufficient to compensate for generally nutritionally insufficient complementary foods.

The fact that all three foods had similar results in terms of impact on nutritional status could reflect a more systemic non-food-related phenomenon in the environment. For example, exposure to environmental hazards may limit the benefits of ASFs through effects on gut integrity (Hetherington et al., 2017; Kaur, Graham & Eisenberg, 2017). Children may suffer from environmental enteric dysfunction (EED) which has been associated with stunting by inflammation-mediated interference with the insulin-growth factor synthesis pathway and through negative impacts on absorption of nutrients (Owino et al., 2016). Another possible reason for no effect of animal foods could be breastfeeding which remained high during the intervention period.

Comparing the body composition data with reference data based on healthy infants from Ethiopia (Admassu et al., 2017) and the United States (Butte et al., 2000), Kenyan children's body fat is low and an intervention with a daily supplement of nutritious complementary food was not able to increase fat deposition, as was observed in the Cambodian population (Skau et al., 2015). The lack of differences in FFM and anthropometric measures among the groups may be explained by the fact that all the groups had comparable nutrient intakes. Furthermore, the lack of differences on length and weight seen were possibly because a majority of the children's weight and length z scores were in the normal range for all the groups.

The overall deterioration of iron status among all food groups, including those receiving foods fortified with micronutrients including iron, may also be caused by non-food factors. Although we did not assess malaria infection, the study area is vulnerable to malaria (Desai et al., 2005). Malaria is known to be strongly associated with iron deficiency anaemia (Spottiswoode, Duffy & Drakesmith, 2014; Friedman et al., 2009). EED is also linked to bacterial overgrowth in the gut epithelia which may lead to increased iron requirements (Owino et al., 2016). The deterioration of iron status and haemoglobin concentration in the non-fortified food (WFC) could be caused by the presence of phytic acids in maize and amaranth grains (Azeke et al., 2011; Albarracín et al., 2015). Although partial germination of grain amaranth was done to reduce phytic acid, the efficiency in the reduction may not have been adequate to remove the inhibition of mineral absorption by phytic acid. Phytic acid content was assessed during the development of the product where it was concluded that the amaranth grain should be germinated for 72 hours to reduce phytic acid to an acceptable level. However, for the scaled up production of the intervention foods the lengthy germination duration was found to increase the risk of growth of pathogenic bacteria and the germination time was limited to a standardized 48 hours (Kinyuru et al., 2015). The fortification of WFL and CSB+ with multiple micronutrient premix had no benefit on iron status.

For secondary anthropometric measures a higher head circumference was found in the WFL group compared to CSB+. The circumference was 0.5 cm larger, for mean head circumference close to 47 cm. This is equal to a difference in the radius of about 0.8 mm.

The results from previous studies examining the effects of micronutrient supplementation on growth have been mixed (Admassu et al., 2017; Labbé & Dewanji, 2004) with some demonstrating a beneficial role, particularly in resource limited settings, where fortified foods have improved growth (Admassu et al., 2017), haemoglobin (Owino et al., 2007) and micronutrients (Faber et al., 2005) and others showing no difference in linear growth among infants supplemented with micronutrients from 6 to 18 months (Lartey et al., 1999; Bauserman et al., 2015). Linear growth is not only as a result of dietary improvement during complementary feeding and therefore other measures beyond increasing the nutrient content of complementary foods needs to be explored (Bauserman et al., 2015). Some of these studies, however, have heterogeneous baseline participant populations, varying measures of anthropometry, various timing of interventions and some lack appropriate control groups emanating from diverse intervention products and study designs (Skau et al., 2015;

Admassu et al., 2017; Owino et al., 2007; Bauserman et al., 2015; Arnold et al., 2013) unlike the present study and a similar parallel one in Cambodia (Skau et al., 2015) which recruited children of similar age, had a control(s), and were conducted in food-insecure settings. Another strength of the current study is that we evaluated locally available food sources for infant feeding with the developed products being acceptable to mothers and infants (Konyole et al., 2012).

Although in our study we did not determine malaria parasitaemia, two acute phase protein biomarkers, CRP and AGP, were measured. CRP was slightly high at but did not differ among the study groups indicating a possibility of infection masking the benefits of the study foods (Shinoda et al., 2012; Thurnham & Mccabe, 2010). Clearly, the low follow-up was a limitation to the findings reporting the effects on iron status. Another limitation of the current study could have been that unlike in the Burkina Faso study which refined procedures for administration of isotope doses and collection of saliva where equilibration time in local context has been found to be 3 h (Fabiansen et al., 2017), in our study we used the average of two and three hours as per the protocol then post dose (IAEA, 2011; Colley, Byrne & Hills, 2007). We thus acknowledge the recent study showing that 3 hours were the most optimum (Fabiansen et al., 2017); however, our study was based on a previous protocol assuming that deuterium equilibration takes less than 3 hours in infants and children (Colley, Byrne & Hills, 2007) when saliva is the primary specimen.

Although we did not demonstrate a clear beneficial effect from supplementing with WFC on FFM, linear growth and Fe status, we cannot exclude insects as a potentially promising food source for people in food-insecure areas. The lack of impact of the insect-based WFC product on improving iron status need further investigations to clarify iron absorption from different blends to isolate the specific impact of the termites. It is also possible that improving the quality of complementary foods is beneficial if other growth-limiting pathologies are prevented. Given the high disease burden among infants in this resource-limited rural area (Spottiswoode, Duffy & Drakesmith, 2014; Friedman et al., 2009), the role of conditions that impair nutrient absorption and utilization is a potential area of further research.

The WinFoods did not differ from the CSB+ in FFM, length gain and weight gain. There was overall deterioration of iron status among all food groups with a significant drop in the non-fortified food group. This study did not include products which were fortified and also contained ASF, and could therefore not confirm the finding in a similar study in Cambodia concluding that complementary food supplements distributed in food-insecure populations can benefit from combined fortification and inclusion of ASF (Skau et al., 2015). Infants in all food groups gained FFM and, unlike the Cambodian infants, the FM was preserved during the 9 months intervention. The long-term implications for health and development of these differences in growth patterns in early childhood between populations need further investigations.

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Figure 1: Participant screening, recruitment and follow up.

Five hundred and twenty seven infant mother pairs were eligible at enrolment. Twenty eight were however excluded for various reasons. The remaining 499 were randomised into the three arms of the study to either receive WinFood Classic (165), Corn soy blend plus (167) or WinFood Lite (167). At 6 months, Body composition was taken from WFC=152, CSB+=147 and WFL=143 participants while blood samples for iron biomarkers was obtained from 87, 83 and 79 participants respectively.

During the follow up, WFC, CSB+ and WFL lost 21, 27 and 15 participants respectively; the main reasons being relocation from the study area.WFC and CSB+ arms each recorded 3 deaths while WFL recorded 2 deaths.

For analysis therefore; 141,137 and 150 completed the study and were included in the analysis with an intention to treat for WFC, CSB+ and WFL respectively. Body composition had 91 each for WFC and CSB+ with 106 being in the WFL group as detailed in **Figure 1**. Analysis was by intention-to-treat, based on available cases.

Table 1: Baseline characteristics of study participants randomised to supplementation with WinFood Classic (WFC), Corn-soy blend+ (CSB+) and WinFood Lite [1]

Number of children by food	WinFood Classic =165	Corn-soy blend+=167	WinFood Lite =167
Child characteristics			
Sex, boys, n (%)	76 (46.1)	83 (49.7)	81 (48.5)
Infant birth order	3.5 ± 2.2	3.1 ± 1.9	3.3 ± 1.9
Child age (months)	6.0 ± 0.2	6.1 ± 0.2	6.0 ± 0.2
Currently breastfeed, n (%)	162 (98.2)	166 (99.4)	166 (99.2)
Age infant introduced to other foods (mo)	3.1 ± 2.1	3.1 ± 2.0	3.4 ± 2.0
Weight, kg	7.6 ± 1.0	7.4 ± 1.0	7.3 ± 1.1
Length, cm	65.9 ± 2.9	65.3 ± 2.8	65.1 ± 3.0
Haemoglobin g/dl	10.8 ± 1.5	10.7 ± 1.3	10.7 ± 1.4
Weight-for-length Z-score (WLZ)	0.25 ± 1.19	0.24 ± 1.19	0.16 ± 1.17
Length-for-age Z-score (LAZ)	-0.47 ± 1.26	-0.76 ± 1.13	-0.85 ± 1.33
Caregiver characteristics			
Age of main caregiver(years)	26.4 ± 6.9	25.6 ± 6.7	25.3 ± 5.6
Education level			
Unable to read and write, n (%)	14 (8.5)	15 (9.0)	7 (4.2)
Primary incomplete, n (%)	62 (37.6)	73 (43.7)	83 (49.7)
Primary completed or higher, n (%)	89 (53.9)	79 (47.3)	77 (46.1)
Marital Status			
Married	154 (93.3)	150 (89.8)	153 (91.6)
Single	9(5.5)	13(7.8)	8 (4.8)
Widowed	2 (1.2)	0 (0.0)	2 (1.2)
Household characteristics			
Total household members	5.9 ± 2.2	5.6 ± 2.2	5.4 ± 2.1
Children <5 years	1.8 ± 0.7	1.9 ± 0.8	1.9 ± 0.7
Use of insecticide treated net, n (%)	161 (97.6)	159 (95.2)	161 (96.4)
Access to Water			
Protected well/borehole, n (%)	77 (48.4)	75 (46.6)	68 (41.2)
Primary income			
Farming, n (%)	90 (55.6)	76 (47)	72 (44)

[1]Values are means ± SDs, unless stated otherwise.

Table 2: Effects on body composition and length of WinFood Classic and WinFood Lite compared with the Corn-soy blend+ after a 9-months intervention from 6 mo to 15 mo[1].

	Body composition, kg		Weight, kg	Length, cm
	Fat-free mass, kg	Fat mass, kg		
Age 6 months				
WinFood Classic	5.98 (5.85,6.11) (152)	1.58 (1.48,1.67) (152)	7.5 (7.3,7.7) (152)	65.7 (65.1,66.4) (152)
WinFood Lite	5.79 (5.65,5.94) (143)	1.54 (1.44,1.65) (143)	7.3 (7.1,7.5) (143)	64.8 (64.3,65.4) (143)
Corn-soy blend+ [2]	5.89 (5.76,6.02) (147)	1.57 (1.46,1.68) (147)	7.3 (7.1,7.5) (147)	65.2 (64.6,65.8) (147)
Age 15 months				
WinFood Classic	8.24 (8.01,8.48) (89)	1.42 (1.25,1.59) (89)	9.6 (9.4,9.9) (89)	75.5 (74.9,76.1) (89)
WinFood Lite	8.16 (7.97,8.35) (102)	1.31 (1.17,1.45) (102)	9.4 (9.2,9.6) (102)	75.2 (74.6,75.8) (102)
Corn-soy blend+ [2]	8.14 (7.90,8.38) (88)	1.42 (1.25,1.60) (88)	9.5 (9.3,9.7) (88)	74.6 (74.0,75.2) (88)
Difference (15-6 months) compared to Corn-soy blend+ [2]				
WinFood Classic	0.00 (-0.30,0.29)	-0.05 (-0.32,0.22)	-0.1 (-0.3,0.2)	-0.3 (-0.9,0.4)
WinFood Lite	0.03 (-0.25,0.32)	-0.10 (-0.37,0.15)	-0.1 (-0.3,0.1)	-0.3 (-0.9,0.3)

[1] Analysis was by intention-to-treat, based on available cases and are presented as mean differences; 95% CIs in parentheses (n).[2]Standard Corn-soy blend+

Table 3: Effects on iron status and haemoglobin of WinFood Classic and WinFood Lite compared with the Corn-soy blend+ after a 9-months intervention from 6 mo to 15 mo[1].

Characteristic	Plasma ferritin, µg/L	Plasma transferrin receptor, mg/L	Haemoglobin, g/dl
Age 6 months			
WinFood Classic	29.9 (24.5,36.2) (87)	11.8 (11.0,12.5) (87)	10.8 (10.6,11.0) (164)
WinFood Lite	33.9 (27.0,39.9) (79)	11.6 (10.6,12.5) (79)	10.8 (10.5,11.0) (166)
Corn-soy blend+ [2]	32.8 (28.4,40.4) (83)	11.9 (11.0,12.7) (83)	10.7 (10.5,11.0) (166)
Age 15 months			
WinFood Classic	16.3 (13.6,19.5) (92)	13.5 (12.5,14.6) (92)	10.5 (10.3,10.8) (142)
WinFood Lite	22.5 (18.5,27.2) (89)	11.6 (10.7,12.5) (89)	11.0 (10.7,11.2) (152)
Corn-soy blend+ [2]	25.8 (21.8,30.4) (87)	11.2 (10.2,12.2) (87)	11.3 (11.1,11.5) (137)
Difference (15-6 months) compared to Corn-soy blend+ [2]			
WinFood Classic	0.6 (0.4,0.8) [3]	3.3 (1.7,4.9)	-0.9 (-1.3,-0.5)
WinFood Lite	0.6 (0.5,0.9) [3]	1.7 (0.1,3.4)	-0.4 (-0.8,0.0)

[1] Analysis was by intention-to-treat, based on available casesand are presented as means or mean differences; 95% CIs in parentheses (n). [2]Standard Corn-soy blend+

[3]The means from the log-transformed plasma ferritin values, back-transformed to get a ratio of means

Table 4: Effects on mid-upper arm circumference, head circumference and skin folds thickness of WinFood Classic and WinFood Lite compared with the Corn-soy blend+ after a 9-months intervention from 6 mo to 15 mo[1]

	Mid-upper arm circumference, cm	Head circumference, cm	Skinfolds, mm			
			Biceps	Triceps	Subscapular	Supra-iliac
Age 6 months						
WinFood Classic	14.4 (14.2,14.5) (165)	43.4 (43.2,43.7) (165)	7.0 (6.7,7.3) (165)	8.5 (8.2,8.8) (165)	8.1 (7.8,8.4) (165)	8.7 (8.3,9.1) (165)
WinFood Lite	14.0 (13.8,14.2) (167)	43.1 (42.9,43.3) (167)	6.9 (6.6,7.1) (166)	8.5 (8.2,8.7) (166)	7.8 (7.5,8.1) (166)	8.7 (8.3,9.2) (166)
CSB+[2]	14.2 (14.0,14.4) (167)	43.5 (43.3,43.8) (167)	7.0 (6.8,7.3) (167)	8.4 (8.2,8.7) (167)	8.0 (7.7,8.3) (167)	8.6 (8.2,9.1) (167)
Age 15 months						
WinFood Classic	14.8 (14.6,15.0) (141)	47.0 (46.7,47.3) (141)	6.0 (5.8,6.3) (140)	7.6 (7.3,7.9) (140)	7.0 (6.8,7.3) (140)	6.7 (6.3,7.1) (139)
WinFood Lite	14.7 (14.5,14.9) (150)	46.8 (46.5,47.0) (150)	6.0 (5.8,6.2) (150)	7.6 (7.3,7.9) (151)	7.1 (6.8,7.4) (150)	6.9 (6.5,7.3) (149)
Corn-soy blend+ [2]	14.8 (14.6,15.0) (137)	46.8 (46.1,47.5) (138)	6.0 (5.8,6.3) (137)	7.6 (7.3,7.9) (137)	6.9 (6.6,7.2) (137)	6.8 (6.4,7.1) (137)
Difference (15-6 months) compared to Corn-soy blend+ [2]						
WinFood Classic	-0.1 (-0.3,0.1) (141)	0.2 (-0.3,0.8) (141)	0.0 (-0.5,0.4)(140)	0.1(-0.4,0.5)(140)	0.2 (-0.2,0.6)(140)	-0.1 (-0.7,0.6)(139)
WinFood Lite	0.1 (-0.2,0.3) (150)	0.5 (0.0,1.1) (150)	0.2 (-0.3,0.6)(150)	0.1(-0.4,0.5)(150)	0.4 (0.0,0.8) (149)	0.1 (-.05,0.7)(148)

[1] Analysis was by intention-to-treat, based on available casesand are presented as mean differences; 95% CIs in parentheses (n).[2]Standard Corn-soy blend+ product.