

1 Effect of locally produced complementary foods on fat-free mass, linear
2 growth and iron status among Kenyan infants: a randomized controlled
3 trial¹⁻¹⁷

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

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43 conceived the idea and designed the study. BBE, SMF, JKHS and VOO reviewed the study design.
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45 quality assurance under supervision by BBE and VOO. SOK, SAO, JNK, BOO, BBE, NR and
46 VOO,: developed the WinFood products; SOK, ,HR and NR analyzed and interpreted the data;
47 SOK: drafted the manuscript. NR, HF and VOO offered overall editorial oversight. All authors
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50

51 **ABSTRACT**

52 The impact of quality complementary food products on infant growth and body composition has not
53 been adequately investigated. This study evaluated the effect on fat-free mass (FFM) accrual, linear
54 growth and iron status of locally produced complementary food products comparing to a standard
55 product. In a randomized, double-blind trial, 499 infants at 6 mo received 9 monthly rations of: 1)
56 WinFood Classic (WFC) comprising germinated amaranth (71%), maize (10.4%), small fish (3%)
57 and edible termites (10%); 2) WinFood Lite (WFL) comprising germinated amaranth (82.5%),
58 maize (10.2%) and multi-micronutrient premix; or 3) fortified Corn-soy blend plus (CSB+). Primary
59 outcomes were changes in FFM, length, and plasma ferritin and transferrin receptors (TfR). FFM
60 was determined using deuterium dilution. Analysis was by intention-to-treat, based on available
61 cases. Compared to CSB+, there were no differences in change from 6 to 15 mo in FFM for WFC
62 0.0 kg, (95% CI:-0.30, 0.29) and WFL 0.03kg, (95% CI:-0.25, 0.32) and length change for WFC -
63 0.3cm (95% CI:-0.9, 0.4) and WFL -0.3cm (95% CI:-0.9, 0.3). TfR increased in WFC group
64 3.3mg/L (95% CI: 1.7, 4.9) and WFL group 1.7mg/L (95% CI: 0.1, 3.4) compared to CSB+..
65 Compared to the increase in Hb in CSB+ group, there was a reduction in Hb in WFC of -0.9 g/dl
66 (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
67 tested WinFoods had the same effect on FFM and length as CSB+, while Hb and iron status
68 decreased, suggesting inhibited iron bioavailability from the amaranth-based WinFoods.

69

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

72 INTRODUCTION

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

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

91 The WinFoods study aimed to develop nutritionally improved foods for infants in LMIC based on
92 improved utilization of locally available foods, together with improved traditional food technologies
93 (e.g. fermentation, malting etc). These foods were dubbed “WinFoods”. The WinFood project was
94 carried out in parallel in Kenya and Cambodia from 2009 to 2012. In each site, processed
95 complementary food products were formulated and produced based on locally available foods and

96 optimized for nutrient composition with emphasis on iron and zinc (Skau et al., 2015, Kinyuru et al.,
97 2012, Kinyuru et al., 2015). Prior to the final decision on formulations, the acceptability of the
98 products was assessed among mothers and infants (Konyole et al., 2012). The efficacy of the
99 developed complementary food products was then tested in randomized trials to assess the impacts
100 of a daily supplement over a 9 month period on growth, nutritional status and development. A
101 Cambodian study found no difference in the primary outcomes of increment in fat-free mass (FFM)
102 and iron status after 9 months intervention, between either of the two versions of WinFood products
103 tested (one fortified and one not fortified with micronutrients) in comparison with either of two
104 corn-soy blend (CSB+ and CSB++) products (Skau et al., 2015). It was concluded that
105 micronutrient fortification may be necessary, and small fish may be an affordable alternative to milk
106 to improve complementary foods. The Cambodian trial also showed that, despite the daily
107 complementary food supplement, the children became increasingly stunted over the intervention
108 period (Skau et al., 2015).

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

113

114 **KEY MESSAGES**

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

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

124

125 **METHODS**

126 **Study setting**

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

131 **Study participant recruitment, inclusion and exclusion criteria**

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

142 recruited into the study if both were healthy and met the inclusion criteria and randomized to
143 receive the same intervention to avoid cross-contamination due to confusing the foods or sharing
144 during feeding.

145

146 **Study design**

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

153

154 **Intervention foods**

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

159 All the foods were centrally processed by extrusion cooking at AllGrain Co. Limited in Nairobi
160 Kenya and packed in opaque food grade white plastic containers, weighed at 500 g, and labelled
161 with computer-generated random numbers corresponding to WFL, WFC and CSB+ under close
162 supervision of the study team. Two complementary foods WFC and WFL based on germinated
163 grain amaranth (*Amaranthus cruentus*) and maize (*Zea mays*) had been developed. WFC had (as %
164 dry w/w) 71 % grain amaranth, 10.4 % maize, 0.6 % soybean oil, 5 % sugar, 10 % edible termites
165 (*Macrotermes subhylanus*) and 3 % small fish (*Rastrineobola argentea*). These fish are the silver
166 cyprinid, a species of ray-finned fish in the family Cyprinidae found in Lake Victoria and locally

167 called *omena* (Kenya), *dagaa* (Tanzania), and *mukene* (Uganda). *Omena* is a rich source of iron and
168 zinc (FAO, 2013; Kinyuru et al., 2013; Capinera et al., 2008; Rumpold & Schlüter, 2013). The grain
169 amaranth was germinated to reduce phytates and potentially enhance micronutrient bioavailability
170 (Kinyuru et al., 2015), especially the bioavailability of iron and zinc. WFL had 82.5 % grain
171 amaranth, 10.2 % maize, 0.6 % soybean oil, 5 % sugar, no ASFs but fortified with micronutrients
172 (vitamins and minerals premix) at 0.2 % of mineral/vitamin premix and 1.56 % mono-calcium
173 phosphate and sodium chloride which are the same rate as CSB+ (World Food Program, 2015).
174 According to World Food Program(2015), CSB+ also called a supercereal plus is made of corn (74
175 %) and soya (19 %), sugar (5 %), oil (0.5 %),Premix (1.5 %) and contains no other ASF not even
176 milk powder and is meant for children 6-23 months. The micronutrients were added to the blends
177 (where applicable) after extrusion cooking to avoid vitamin losses at high processing temperatures
178 (World Food Program, 2015). WFC provided, per 100 g dry weight, 423.6 kcal, 19 g protein, 12.2
179 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;
180 and CSB+ provided 391.7 kcal, 15.1 g protein, 7.7 mg Fe and 5.1 mg Zn. All the study foods were
181 given in daily rations adjusted to the age of the child with children in the age-group 6-8 months, 9-
182 11 months and 12-15 months receiving 50 g/day, 75 g/day and 125 g/day of flour, respectively,
183 based on the WHO recommendations for complementary feeding of breastfed infants to supply 200,
184 300, or 550 kcal/d (Pan American Health Organization, 2001; Dewey & Brown, 2003).

185 The food ration was a complement to breast milk and other foods. The daily rations were delivered
186 in monthly rations packages with instructions to caregivers not to share the food with other young
187 children not in the study and how to correctly measure quantities for daily use. Compliance was
188 assessed by asking the caregivers how much of the study foods the child consumed while checking
189 for any spoilage, spillages and the frequency of feeding (results not shown). A regimen compliance
190 study was also done once mid-way through the intervention in a sub-sample of 254 participants to
191 confirm compliance with the prescribed feeding regime; adequate compliance, defined as

192 consuming at least 60 % of the amount provided, was achieved by 65 % of the group (results not
193 shown). The degree of sharing with other household members was also assessed by occasional
194 home visits and caregiver's recall at the health facility during the monthly visits. The caregivers
195 were to keep all the distributed packets, including those used, to be counted on a monthly basis.

196

197 **Randomization and blinding**

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

203

204 **Participant visits**

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

210

211 **Body composition measurement**

212 Fat free mass (FFM) and fat mass (FM) were assessed at 6 months and 15 months using the
213 deuterium dilution technique. Briefly, a predose sample of about 2 ml of saliva was taken from the
214 child's mouth using a cotton ball. Each child was given a standardized oral dose of deuterium
215 labelled water (15 ml of $^2\text{H}_2\text{O}$ solution comprising 3 g deuterium [99.8 % $^2\text{H}_2\text{O}$ -Cambridge Isotope

216 Laboratories Inc.] and 12 ml of mineral water) which had been accurately weighed at the Kenya
217 Medical Research Institute (KEMRI) laboratories in Nairobi, Kenya and transported refrigerated at
218 4 °C to the field following guidelines from the International Atomic Energy Agency (IAEA) (IAEA,
219 2011). Post-dose saliva samples were taken at 2 hours and 3 hours. Saliva samples were collected
220 into a tightly capped 1.5 mL cryogenic tube by squeezing the saliva from the wet cotton ball
221 removed from the child's mouth, using a syringe. Samples were kept in a cooler box with ice packs
222 and were transported the same day to a central collection point at Lusheya health centre where they
223 were stored in a chest freezer at -20 °C pending transfer in dry ice package to KEMRI in Nairobi for
224 analysis. Enrichment of deuterium in saliva samples was determined using Fourier Transform
225 Infrared (FTIR) spectrophotometer (Shimadzu model 8400s, Shimadzu Corporation, Kyoto, Japan).
226 Enrichment of the pre-dose sample from the child was used for background correction of post-dose
227 samples. Our study was based on a previous protocol assuming that deuterium equilibration takes
228 less than 3 hours in infants and children when saliva is the primary specimen (Colley, Byrne & Hills
229 2007). Using the mean of deuterium enrichment based on the two post-dose samples (Colley, Byrne
230 & Hills 2007) as per the protocol at the time (IAEA, 2011), the dilution space and Total Body Water
231 (TBW) were calculated accordingly. FFM was calculated by dividing TBW by an age specific
232 hydration factor as: $TBW/0.79$ for both sexes. FM was calculated as body weight minus FFM
233 (IAEA, 2011).

234

235 **Iron status**

236 Three (3)-mL blood samples were drawn by venepuncture from non-fasting subjects both at 6 months
237 and 15 months. Haemoglobin concentration was measured on blood drop aliquots using a HemoCue
238 HB301 photometer (HemoCue Sheffield, United Kingdom). Blood left in the syringe was put into a
239 plain Vacutainer (Becton Dickinson), kept chilled at 4 °C, and separated within 4 hours by
240 centrifugation (1300 x g, 10 min at 4 °C). Plasma samples were kept frozen at -20 °C for 3 months

241 at Lusheya health centre until they were sent to the University of Nairobi Institute of Tropical and
242 Infectious Diseases, Nairobi, Kenya for further storage at -80 °C. Plasma samples were
243 subsequently transported by air to the VitMin Lab (Willstaett, Germany) for analysis of plasma
244 ferritin, plasma transferrin receptors, alpha-1-acid glycoprotein (AGP) and C-reactive protein (CRP)
245 concentrations using enzyme immunoassays using commercial ELISA test kits (Ramco
246 Laboratories) as described by Erhardt et al. (2004).

247

248 **Anthropometry**

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

262

263 **Morbidity**

264 Morbidity data were collected based on caregivers' recall about specific symptoms and clinic visits
265 in the past seven days especially for the upper respiratory tract infection (URTI) and diarrhoea as

266 defined by WHO respectively (WHO, 2001; WHO, 2017). General assessment of overall morbidity
267 in the last month (scored as healthy; mild, self-limited illness; moderate illness requiring
268 symptomatic treatment at the clinic; severe illness requiring antibiotics or other medical
269 intervention) for the child during their monthly visits to clinic using questionnaires was also done.
270 Caregivers were encouraged to bring their children to the clinic in the event of severe illness prior to
271 the next visit.

272 **Sample size consideration**

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

279

280 **Data analysis**

281 Primary outcomes were changes in FFM, length, plasma ferritin and plasma transferrin receptors.
282 Analysis was by intention-to-treat, based on available cases. Case record forms were checked daily
283 and entered within 2 weeks. Quantitative data was double entered in Microsoft Excel™ with length
284 and weight measurements converted to Z-scores using WHO Anthro™ v3.2.2 based on the WHO's
285 2006 Child Growth Standards (WHO, 2014). Frequencies, means and median values were
286 calculated using STATA® version 12 (A Stata Press Publication, 2011). Analysis of variance
287 (ANOVA) was used to determine differences between groups in change in parameters from 6 to 15
288 months. Plasma ferritin concentrations were log-transformed after correction for inflammation using
289 CRP and AGP concentrations and the correction factors as published elsewhere (Thurnham et al.,

290 2010). The means from the log-transformed plasma ferritin values were then back-transformed to
291 get a geometric mean. The same was done for the differences and back-transformed to give a ratio.
292 Selected pair-wise comparisons were considered with CSB+ used as the reference group. Stunting,
293 underweight and wasting were defined as length-for-age, weight-for-age and weight-for-length,
294 respectively, < -2 standard deviations of the WHO reference standards while moderate-to-severe
295 and severe acute malnutrition in infants were defined as MUAC < 12.5 cm and MUAC < 11.5 cm,
296 respectively (WHO, 2014). Before the study was unblinded, all infants with negative % FM were
297 considered implausible and removed because negative values occur when the deuterium dose has
298 not had sufficient time to fully equilibrate with body water, or the dose was not completely
299 consumed (IAEA, 2011). We also reviewed and checked with field notes regarding problems
300 administering the $^2\text{H}_2\text{O}$ to the child. Any uncertainty of how much $^2\text{H}_2\text{O}$ the child consumed led to
301 his or her exclusion from the deuterium analyses. Furthermore, in cases of poor agreement between
302 pairs of enrichment values, we discarded all of those where the two values differed by >50 ppm
303 based on expert opinion of what is plausible but these variations could be due to spillages of
304 deuterium during dosing. We also rejected outliers which fitted very poorly with the general
305 association of body water with weight and height as described by other workers (IAEA, 2011;
306 Colley, Byrne & Hills, 2007). More samples were removed at 15 months than 6 months because
307 more had poor agreement due to longer equilibration times in older children as observed previously
308 by Colley, Byrne & Hills, (2007).

309

310 **Ethical considerations**

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

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

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

319

320 **RESULTS**

321 We screened 527 infants of whom 499 (94.6 %) met the inclusion criteria and were randomized to
322 one of the three food groups (**Figure 1**). Four hundred and twenty-eight children (86 %) completed
323 the study. Of the 71 (14 %) children lost to follow-up, 63 (89 %) relocated from the study area while
324 8 (11 %) died. The dropout rate did not differ between groups. Of the 499 included, we obtained
325 body composition data from 442 (89 %) at 6 months and 288 (58 %) at 15 months. The numbers at
326 15 months being lower compared to 6 months due to longer equilibration time as explained by
327 Colley, Byrne & Hills, (2007).

328

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

335

336 No differences in body composition were observed among the three intervention groups over the 9
337 month intervention (**Table 2**). There were no differences in FFM gain in WFC 0.0 kg (95 % CI:-
338 0.30, 0.29) or WFL 0.03 kg (95 % CI:-0.25, 0.32), compared with the CSB+ group. Similarly,

339 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
340 was not different compared to CSB+. The weight gained in all three groups was mainly FFM, while
341 FM remained unchanged.

342
343 There was a decrease in plasma ferritin in the WFC group ratio of geometric means: 0.6 µg/L (95 %
344 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
345 was also an increase in plasma transferrin receptor in the WFC group 3.3 mg/L (95 % CI: 1.7, 4.9)
346 and the WFL group 1.7 mg/L (95 % CI: 0.1, 3.4). As seen in Table 3, compared to the increase in
347 hemoglobin over time in the CSB+ group, there was a reduction in hemoglobin in the WFC group -
348 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,
349 0.0).Despite all these findings, the low follow-up was a limitation.

350
351 As defined by WHO cut offs (WHO, 2001), 67 % of all children were anemic at 6 months while 73
352 %, 64 % and 63 % respectively were anemic at 15 months for WFC, WFL and CSB+, respectively;
353 the WFC group was different from the CSB+ group (p=0.01). A similar trend was observed for
354 mild anaemia (Hb between 10-10.9g/dl) where a greater proportion (p=0.04) of children (41.8 %) in
355 the WFC group had mild anaemia at 15 months compared to children in the CSB+ group (22.4 %).
356 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
357 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)
358 g/L at 15 months.

359
360 There were no differences between the WinFoods and the CSB+ in the relative changes in MUAC
361 and biceps triceps, subscapular and supra-iliac skinfolds. In contrast, there was a slight positive
362 change in head circumference for WFC 0.2 cm (95 % CI:-0.3, 0.8) and WFL 0.5 cm (95 % CI:-0.0,
363 1.1) relative to CSB+ (**Table 4**).

364

365 **DISCUSSION**

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

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

387 a non-fortified food supplement may not be sufficient to compensate for generally nutritionally
388 insufficient complementary foods.

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

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

405 The overall deterioration of iron status among all food groups, including those receiving foods
406 fortified with micronutrients including iron, may also be caused by non-food factors. Although we
407 did not assess malaria infection, the study area is vulnerable to malaria (Desai et al., 2005). Malaria
408 is known to be strongly associated with iron deficiency anaemia (Spottiswoode, Duffy &
409 Drakesmith, 2014; Friedman et al., 2009). EED is also linked to bacterial overgrowth in the gut
410 epithelia which may lead to increased iron requirements (Owino et al., 2016). The deterioration of

411 iron status and haemoglobin concentration in the non-fortified food (WFC) could be caused by the
412 presence of phytic acids in maize and amaranth grains (Azeke et al., 2011; Albarracín et al., 2015).
413 Although partial germination of grain amaranth was done to reduce phytic acid, the efficiency in the
414 reduction may not have been adequate to remove the inhibition of mineral absorption by phytic
415 acid. Phytic acid content was assessed during the development of the product where it was
416 concluded that the amaranth grain should be germinated for 72 hours to reduce phytic acid to an
417 acceptable level. However, for the scaled up production of the intervention foods the lengthy
418 germination duration was found to increase the risk of growth of pathogenic bacteria and the
419 germination time was limited to a standardized 48 hours (Kinyuru et al., 2015). The fortification of
420 WFL and CSB+ with multiple micronutrient premix had no benefit on iron status.

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

424 The results from previous studies examining the effects of micronutrient supplementation on growth
425 have been mixed (Admassu et al., 2017; Labbé & Dewanji, 2004) with some demonstrating a
426 beneficial role, particularly in resource limited settings, where fortified foods have improved growth
427 (Admassu et al., 2017), haemoglobin (Owino et al., 2007) and micronutrients (Faber et al., 2005)
428 and others showing no difference in linear growth among infants supplemented with micronutrients
429 from 6 to 18 months (Lartey et al., 1999; Bauserman et al., 2015). Linear growth is not only as a
430 result of dietary improvement during complementary feeding and therefore other measures beyond
431 increasing the nutrient content of complementary foods needs to be explored (Bauserman et al.,
432 2015). Some of these studies, however, have heterogeneous baseline participant populations,
433 varying measures of anthropometry, various timing of interventions and some lack appropriate
434 control groups emanating from diverse intervention products and study designs (Skau et al., 2015;

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

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

452

453 Although we did not demonstrate a clear beneficial effect from supplementing with WFC on FFM,
454 linear growth and Fe status, we cannot exclude insects as a potentially promising food source for
455 people in food-insecure areas. The lack of impact of the insect-based WFC product on improving
456 iron status need further investigations to clarify iron absorption from different blends to isolate the
457 specific impact of the termites. It is also possible that improving the quality of complementary foods
458 is beneficial if other growth-limiting pathologies are prevented. Given the high disease burden

459 among infants in this resource-limited rural area (Spottiswoode, Duffy & Drakesmith, 2014;
460 Friedman et al., 2009), the role of conditions that impair nutrient absorption and utilization is a
461 potential area of further research.

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

471

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627

628 **Figure 1: Participant screening, recruitment and follow up.**

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

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

638 For analysis therefore; 141, 137 and 150 completed the study and were included in the analysis with
639 an intention to treat for WFC, CSB+ and WFL respectively. Body composition had 91 each for
640 WFC and CSB+ with 106 being in the WFL group as detailed in **Figure 1**. Analysis was by
641 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)

¹Values 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 mo¹.

	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).²Standard 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 mo¹.

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 cases and are presented as means or mean differences; 95% CIs in parentheses (n). ²Standard Corn-soy blend+

³The 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 mo¹

	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 cases and are presented as mean differences; 95% CIs in parentheses (n).²Standard Corn-soy blend+ product.