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Food-based dietary guidelines for optimizing calcium intakes for reproductive-aged women in Ethiopia using local foods

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Abstract

Increasing dietary calcium intakes of Ethiopian women of reproductive age (WRA) is a public health priority for reducing pre-eclampsia in pregnancy. Using linear programming, we determined whether locally available foods consumed by WRA in nine regions (urban and rural) and two administrative cities of Ethiopia could provide 1000 mg/day of dietary calcium, and we identified food-based recommendations (FBRs) to improve dietary calcium adequacy in each region. Results showed that diets providing 1000 mg/day of calcium were feasible in eight regions (40%) of the target populations examined. It would, however, require marked changes for most populations (90%), increasing the number of servings per week of several food groups to levels close to those of high consumers in each population. The selected calcium-specific FBRs integrate well into the 2022 Ethiopian Dietary Guidelines, requiring additional messages to consume green leafy vegetables, milk, root crops, or teff *(Eragrostis tef)* or to consume a higher number of servings of vegetables than currently recommended, depending on the population. In conclusion, these analyses show that a food-based approach can be used to achieve dietary calcium adequacy among WRA in 40% of the populations examined. For the other populations, food-based interventions alone may be inadequate and other interventions are likely needed.

KEYWORDS
calcium, diet modeling, Ethiopia, food-based recommendations, linear programming, Optifood, pregnancy, women of reproductive age

PURPOSE

The Nutrition Science Program of the New York Academy of Sciences (NYAS) and the Children's Investment Fund Foundation (CIFF) formed the Calcium Task Force in 2021. This interdisciplinary task force comprises specialists in areas including micronutrients, gynecology and obstetrics, and public health. An objective of the task force was to identify gaps where the latest evidence could inform interventions and policies, and a follow-up grant included the provision of Technical Assistance for Calcium Programs in Ethiopia. In this article, NYAS, in collaboration with members in the United Kingdom and Ethiopia from the London School of Hygiene & Tropical Medicine (LSHTM), the Micronutrient Action and Policy Support (MAPS) team, and the Centre for Food Science & Nutrition, Addis Ababa University, discuss the analysis to identify food-based strategies focused on improving dietary calcium intakes among women of reproductive age (WRA) in different regions of Ethiopia. These region-specific food-based recommendations (FBRs) were selected to align with the 2022 Ethiopian Dietary Guidelines to facilitate their promotion within this broader set of guidelines.

INTRODUCTION

Dietary intakes of calcium in many low- and middle-income countries, including Ethiopia, are well below recommended levels.[1,2] These low intakes are a public health concern, especially during pregnancy.[1,2] Suboptimal calcium intakes increase risks of pregnancy-induced hypertensive disorders, including pre-eclampsia, which is the leading cause of maternal deaths worldwide.[3] In Ethiopia, pre-eclampsia affects between 7.2% and 8.4% of pregnancies and contributes to over 50,000 maternal deaths per year.[4] Specifically, in Addis Ababa, Ethiopia, low calcium intakes have been found to be associated with an increased risk of pre-eclampsia among pregnant women.[4] Strategies to help increase dietary intakes of calcium of WRA in Ethiopia is a public health priority.

The recent Ethiopian National Nutrition Survey found that WRA consumed on average 300 mg/day of calcium, which is well below the 1000 mg/day recommended for pregnant women.[1] This is mainly associated with intakes of high-energy diets with low calcium concentration.[1] Modifying food choices within realistic modifications could meet calcium requirements.

The Ethiopian government is prioritizing the improvement of dietary practices to reduce malnutrition and noncommunicable disease risks, with a special focus on WRA and children.[5] One of the factors contributing to inadequate intakes is the lack of nutrition knowledge.[6,7] Therefore, the 2022 Ethiopian Food-Based Dietary Guidelines (EFBDG) were recently developed as one strategy for promoting the intake of quality diets and reducing health risks among populations in Ethiopia.[5] The EFBDG provide general guidance on the quantities of foods from selected food groups that Ethiopian children and adults should consume.[5] The recommendations are specific for nonfasting and continuous or intermittent fasting situations.[5] In the Orthodox Christian religion in Ethiopia, fasting involves abstaining from animal-sourced foods and no eating or drinking before a specific time (between 12 and 3 p.m.) in the afternoon. Continuous fasting occurs during designated fasting periods (ranging from 2 to 8 weeks) and intermittent fasting on Wednesdays and Fridays.[6] During continuous fasting periods, the EFBDG recommend that the number of servings per day for legumes, nuts, and seeds increases, and calcium and vitamin B12 supplements are recommended.[5] However, they do not provide specific recommendations for increasing intakes of individual nutrients or tailored recommendations for different regions in Ethiopia.[5] As increasing calcium intake for WRA is a priority in Ethiopia, the integration of specific recommendations for calcium into these dietary guidelines is required.

Previous modeling studies have examined if calcium requirements can be met using locally consumed foods with usual portion sizes in Uganda, Guatemala, and Bangladesh.[8] They showed that even though achievement of dietary recommendations for calcium is challenging, it was possible for some target groups in these countries, including nonpregnant and nonbreastfeeding WRA.[8] To date, no modeling studies have looked at using locally consumed foods for modifying realistic food choices to meet the calcium requirements of WRA in Ethiopia. Therefore, team members from LSHTM, MAPS, and Addis Ababa University, in collaboration with the NYAS, undertook secondary data analysis to identify possible food-based strategies for improving calcium intakes among urban and rural WRA, including pregnant women, in different regions of Ethiopia. Additionally, this analysis would serve to enrich the evidence base on food-based sources of calcium, demonstrate the potential for meeting calcium needs, and help refine the dietary guidelines as regards to calcium. These region-specific FBRs were selected to align with the 2022 Ethiopian Dietary Guidelines to facilitate their promotion within this broader set of guidelines. They will be used by the Nutrition group of NYAS to inform the development of Ethiopian-specific education materials, job aids, and policy briefs for promoting improved dietary calcium intakes of WRA in urban and rural regions across Ethiopia.

The objectives of the analyses for WRA in each region of Ethiopia were to (1) determine whether calcium reference values of 1000 mg of calcium per day can be met in diets based on locally available foods given the regional food consumption patterns, (2) identify the best food sources of calcium, (3) identify alternative sets of region-specific FBRs for increasing dietary calcium intakes, indicating the most promising sets of FBRs to incorporate into education materials, and (4) integrate the FBRs into the new EFBDG.

METHODS

Defining model parameters for linear programming analysis

Secondary data analysis was conducted using the 2015/16 Ethiopian Household Expenditure and Consumption Survey (EHCES) and linear programming analysis (LPA).[9–12] The EHCES was conducted over 1 year between July 2015 until July 2016, where a two-stage sampling design was used to survey 2106 enumerator areas. Sampling was spread out over the year and, therefore, both temporal and spatial variation was included and representative of the population. The EHCES was used to identify foods consumed by a household at two visits within a 1-week period (i.e., first visit = 3 day recall and second visit = 4 day recall).[9] The 20 target populations for the LPA included WRA living in nine urban and rural regional regions of Ethiopia and the administrative cities of Addis Ababa and Dire Dawa.[9] LPA model parameters were estimated by redistributing the EHCES household food consumption data for each target population, using the apparent intake method per adult female equivalent (AFE).[13,14] Specifically, in all eligible households, the estimated energy requirement of each household member was divided by the energy requirement of a nonpregnant, nonlactating WRA.[14] Each individual was then allocated an AFE based on their energy requirements. These ratios were summed across all household members to provide the total number of AFEs per household.

The energy and nutrient content of each food were obtained from food composition studies conducted in Ethiopia or Food Composition Tables in the following hierarchical order: Ethiopia, Kenya, West

TABLE 1 Calcium content (%NRV) of the nutritionally best[a] and calcium maximized[b] diets and the other nutrients that did not achieve their NRVs[c] in the nutritionally best diets presented for urban and rural women in each region.

Population	*n*[d]	Optimized diet (%)[a]	Maximum Ca (%)[b]	Other nutrients[c]
Addis Ababa city	3832	108.0	118.3	Vitamin A, iron
Afar urban	768	96.9[e]	101.6	Vitamin A, iron, B12
Afar rural	576	109.5	132.4	Vitamin A, C, iron, folate
Amhara urban	3360	114.6	129.7	Vitamin A, iron
Amhara rural	2016	90.9	91.5[f]	Vitamin A, B12
Benishangul-Gumuz urban	768	100.0	146.3	
Benishangul-Gumuz rural	576	100.0	120.3	Vitamin A, B12
Dire Dawa city	672	119.2	129.9	Vitamin A, iron
Gambella urban	768	107.6	172.5	Iron, folate
Gambella rural[a]	576	162.6	217.6	
Harari urban	384	108.7	131.3	Iron
Harari rural	288	67.7	71.3[f]	Vitamin A, iron, B12, folate
Oromia urban	4128	120.3	136.8	Iron
Oromia rural	2304	107.1	167.6	B12
SNNPR[g] urban	3165	180.4	201.6	Iron
SNNPR rural	2016	229.4	260.9	B12
Somali urban	1152	84.8	89.2[f]	Vitamin A, iron, B12, folate
Somali rural	576	62.3	62.4[f]	Vitamin A, C, iron, folate, B12
Tigray urban	1152	112.2	124.6	Vitamin A, iron
Tigray rural	1152	98.6[e]	100.0	Vitamin A

[a]Module 2 optimized diet (Diet B), which was the Module 2 diet that aimed to meet only the WHO nutrient reference values.[21]
[b]Module 3 maximized calcium diet that was selected to have the highest calcium content possible given model constraints.
[c]Other nutrients—these nutrients did not achieve their reference nutrient values (NRVs) in the Module 2 nutritionally best diet (Diet B).
[d]*n*—number of households that defined the model parameters.
[e]Diet achieved 1000 mg/day for calcium, but compromised other nutrients.
[f]Diet did not provide 1000 mg/day of calcium for target populations.
[g]Southern Nations, Nationalities, and Peoples' Region.

Africa, the United States Department of Agriculture, India, and the literature.[15–20]

Optifood software Modules 1–3 were used to do the LPA.[10–12] Module 1 is used to (1) set up the target group (e.g., WRA, country, region, reference nutrient intake group, mean body weight, and physical activity levels [PALs]), (2) enter details about locally available foods, (3) enter the constraints of those foods, and (4) test the model parameters. Module 2 identifies the main source of calcium (Tables 1 and 2) and generates the nutritionally best diets using locally consumed foods and identifies the FBRs that are then tested in Module 3, which compares alternative FBRs and generates the maximized and minimized calcium diets (Table 3).[a] Two to three sets of FBRs were selected for each of these target populations that included: (1) animal-sourced foods that can be consumed during a nonfasting period; (2) no animal-sourced foods, which occurs during a fasting period; and (3) in some regions where teff (*Eragrostis tef*, a high calcium grain) is not widely consumed, sets of FBRs that did not include teff. All sets of FBRs were selected to allow integration within the 2022 EFBDG.[5]

The input model parameters for the LPA included World Health Organization (WHO) nutrient reference values (NRVs) for 12 nutrients,[21] a list of food items consumed by each target group, the average daily serving size for each food item (g/day), and the upper and lower constraint values on the number of servings per week for each food item. The values for these model parameters are detailed in Tables S1–S4. The list of foods modeled for each target population included all foods reported as consumed in ≥5% of eligible households and some foods consumed by <5% of households but were good food sources of calcium and other nutrients. Food items assumed to have no/minimal nutritional value (e.g., water), herbs or spices used in recipes (e.g., garlic, chili), or were alcoholic (e.g., beer, spirits, tella) were excluded even if consumed in >5% of households.

Values for model constraints on the minimum and maximum number of food servings per week that could be included in a simulated diet were derived from the EHCES data to ensure all modeled diets fell within the reported food patterns of each target population (Table S5). In most cases, the minimum constraint value was zero. The exceptions for some target populations were the food groups of cereals, staples, vegetables, and fats & oils. The minimum value in these cases was set as 6 servings per week instead of 7 servings per week to accommodate smaller serving sizes.

TABLE 2 Main food sources of calcium[a] in the Module 2 nutritionally best diets as % age of total diet calcium.

Food, % calcium Population	Cows milk %	Teff %	Kale %	Chick peas %	Wheat flour %	Sour milk %	Sama-Kenkez %	Goat milk %	Sorghum %	Dinich be-siga %	Shifer awAleko %	Wild greens %	Qocho %	Butter milk %	Kidney bean %
Addis Ababa	10.7	43.4	19.5												
Afar urban		34.8	13.8												
Afar rural	34.7	35.7				14.1									
Amhara urban	10.4	40.7	16.6	6.5											
Amhara rural	5.9	26.4	20	9.9	6.3										
Benishangul-Gumuz urban	11.4	34.1	20.5				7.2								
Benishangul-Gumuz rural	6.8	15.4	30.1				11.9								
Dire Dawa city	8.6	32.8	17.2							21.4					
Gambella urban	7.1	16.0										47.2			
Gambella rural		16.6									38.8	24.5			
Harari urban		23	21.3									17.7			
Harari rural	20.2	20.8	30.3						10.7						
Oromia urban		38.8	25.3							14					
Oromia rural			42.8										20.4	12.8	
SNNPR[b] urban		24.1	27.5								19.4				
SNNPR rural		13.0	33.8			6.5					32.9				
Somali urban	29.9	36.7													7.6
Somali rural	28.3				13.5			37.6	5.6						9.4
Tigray urban	8.9	46.4								12.2					
Tigray rural		34.5		8.4	8.5									5.9	

[a]Main food sources—defined as foods that provide ≥5% of the Module 2 nutritionally best diet's Ca content (i.e., diet selected to come as close as possible to meeting nutrient NRVs).
[b]SNNPR—Southern Nations, Nationalities, and Peoples' Region.

In addition, all models included an energy constraint of 2282 kcal/day to ensure that the energy contents of all simulated diets were equal to the target population's estimated average energy requirement, which was calculated using the WHO/Food and Agriculture Organization algorithms,[22] assuming an average body weight of 50.4 kg and a PAL of 1.85 (i.e., moderate activity). This value was slightly lower than the estimated median energy intakes of WRA used when developing the 2022 EFBDG, which ranged from 2341 to 2703 kcal/day.[5]

Quality control

The average serving size for each food item was derived from households where the food item was consumed. This approach could result in model parameters that overestimated the grams of food consumed from different food groups. Thus, for both consumers and nonconsumers, if the parameters allowed the selection of a diet in which the total grams of food selected per week from an individual food group exceeded the 90th percentile for all households, the distribution of grams of foods consumed from each food group was examined for each target population and the model parameters adjusted.

Data analysis

Table 4 summarizes the objectives of each LPA and the model parameters used when doing the analyses in Modules 2 (nutritionally best diet) and 3 (maximized calcium diet) of the Optifood software program. For all simulated diets, the model constraints shown for each analysis ensured the diets resembled reported diets from the Ethiopian Household Consumption and Expenditure Survey data. To answer study objective 1 (to determine whether calcium reference values of 1000 mg/day can be met based on locally available foods), the calcium content of the maximized calcium diet (examined using Module 3) was determined for each target population and whether it achieved

TABLE 3 Food-based recommendations for promoting calcium intakes for women of reproductive age on nonfasting (NF), fasting (F), and no teff (NT) expressed as the number of servings per week from food groups, food subgroups, or specific food (note the daily serving sizes are not necessary those consumed by women in these urban and rural populations), and the calcium content of the minimized calcium diet expressed as %1000 mg/day, and the other nutrients not achieving 65% of their nutrient reference values in their minimized diets.

Population	Diet type	Dairy #S/w[a]	Milk #S/w	Whole grains #S/w	Teff #S/w	Millet #S/w	Vegetables #S/w	GLV[b] #S/w	Legumes #S/w	Roots #S/w	Small fish #S/w	% Ca[c]	Nutrients[d]
Addis Ababa	NF[e]		7	21	7			7				79.6	8
Addis Ababa	F[f]			21	7		35	7				70.3	8
Addis Ababa	NT[g]		7	21			35	7	14			48.8	7
Afar urban	NF		7	21	7			7				45.9	7
Afar urban	NT		7	21				7				25.9	6
Afar rural	NF	14			7			3				70.2	7
Afar rural	NT	14		14				3				36.6	6
Amhara urban	NF		7	21	7				14			59.3	6
Amhara urban	F			21	7		21		14			50.0	6
Amhara urban	NT		7	21			21		14			24.4	6
Amhara rural	NF		7		7	7		7	7			50.9	8
Amhara rural	F				7	7		7	7			46.6	8
Amhara rural	NT		7				21	7	14			34.0	7
Benishangul-Gumuz urban	NF		7		7		35			14		57.1	8
Benishangul-Gumuz urban	NT		7				35			14		25.2	8
Benishangul-Gumuz rural	NF		7	21	7			7		7		47.7	7
Benishangul-Gumuz rural	NT		7	21				7		7		30.9	7
Dire Dawa	NF		7		7			7	14			67.7	7
Dire Dawa	F				7		35	7	14			61.7	6
Dire Dawa	NT		7				35	7	14			36.9	4
Gambella U	NF		7	14				7			7	78.4	9
Gambella urban	F			14	3		35	7				76.9	8
Gambella rural	NF		7		7						7	79.2	8
Gambella rural	F				7		28	7				71.9	8
Gambella rural	NT		7				28				7	58.4	5
Harari urban	NF		7		7		35	7				60.9	6
Harari urban	NT		7				35	7	14			42.5	5
Harari rural	NF		7		7		21	7				56.3	7
Harari rural	NT		7				21	7	7			44.0	7
Oromia urban	NF		7		7			7				78.7	7
Oromia urban	F				7			7				76.3	7
Oromia urban	NT							7	14			36.8	4
Oromia rural	NF		7		7					14		65.7	9
Oromia rural	F			21	7			7				60.5	9

(Continues)

TABLE 3 (Continued)

Population	Diet type	Dairy #S/w[a]	Milk #S/w	Whole grains #S/w	Teff #S/w	Millet #S/w	Vegetables #S/w	GLV[b] #S/w	Legumes #S/w	Roots #S/w	Small fish #S/w	% Ca[c]	Nutrients[d]
Oromia rural	NT		7	21					14			34.4	7
SNNPR[h] urban	NF		3		3			7		14		71.1	8
SNNPR urban	NT		7					7	14	14		65.5	7
SNNPR rural	NF		7					7		14		82.5	7
Somali urban	NF		14		7		28	2				54.3	6
Somali urban	NT		14				28	2	14			27.7	2
Somali rural	NF	14		14			21		7			31.8	6
Tigray urban	NF	7			7			7				65.2	6
Tigray urban	F				7		35	7				59.2	6
Tigray urban	NT	7					35	7	14			28.2	6
Tigray rural	NF		7		7		35	7	14			51.2	6
Tigray rural	F				7		35	7	14			46.4	6
Tigray rural	NT		7				35	7	14			24.4	6

[a]#S/w—number of servings per week.
[b]GLV—green leafy vegetables.
[c]The calcium content of the Module 3 minimized calcium diet expressed as a percentage of 1000 mg Ca per day.
[d]Nutrients—following the food-based recommendations would likely mean the population would be at low risk of inadequate intakes of this number of the 12 nutrients modeled.
[e]NF—Nonfasting.
[f]F—Fasting.
[g]NT—No teff.
[h]SNNPR Southern Nations, Nationalities, and Peoples' Region.

or exceeded 100% of the calcium (Ca) NRV (i.e., 1000 mg/day). A result of less than 100% indicated that the recommended calcium intakes for the target population would be challenging to meet using acceptable quantities of local foods given local food patterns. Additionally, if 100% of the Ca NRV was met in the maximized calcium diet but it was not met in the nutritionally best diet (examined using Module 2), it suggested that Ca NRVs could be met using local foods, but only at the expense of not meeting the NRVs for the other 11 nutrients. The nutritionally best diet was selected to come as close as possible to achieving the NRVs for 12 nutrients (protein, calcium, iron, zinc, thiamine, riboflavin, niacin, vitamins A, C, B_6, B_{12}, and folate).

To answer study objective 2 (to identify the best food sources of calcium), the best food sources of calcium for each target population were those providing at least 5% of calcium in the target group's Module 2 nutritionally best diet. The best food sources of calcium were identified from this diet instead of the maximized calcium diet because these foods were also consistent with a balanced nutritious diet.

To answer study objective 3 (to identify alternative sets of region-specific FBRs), up to eight FBRs were evaluated individually and in combination with other individual FBRs to select favorable sets of FBRs for each of the 20 target populations. These FBRs were reported as the number of servings per week from specific food subgroups or food groups rather than individual calcium-rich foods to avoid selecting a rigid set of FBRs that reduced the choice for the target populations. The exception was teff and finger millet, because they were good food sources of calcium, and the calcium content of teff, in particular, was higher than other grains in the whole grain subgroup category.[23,24] These alternative sets of FBRs were tested by selecting the diet with the lowest Ca content possible and compared in Module 3. In this module, 12 diets were selected that had the minimum content possible for each of the 12 nutrients modeled, given the model constraints. The criteria for selecting sets of FBRs for each target population were the sets of FBRs that met at least 65% of the Ca NRV[10] in the minimized calcium diet (examined using Module 3) using the lowest number of individual FBRs. The minimized diets for other nutrients were also examined when selecting FBRs for calcium to select those that would also recommend dietary adequacy for other nutrients. When 65% of the Ca NRV was not achieved, the sets with the highest % Ca NRVs using the lowest number of individual FBRs were used. For each target population, at least two sets of promising FBRs were selected, in which one could be recommended on nonfasting days and the other on fasting days. For populations where teff was not widely consumed, a set of FBRs that excluded teff was also selected. The need to recommend the fasting recommendations is less important in regions where Orthodox Christianity is not practiced by the majority of the population, therefore, only nonfasting days were selected for the regions of Afar, Benishangul-Gumuz, Harari, Somali, and SNNP.

TABLE 4 Description of the linear programming models used to answer each study objective, including the model's objective function[a], model constraints, and the outcomes of interest.

Purpose (module)	Model objective[a]	Model constraints	Outcomes of interest
Study objective 1: To determine if the Ca content of any diet would achieve 1000 mg/day (Module 3, maximized Ca diet)	Select the diet with highest Ca content (objective function maximizes the diet's Ca content)	• Diet's energy content = the average energy requirement[b] • Grams of each food ≥ 0 g • Grams of each food ≤ a maximum amount • # Servings from each food subgroup ≥ minimum # of servings • # Servings from each food subgroup ≤ maximum # of servings • # Servings from each food group ≥ minimum # of servings • # Servings from each food group ≤ maximum # of servings • # Servings from all staple foods ≥ minimum # of servings • # Servings from all staple foods ≤ maximum # of servings	The Ca content of the simulated diet expressed as a % of 1000 mg/day
Study objective 2: To identify good food sources of calcium for the target population (Module 2 analyses; diet selected to meet NRVs[c] of 12 nutrients)	Select the diet that comes as close as possible to meeting 1000 mg/day for Ca and the WHO reference nutrient values for 12 nutrients[c] (objective function minimizes sum of deviations below the NRVs)	• Same constraints as above	List of foods and food subgroups providing ≥5% of the model diet's calcium content
Study objective 3: Test and compare alternative sets of FBRs[d] for improving dietary Ca intakes (Module 3, minimized Ca diet)	Select the diet with the lowest Ca content possible (objective function minimizes the diet's Ca content)	• Same constraints as above • Additional constraints to ensure the FBRs being tested are met. FBRs are expressed as # servings/week of either a food, food subgroup, or food group, thus the constraints can include: o # Servings from a food ≥ FBR o # Servings from a food subgroup ≥ FBR o # Servings from a food group ≥ FBR	The Ca contents of the minimized Ca diets, which are expressed as a % of 1000 mg/day, for all FBRs tested. These values are compared.

[a]Criteria for selecting the optimized diet in each linear programming analyses.
[b]Energy requirement = 2282 kcal/day calculated using equations, assuming an average body weight of 50.4 kg and a physical activity level (PAL) of 1.85.[19]
[c]NRVs—Nutrient reference values.[18]
[d]FBRs—Food-based recommendations, which can be the number of servings per week of a specific food or from a food subgroup, or a food group.

Adjusting results to align with the 2022 Ethiopian Food-based Dietary Guidelines

To answer study objective 4 (to integrate the FBRs into the new EFBDG), the sets of FBRs selected for each target population in the Optifood analyses were adapted and integrated into the new EFBDG.[5] Initially, the food serving sizes were adapted to align with those used in the EFBDG. To do this, the energy per week recommended from individual foods, food subgroups, or food groups from the Optifood analyses was divided by the recommended energy equivalent serving sizes for foods in specific food groups as reported in the EFBDG manual.[5] These calculations resulted in an adjustment of the number of servings per week recommended for each FBR from the Optifood-derived calcium-specific sets of FBRs. Examples of the calculations for the number of servings of individual foods and food subgroups are in Supplementary Calculation SC1.

For food subgroups and food groups, a similar procedure was used except that the serving size per day was a weighted (based on the number of consumers) serving size for the food group or food subgroup, which was multiplied by the number of servings selected in the Optifood analyses. These adjusted sets of Ca-specific FBRs were then incorporated into the 2022 EFBDG. Examples of calculating the number of servings of food subgroup per day and per week using the EFBDG are in Supplementary Calculation SC2.

Sensitivity analyses

Two types of sensitivity analyses were done, which were (1) the sensitivity of model results to the energy requirements modeled and (2) the sensitivity of results to the upper constraints placed on the food item, food subgroups, and food groups. For the first type of sensitivity analysis, the PAL chosen to estimate the average energy requirements of the target population was reduced from 1.85 (moderately active; 2282 kcal/day) to 1.55 (sedentary; 1912 kcal/day), and the Module 2 analyses were rerun. For the second type of sensitivity analysis, the 75th percentiles instead of the 90th percentiles were selected to define the upper constraint levels on food subgroups and food groups. The analyses in Modules 2 and 3 were rerun by a second independent researcher and the results were compared. Consistency between the main and adjusted results would suggest relative stability of the model and low risk of bias due to parameter assumptions.

RESULTS

The number of households that have at least one WRA living in the household for urban and rural populations in each region are presented in Table 1. These numbers ranged from 288 to 4182 households, indicating that model parameters for each target population were derived from a relatively large number of households, especially in Addis Ababa, Amhara, Oromia, and Tigray, which were over 1000 households.

The maximized calcium diets (Module 3) showed it was possible to select a diet that provided 1000 mg/day of calcium for all target populations, except rural populations in Amhara and Harari and both rural and urban populations in Somali (Table 1). However, choosing a diet that achieves the Ca NRV in WRA might compromise other nutrients in the diets of urban populations in Afar and rural populations in Tigray because their nutritionally best diets (Module 2, Diet B), which are selected to come as close as possible to achieving the NRVs of 12 nutrients, did not achieve 100% of the calcium NRV.

The most common main food sources of calcium for over 50% of the target populations were teff, cows' milk, and Ethiopian kale (Table 2). Other good food sources of calcium for 5–15% of the target populations were other types of milk, wild greens, some legumes (chickpeas and kidney beans), sorghum, other composite dishes, and qocho, which is made from the starchy stem of enset (*Ensete ventricosum*) (Table 2). Similarly, the main food groups (food subgroups) for dietary calcium adequacy for Ethiopian women were dairy (milk), cereals (whole grains), vegetables (green leafy vegetables), legumes (beans), and some main meal dishes (Table S6). These results guided the selection of FBRs to test in the Module 3 analyses.

The final sets of FBRs selected for the 20 target populations on nonfasting days usually included milk or dairy products (100% of populations), teff (90% of populations), vegetables (60%), especially green leafy vegetables (85%), and legumes (60%). Small fish eaten with bones were also selected as an FBR for both urban and rural populations in Gambella, and starchy roots for populations living in Benishangul-Gumuz and SNNPR because consumption of these food items was specific to these regions (Table 3). Almost half ($n = 8$; 40%) of the target regions had at least one recommendation that met at least 65% of the Ca NRV (Table 3). In the sets of recommendations selected for fasting days, a recommendation was often incorporated into the set to increase dietary calcium that was not included in the nonfasting set ($n = 12$ target populations; 60%). These additional recommendations were vegetables ($n = 6$; 50%), green leafy vegetables ($n = 2$; 16.7%), teff/millet/whole grains ($n = 4$; 33.3%), or legumes ($n = 3$; 25%). Teff was also an important food for increasing dietary calcium adequacy because the calcium contents of the Module 3 minimized calcium diets were always much lower when teff was excluded from the set of recommendations (Table 3). Teff is more often consumed by urban than rural populations, and its consumption is low in the Somali, western Oromia, SNNPR, Gambella, and Benishangul-Gumuz regions.[24]

The integrated sets of FBRs are shown in Tables 5A and B, where the adjusted Optifood-generated Ca-specific FBRs are shown in bold italics for urban and rural populations in each region. Where the diet with current recommendations could not meet the calcium requirements, specific recommendations were made. All cases integrated well, except for legumes and vegetables, where recommendations were higher than current recommendations in some regions (urban: Addis Ababa, Benishangul-Gumuz, Dire Dawa, Gambella, Harari and Tigray; and rural: Gambella). There were also specific recommendations for either teff, green leafy vegetables, roots, whole grains, small fish eaten with bones, and milk for all regions.

DISCUSSION

Our findings indicate that it is possible to achieve recommended dietary calcium intakes for WRA using locally consumed foods in Ethiopia in eight (40%) of the target regions examined. These include the cities of Addis Ababa and Dire Dawa; both urban and rural populations in Gambella, Oromia, and SNNPR; urban populations in Tigray; and rural populations in Afar. In contrast, the use of a realistic (i.e., remained within the observed dietary pattern) food-based approach to ensure dietary calcium adequacy in both urban and rural populations in Somali, rural populations in Amhara, Benishangul-Gumuz, and Tigray and urban populations in Afar is not likely to be possible. The teff consumption in these populations was also low, consistent with previous reports,[25] as reflected in the model constraints. In Harari, the relatively high amounts of milk that could be selected partially compensated for the low amounts of teff. In the short-term for these populations, especially rural Somali, food-based intervention alone might be inadequate, and other interventions, such as calcium supplementation, are likely needed. These results reflect regional- and population-specific

TABLE 5 The calcium-specific food-based recommendations (in bold italics, and adjusted) positioned within the 2022 Ethiopian Dietary Guidelines for fasting and nonfasting day, presented for urban and rural population from each region.

A. Urban populations								
Food group **Population**	**Legumes[a]** **serves/w**	**Cereals[b] & roots[c]** **serves/w**	**Fruits[d]** **serves/w**	**Vegetables[e]** **serves/w**	**Fats & oils[f]** **serves/w**	**Nuts & seeds[g]** **serves/w**	**MFE[h]** **serves/w**	**Dairy[i]** **serves/w**
Addis Ababa Nonfasting Fasting[k] No teff	7–14 14–21 ***9–14***	21–28 C&R; ***20 teff*** 21–28 C&R; ***20 teff*** 21–28	14–21 14–21 14–21	14–21 veg; ***3 GLV***[j] ***21 veg; 3 GLV*** ***21 veg; 3 GLV***	14–21 14–21 14–21	7–21 14–21 7–21	4–9 0 4–9	4–9 dairy; ***6 milk*** 0 4–9 dairy; ***6 milk***
Afar Nonfasting No teff	7–14 7–14	21–28 C&R; ***13 teff*** 21–28	14–21 14–21	14–21 veg; ***2 GLV*** 14–21 veg; ***2 GLV***	14–21 14–21	7–21 7–21	4–9 4–9	4–9 dairy; ***4 milk*** 4–9 dairy; ***4 milk***
Amhara Nonfasting Fasting No teff	***11***–14 ***11***–21 ***11***–14	21–28 C&R; ***19 teff*** 21–28 C&R; ***19 teff*** 21–28	14–21 14–21 14–21	14–21 14–21 14–21	14–21 14–21 14–21	7–21 14–21 7–21	4–9 0 4–9	4–9 dairy; ***5 milk*** 0 4–9 dairy; ***5 milk***
Benishangul-Gumuz Nonfasting No teff	7–14 7–14	21–28 C&R; ***17 teff, 4 roots*** 21–28 C&R; ***4 roots***	14–24	***21*** ***21***	14–21 14–21	7–21 7–21	4–9 4–9	4–9 dairy; ***4 milk*** 4–9 dairy; ***4 milk***
Dire Dawa Nonfasting Fasting No teff	***7***–14 ***7***–21 ***7***–14	21–28 C&R; ***17 teff*** 21–28 C&R; ***17 teff*** 21–28	14–24 14–24 14–24	14–21 veg; ***3 GLV*** ***27 veg; 3 GLV*** ***27 veg; 3 GLV***	14–21 14–21 14–21	7–21 14–21 7–21	4–9 0 4–9	4–9 dairy; ***4 milk*** 0 4–9 dairy; ***4 milk***
Gambella Nonfasting Fasting	7–14 14–21	21–28 C&R; ***21 w/g***[l] 21–28 C&R; ***11 teff***	14–24 14–24	14–21 veg; ***8 GLV*** ***28 veg; 8 GLV***	14–21 14–21 14–21	7–21 14–21	4–9 0	4–9 dairy; ***9 milk*** 0
Harari Nonfasting No teff	7–14 ***7–14***	21–28 C&R; ***11 teff*** 21–28	14–24 14–24	***22 veg; 4 GLV*** ***22 veg; 4 GLV***	14–21 14–21	7–21 7–21	4–9 4–9	4–9 dairy; ***8 milk*** 4–9 dairy; ***8 milk***
Oromia Nonfasting Fasting No teff	7–14 7–21 ***8–14***	21–28 C&R; ***21 teff*** 21–28 C&R; ***21 teff*** 21–28	14–24 14–24 14–24	14–21 veg; ***5 GLV*** 14–21 veg; ***5 GLV*** 14–21 veg; ***5 GLV***	14–21 14–21	7–21 14–21 7–21	4–9 0 4–9	4–9 dairy; ***4 milk*** 0 4–9 dairy; ***4 milk***
SNNPR[m] Nonfasting No teff	7–14 ***9–14***	21–28 C&R; ***8 teff, 7 roots*** 21–28 C&R; ***7 roots***	14–24 14–24	14–21 veg; ***7 GLV*** 14–21 veg; ***7 GLV***	14–21 14–21	7–21 7–21	4–9 4–9	4–9 dairy; ***4 milk*** 4–9 dairy; ***4 milk***
Somali Nonfasting No teff	7–14 ***7–14***	21–28 C&R; ***14 teff*** 21–28	14–24 14–24	14–21 veg; ***1 GLV*** 14–21 veg; ***1 GLV***	14–21 14–21	7–21 7–21	4–9 4–9	4–9 dairy; ***6 milk*** 4–9 dairy; ***6 milk***
Tigray Nonfasting Fasting No teff	7–14 7–21 ***8–14***	21–28 C&R; ***21 teff*** 21–28 C&R; ***21 teff*** 21–28	14–24 14–24 14–24	14–21 veg; ***2 GLV*** ***16***–21 veg; ***2 GLV*** ***16***–21 veg; ***2 GLV***	14–21 14–21 14–21	7–21 14–21 7–21	4–9 0 4–9	***4–9*** 0 ***4–9***
B. Rural populations								
Food groups **Population**	**Legumes** **serves/w**	**Cereals & roots** **serves/w**	**Fruits** **serves/w**	**Vegetables** **serves/w**	**Fats & oils** **serves/w**	**Nuts & seeds** **serves/w**	**MFE** **serves/w**	**Dairy** **serves/w**
Afar Nonfasting No teff	7–14 7–14	21–28 C&R; ***17 teff*** 21–28 C&R; ***28 w/g***	14–21 14–21	14–21 veg; ***1 GLV*** 14–21 veg; ***1 GLV***	14–21 14–21	7–21 7–21	4–9 4–9	***16 dairy*** ***16 dairy***

(Continues)

TABLE 5 (Continued)

B. Rural populations Food groups Population	Legumes serves/w	Cereals & roots serves/w	Fruits serves/w	Vegetables serves/w	Fats & oils serves/w	Nuts & seeds serves/w	MFE serves/w	Dairy serves/w
Amhara Nonfasting Fasting No teff	*7*–*14* *7*–*21* ***12***–*14*	21–28 C&R; ***9 teff, 9 millet*** 21–28 C&R; ***9 teff, 9 millet*** 21–28	14–21 14–21 14–21	14–21 veg; ***3 GLV*** 14–21 veg; ***3 GLV*** 14–21 veg; ***3 GLV***	14–21 14–21 14–21	7–21 14–21 7–21	4–9 0 4–9	4–9 dairy; ***1 milk*** 0 4–9 dairy; ***1 milk***
Benishangul-Gumuz Nonfasting No teff	7–14 7–14	21–28 C&R; ***11 teff, 21 w/g, 2 roots*** 21–28 C&R; ***21 w/g***	14–21 14–21	14–21 veg; ***4 GLV*** 14–21 veg; ***4 GLV***	14–21 14–21	7–21 7–21	4–9 4–9	4–9 dairy; ***3 milk*** 4–9 dairy; ***3 milk***
Gambella Nonfasting Fasting No teff	7–14 14–21 7–14	21–28 C&R; ***12 teff*** 21–28 C&R; ***12 teff*** 21–28	14–21 14–21	14–21 ***22 veg; 8 GLV*** ***22 veg***	14–21 14–21	7–21 14–21 7–21	4–9 MFE; ***6 Sfish***[n] 0 4–9 MFE; ***6 Sfish***	***18 milk*** 0 ***18 milk***
Harari Nonfasting No teff	7–14 ***7–14***	21–28 C&R; ***6 teff*** 21–28	14–21 14–21	***9***–21 veg; ***4 GLV*** ***9***–21 veg; ***4 GLV***	14–21 14–21	7–21 7–21	4–9 4–9	4–9 dairy; ***6 milk*** 4–9 dairy; ***6 milk***
Oromia Nonfasting Fasting No teff	7–14 7–21 ***11***–21	21–28 C&R; ***18 teff, 18 roots*** 21–28 C&R; ***18 teff, 21 w/g*** 21–28 C&R; ***21 w/g***	14–21 14–21 14–21	14–21 14–21 veg; ***7 GLV*** 14–21	14–21 14–21 14–21	7–21 14–21	4–9 0 4–9	4–9 dairy; ***4 milk*** 0 4–9 dairy; ***4 milk***
SNNPR Nonfasting	7–14	21–28 C&R[l]; ***35 roots***	14–21	14–21 veg; ***12 GLV***	14–21	7–21	4–9	4–9 dairy; ***4 milk***
Somali Nonfasting	***7***–14	21–28 C&R[l]; ***15 w/g***	14–21	14–21	14–21	7–21	4–9	***8***
Tigray Nonfasting Fasting No teff	***11***–14 ***11–21*** ***11***–14	21–28 C&R; ***14 teff*** 21–28 C&R; ***14 teff*** 21–28	14–21 14–21 14–21	***10***–21 veg; ***2 GLV*** ***10***–21 veg; ***2 GLV*** ***10***–21 veg; ***2 GLV***	14–21 14–21 14–21	7–21 14–21 7–21	4–9 0 4–9	4–9 dairy; ***3 milk*** 0 4–9 dairy; ***3 milk***

Note: The nonfasting days in some regions are presented both with and without a recommendation to consume teff. In the regions of Afar, Benishangul, Harai, Somali, and SNNPR, the religion is predominantly Muslim and, therefore, fasting day recommendations were not included for these regions.
[a]Legumes—serving size (kcal) = 115 kcal/day.
[b]Cereals—serving size (kcal) = 300 kcal/day.
[c]Roots—serving size (kcal) = 300 kcal/day.
[d]Fruits—serving size (kcal) = 80 kcal/day.
[e]Vegetables—serving size (kcal) = 30 kcal/day.
[f]Fats & oils—serving size (kcal) = 130 kcal/day.
[g]Nuts & seeds—serving size (kcal) = 50 kcal/day.
[h]MFE—meat, fish & eggs, serving size (kcal) = 65 kcal/day.
[i]Dairy—serving size (kcal) = 90 kcal/day.
[j]GLV—green leafy vegetables.
[k]Fasting refers to intermittent fasting, which is the same value as continuous fasting except for legumes (21–28 instead of 14–21) and nuts and seeds (14–42 instead of 14–21).
[l]w/g—whole grains.
[m]Southern Nations, Nationalities, and Peoples' Region.
[n]Sfish—small dried fish eaten with bones.

differences in food patterns, including the types and quantities of food consumed, as recorded in the EHCES data used to define the model parameters.

The FBRs do, however, rely on teff being recommended in relatively high amounts (Table S7). The final sets of FBRs selected for the 20 target populations on nonfasting days usually included milk or dairy products, teff, vegetables (especially green leafy vegetables), and legumes as well as small fish eaten with bones for populations in Gambella, and starchy roots for populations living in Benishangul-Gumuz and SNNPR. In the sets of recommendations selected for fasting periods/days, the minimized calcium content for these sets of recommendations were always lower than when animal-sourced foods were included, because milk or dairy products and small fish eaten with bones are excellent food sources of calcium.[16,26]

Our findings highlight that the calcium-specific FBRs selected through these analyses integrate well into the 2022 EFBG general set of 11 key messages for the public to improve population health.[5] However, increasing intakes of selected foods (e.g., teff), and foods from specific food subgroups (e.g., milks) or food groups (e.g., dairy) are necessary to improve the nutrient adequacy of WRA diets in Ethiopia. The calcium-specific adjustments, depending on the target population, will encourage the consumption of green leafy vegetables (ranging from 1 to 7 servings per week) within the key message to *consume vegetables*, encourage the consumption of teff (ranging from 8 to 20 servings per week) within the key message to *consume whole-grain cereals*, and encourage the consumption of milk (ranging from 3 to 18 servings per week) within the key message to *consume dairy products*. For two populations (rural Afar and rural Gambella), they would also encourage a slightly higher consumption of milk or dairy products than are currently specified in the 2022 EFBG messages. Conversely, our findings also indicate that some EFBDG recommendations are not critical for dietary calcium adequacy, including recommendations for fruits, fats and oils, nuts and seeds, and meat, fish, and eggs, except for small fish eaten with bones in Gambella. The recommendation for nuts and seeds, however, could be important for improving dietary calcium intakes, especially in populations where sesame seeds are widely consumed, given the high calcium content of sesame seeds.[27] Nonetheless, these seeds were not selected in the Optifood analyses because the number of households in which they were reported as consumed were generally low (<5%). If the consumption levels of calcium-rich nuts and seeds, however, could be increased through supportive agricultural interventions to increase their availability and/or decrease their costs, then these food items should be included in sets of Ca-specific FBRs for WRA. The current analyses were restricted to food items that were reported as commonly consumed in households from each target population.

These considerations underscore the importance of fully testing sets of FBRs before promoting them, using methods such as Trial of Improved Practices and expert consultation.[28,29] Cereal grains are widely consumed in many regions of Ethiopia, providing 60–70% of energy intakes in some regions.[30] In these cereal-consuming areas, dietary calcium adequacy will be driven by variations in the types of cereals consumed and the grain's mineral concentration, especially teff, because the grams of cereals consumed are substantially higher than the grams of dairy products consumed. Our analyses clearly highlight the importance of teff for improving dietary calcium intakes of rural and urban WRA in Ethiopia. Teff is a small-grained gluten-free cereal crop that was domesticated in the Horn of Africa and is a staple food in much of Ethiopia and Eritrea.[30,31] It is an important crop for generating income and is mainly consumed as injera, a traditional fermented flat-bread.[30] There are 12 different varieties of teff, which have been divided into three categories—white, red, and mixed—where red teff typically contains the highest calcium concentration.[30] A recent national survey of crop elemental composition in Ethiopia determined a median calcium concentration in teff grain of 147 mg/100 g ($n = 362$), which was substantially greater than wheat (42 mg/100 g; $n = 325$), barley (41 mg/100 g; $n = 175$), sorghum (18 mg/100 g; $n = 135$), and maize (6 mg/100 g, $n = 290$), although lower than finger millet (461 mg/100 g; $n = 37$).[23,24] As with other whole grains, teff contains high amounts of phytates that can affect the bioavailability of calcium.[32] However, food processing techniques such as fermentation and cooking help break down phytates before consumption.[32] Oxalates, present in high amounts in spinach, are similar to phytates in that they inhibit calcium absorption, but cooking methods such as boiling help reduce them.[33] Previous studies show that teff is more often consumed by urban than rural populations due to its availability and increasing price.[25,34] Its consumption is low in Somali, SNNPR, Gambella, Benishangul-Gumuz, and western Oromia regions.[1] The price of teff is higher than other grains; however, monitoring of teff's food value chain is limited.[25,34,35] Its intake is also lower compared with other grains in some regions. Increasing the promotion of the nutritional advantages of consuming teff through FBRs might help to increase consumption in the population.

Adherence to FBRs in regions where calcium levels can be achieved should reduce the number of WRA at risk of inadequate calcium intakes; however, the recommendations need to be affordable, accessible, and acceptable.[8,36] We did not model the price of food items in these analyses, but with the potential rise in prices of some of the foods with higher calcium content, government strategies may be needed to increase the production and reduce the purchase prices of these foods. For example, farming input subsidies or subsidizing the cost of calcium-rich food items might increase the availability and affordability of these foods.[37,38] It is recommended that appropriate health promotion strategies are also developed to encourage their consumption.[39]

In regions where adequate calcium FBRs are not possible, other strategies such as supplying local high-calcium foods, calcium-fortified foods, and supplementation are necessary.[8] Iron and folic acid (IFA) supplements are provided to women in Ethiopia attending antenatal clinics.[40] Research has indicated that the addition of calcium supplements would be acceptable, but implementation should consider lessons learned from IFA supplement programs.[40]

Previous studies have shown that 89–96% of WRA in Ethiopia are at risk of inadequate calcium intakes.[41] Such low intakes are of concern because they increase the risks of pre-eclampsia, which cause an estimated 16% of maternal deaths in Ethiopia.[41] In addition to pregnancy risk factors, chronic low intakes of calcium can increase the risk of osteoporosis. Definitive figures for osteoporosis are limited for Ethiopia, though there are an estimated 7.3 million cases.[42] During pregnancy and lactation, a loss of 3–5% of maternal calcium stores can occur.[43] This loss is usually compensated by calcium homeostasis where more dietary calcium is absorbed,[43] although the increase in calcium absorption is not possible if the calcium intake is below 500 mg/day.[43] Short birth spacing can also hinder the calcium stores returning to normal.[44] The WHO recommends birth spacing of more than 2 years; however, birth spacing is often less than this in Ethiopia.[45,46] Furthermore, the median age for first-time mothers is 18.7 years, which also compromises the calcium stores as peak bone mass has not yet been reached.[44,46] Vitamin D deficiency, impacting intestinal calcium absorption, is also increasing in WRA in Ethiopia.[47,48] These additional risk factors highlight the importance of increasing the intakes of calcium during pregnancy in Ethiopia.

Strengths and limitations

The main strength of this study was the inclusion of populations that were representative of both urban and rural geographic regions in Ethiopia to set model parameters and that it explicitly considered fasting. Routinely collected EHCES data informed the types and amounts of locally consumed foods.[9] Setting up the parameters within Optifood is time-consuming; however, once this is complete, the analyses are quick to run. Therefore, comparable analyses could be run for other micronutrients in the same target populations. Another unique strength of this study was that the findings were integrated into the new EFBDG, which will ensure consistent recommendations are included in educational materials developed to improve dietary calcium intakes.

We also recognize the limitations of this study. First, the model parameters were derived from 7-day EHCES data, which assumes equal intrahousehold food distribution based on the estimated average energy requirements of individual household members. Second, the respondents were asked to recall the quantities of food consumed for the past 3 and 4 days, which is prone to recall bias. Despite these limitations, the results showed some agreement with the modeling results done to inform the development of the 2022 EFBDG.[28] Similar to the current study, the study by Bekele et al. also identified the importance of increasing milk and dairy products for improving dietary adequacy among WRA in Ethiopia.[6] However, differences in the modeling approach they used and the nutrients modeled would at least partially account for the differences in the results. Another limitation in the current analyses is that only the total calcium content of modeled foods was estimated, rather than bioavailable calcium, which might be low in some of the foods selected.[49] The selection of specific FBRs to improve dietary calcium intakes for WRA, especially during pregnancy, using diet modeling is somewhat subjective given there are often several options to select from. Lastly, price analysis was not included in the modeling as it was beyond the scope of this study.

CONCLUSION

In conclusion, the analyses undertaken in this project have shown that a food-based approach can be used to achieve dietary calcium adequacy among WRA in eight target populations examined, and to improve dietary calcium adequacy in the other populations. For the other populations, food-based interventions alone may be inadequate and other interventions are likely needed. These recommendations can be integrated into messages recommended in the 2022 EFBDG. To improve dietary calcium adequacy among WRA and reduce risks of complications in pregnancy, it will require changes to the average food consumption in most areas of Ethiopia, although the sets of recommendations selected remain within the range of food patterns observed in each region. The sets of recommendations identified through these analyses can be used to inform the development of Ethiopian-specific educational materials, job aids, and policy briefs for promoting improved dietary calcium intakes of urban and rural Ethiopian WRA in different regions of Ethiopia.

AUTHOR CONTRIBUTIONS

Z.H.R., F.G., E.L.F., E.L.A., and E.J.M.J. conceptualized the project. E.L.F. conceptualized the analyses, K.T. did the EHCES analysis, H.D.-K. and E.L.F. did the Optifood analyses., S.M.S. and D.G. consulted on the findings of the analysis, H.D.-K. and E.L.F. wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version.

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COMPETING INTERESTS

The authors declare no competing interests.

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Note

[a] The 90th and 10th percentiles were used as upper and lower constraints, respectively.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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