AJCN. First published ahead of print October 22, 2014 as doi: 10.3945/ajcn.114.090670.

A comprehensive linear programming tool to optimize formulations of ready-to-use therapeutic foods: an application to Ethiopia[1–4]

Kelsey N Ryan, Katherine P Adams, Stephen A Vosti, M Isabel Ordiz, Elizabeth D Cimo, and Mark J Manary

ABSTRACT

Background: Ready-to-use therapeutic food (RUTF) is the standard of care for children suffering from noncomplicated severe acute malnutrition (SAM).

Objective: The objective was to develop a comprehensive linear programming (LP) tool to create novel RUTF formulations for Ethiopia.

Design: A systematic approach that surveyed international and national crop and animal food databases was used to create a global and local candidate ingredient database. The database included information about each ingredient regarding nutrient composition, ingredient category, regional availability, and food safety, processing, and price. An LP tool was then designed to compose novel RUTF formulations. For the example case of Ethiopia, the objective was to minimize the ingredient cost of RUTF; the decision variables were ingredient weights and the extent of use of locally available ingredients, and the constraints were nutritional and product-quality related.

Results: Of the new RUTF formulations found by the LP tool for Ethiopia, 32 were predicted to be feasible for creating a paste, and these were prepared in the laboratory. Palatable final formulations contained a variety of ingredients, including fish, different dairy powders, and various seeds, grains, and legumes. Nearly all of the macronutrient values calculated by the LP tool differed by <10% from results produced by laboratory analyses, but the LP tool consistently underestimated total energy.

Conclusions: The LP tool can be used to develop new RUTF formulations that make more use of locally available ingredients. This tool has the potential to lead to production of a variety of low-cost RUTF formulations that meet international standards and thereby potentially allow more children to be treated for SAM. *Am J Clin Nutr* doi: 10.3945/ajcn.114.090670.

Keywords RUTF, formulation, linear programming, optimization, severe acute malnutrition

INTRODUCTION

Ready-to-use therapeutic food (RUTF)[5] has saved the lives of untold thousands of children suffering from severe acute malnutrition (SAM) over the past decade. This shelf-stable, ready-to-eat, complete diet is the WHO standard of care for treatment of noncomplicated SAM (1, 2) and has the benefit of being administered in the home. The standard RUTF is a peanut-based paste with added oil, milk or whey powder, sugar, a micronutrient premix, and an emulsifier; 50% of the protein should come from dairy ingredients. In 2007, nutritional specifications for RUTF were published (1), and international entities that purchase RUTF set additional quality and microbiological requirements.

The demand for RUTF to treat SAM in developing countries is increasing (3). Most RUTFs are produced in developed countries, and almost all consist of the standard RUTF formulation. There have been attempts to improve RUTF formulations, most of which have focused on ingredients of special interest to the investigators or on efforts to reduce cost (4–9). Thus, most research has used a small number of ingredients available in a specific geographic region, limiting innovation. Linear programming (LP) has been used to develop therapeutic and supplementary foods for developing countries to minimize the cost of a product that meets a given nutritional standard or to maximize nutritional value of a product given a cost constraint (6, 9, 10).

The objective of this research was to develop a comprehensive candidate ingredient, nutrient, and price database and to integrate that database into a user-friendly, publically available LP tool. The LP tool was designed to identify low-cost optimal ingredient combinations for RUTF that *1*) meet RUTF nutrient requirements of the joint United Nations agency statement, *2*) can be produced in a full-scale production facility, and *3*) are acceptable to consumers. An example of applying the LP tool to develop new RUTF formulations for Ethiopia using local and imported ingredients is presented.

MATERIALS AND METHODS

Overview

A comprehensive database of all potential RUTF candidate ingredients was compiled, along with quantitative information

[1] From the Department of Pediatrics, Washington University School of Medicine, St. Louis, MO (KNR, MIO, EDC, and MJM), and the Department of Agricultural and Resource Economics, University of California, Davis, Davis, CA (KPA and SAV).

[2] Supported by the Children's Investment Fund Foundation.

[3] Supplemental Figure 1 and Tables 1–3 are available from the "Supplemental data" link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

[4] Address correspondence to M Manary, Department of Pediatrics, St. Louis Children's Hospital, One Children's Place, St. Louis, MO 63110. E-mail: manary@kids.wustl.edu.

[5] Abbreviations used: AOAC, Association of Official Analytical Chemists; LP, linear programming; RUTF, ready-to-use therapeutic food; SAM, severe acute malnutrition.

Received April 23, 2014. Accepted for publication September 24, 2014.
doi: 10.3945/ajcn.114.090670.

regarding the nutrient content, food-safety properties, and geographic availability of each ingredient (**Figure 1**). Ingredients deemed unsuitable for incorporation in RUTF were removed to create a database of candidate ingredients. Linear optimization was used to select a minimum-cost combination of ingredients from the candidate ingredients that met all nutrient and safety requirements of RUTF, as defined by the WHO (1). Multiple candidate RUTF formulas were created by varying the constraints of the optimization problem and assumptions applied to the database. The assumptions were applied with the understanding that these RUTF formulations were to be targeted to Ethiopia. The formulations for Ethiopia were then prepared in our food formulation laboratory. Each prepared formulation was screened for taste, texture, and viscosity. From this group of candidate Ethiopian RUTF formulations, 4 were chosen for further testing.

Ingredient database

A comprehensive list of global candidate ingredients was compiled by combining those identified in the Food and Agricultural Organization of the United Nations, Statistics Division Database (FAOSTAT) database (http://faostat3.fao.org/faostat-gateway/go/to/home/E), in country-specific food composition tables, and via communication with in-country collaborators and the project's Scientific Advisory Committee. The list included all identified cereals, legumes, seeds, nuts, and edible oils. For 12 countries with many children with SAM (Ethiopia, Ghana, Pakistan, India, Cambodia, Bangladesh, Nigeria, Sierra Leone, Malawi, Mozambique, Niger, and Laos), country-specific agricultural reports, including FAOSTAT reports, were used to identify commonly consumed ingredients. Food composition tables from these countries were reviewed and used to further augment the candidate ingredient database. Care was taken to include ingredients rich in MUFAs and PUFAs (i.e., oils with $<20\%$ saturated fat), bioavailable calcium and phosphorus (from animal ingredients), and ingredients containing large fractions of high-quality protein (plant proteins with known complete amino acid profiles and animal protein). Each country-specific list was sent to local nutritionists for review, and any omissions identified were added to the database.

Exclusion of ingredients incompatible with RUTF was done using a 2-step approach. For example, meats (other than fish), insects, highly perishable ingredients, ingredients with a high moisture content, and ingredients with a high risk of harboring potential pathogens were excluded from the database in the first step (**Supplemental Figure 1**). Potential RUTF producers may not have refrigerated storage, so only ingredients that can be stored at ambient conditions for $\geq$6 mo were considered viable candidate ingredients (11–16). Dried fish were included because of the interest of using fish as an animal source of protein, fat, and minerals, and because fish is available and commonly consumed in many developing countries, it may be acceptable in RUTF (17). Fish processing costs, such as drying and grinding, were included in the ingredient cost; these processing methods may reduce microbiological contamination. In the second step of the ingredient screening process, duplicate entries, entries further classified as perishable, and ingredients with limited or no nutrient information were excluded.

All candidate ingredients were added to a food composition table, and relevant nutrition information was collected from the following sources (in order of preference): U.S. Department of

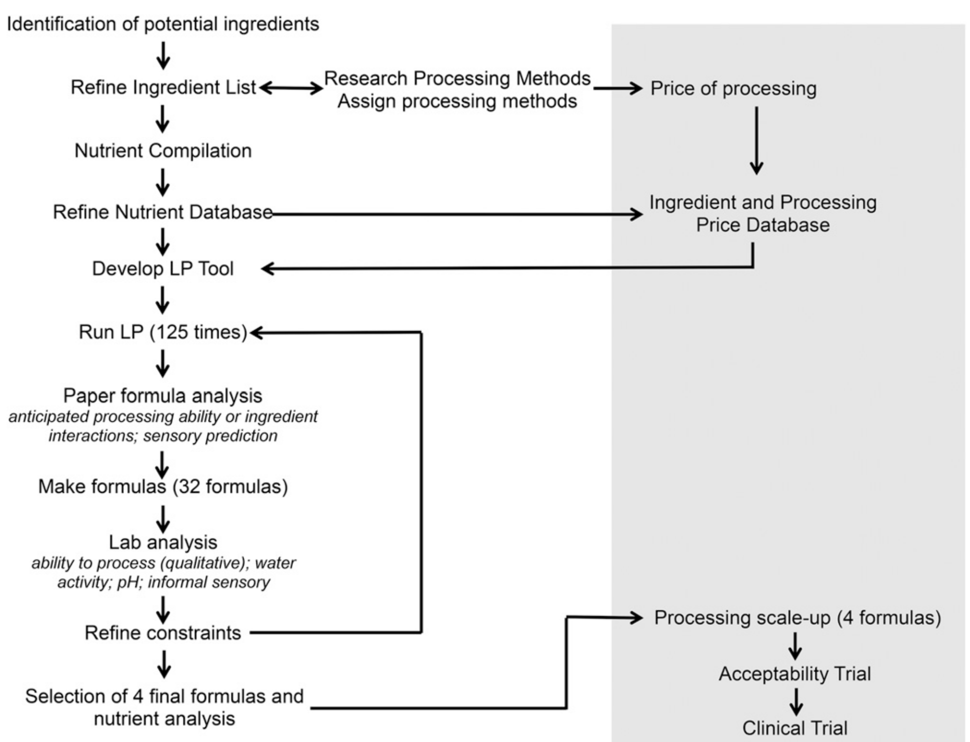

FIGURE 1 Method used to create the LP tool and how it was used to formulate ready-to-use therapeutic food for Ethiopia. The gray box highlights methods and data that are not presented in this article. LP, linear programming.

Agriculture National Nutrient Database (2012), West African Food Composition Table (2012), Tanzania Food Composition Tables (2008), and the food and nutrition literature. For some ingredients, specific nutrient information could not be found. In these cases, nutrient information for a similar ingredient was substituted (e.g., pumpkin seed for generic melon/squash seed). We assumed that the nutrient content was not changed by processing. The nutrient contents of some ingredients were calculated from component or similar foods. Some fatty acid assignments for oils, for example, were made based on the fatty acid composition of the whole seed from which the oil is derived.

Imported ingredient prices were identified by consulting international trade resources or ingredient suppliers, and oceanic and overland transport costs were estimated and added to the LP model. Local ingredient prices for 2012, where "local" in the Ethiopia case is defined as having 500 metric tons or more of a given candidate ingredient available, whether nationally produced or imported, in the Addis Ababa market area (the expected locale of RUTF production), were identified by using a 4-step approach. First, for major basic grains, monthly average wholesale prices from the Ethiopian Grain Trade Enterprise for the Addis Ababa market area were used to generate unweighted average 2012 annual prices. Second, 2012 annual wholesale prices from multiple secondary sources were used to fill gaps. Third, 2012 FAO commodity price data were used to estimate prices for imported commodities, for example, white rice in the Ethiopia case. Fourth, final ingredient price gaps were filled by collecting retail prices in late 2013 and adjusted for inflation (using a food price deflator) and a wholesale/retail mark-up. Estimated processing costs (extrusion, roasting, milling, and grinding) were gathered from millers in the Addis Ababa area and were added to raw ingredient prices.

Linear programming

LP is a mathematical technique used to minimize or maximize a linear objective function subject to a set of constraints (18). Many objective functions can be chosen, for example, minimizing or maximizing a particular nutrient, minimizing cost, or maximizing the proportion of local ingredients chosen. In this exercise, the LP tool was configured to choose ingredient weights to minimize the total cost per 96-g unit of RUTF (the objective function) while meeting a set of nutrient-composition constraints [as specified by the WHO (1) for RUTF], food quality requirements, and a targeted amount of locally available ingredients (**Table 1** and **Supplemental Table 1**). Food quality refers to taste and processing considerations unrelated to safety and nutritional quality. The free Microsoft Excel add-in Solver (Frontline Systems Inc.) was used to find optimal formulations.

All required (Supplemental Table 1) macronutrients, including $n-3$ and $n-6$ fatty acids and protein from dairy ingredients, were included as constraints in the optimization problem because these nutrients must come from food ingredients. Calcium and phosphorus constraints were included because these minerals may be better absorbed from certain complex food matrices, rather than inorganic salts (20, 21). Phosphorus from plant ingredients was multiplied by 0.3 to estimate bioavailable, nonphytate phosphorus from plants (19). A maximum sodium concentration was included to limit ingredients with added salt in the formulation and thereby ensure that the formulation met international standards. The only antinutrient included in the model was fiber, because it is the only antinutrient specified by UNICEF for RUTF (22).

Sugar and peanut constraints were added as optional food quality constraints based on previous research (6) and initial LP tool experimentation. Levels of nutrients contained in selected formulas were constrained to be within UNICEF-specified ranges (**Supplemental Table 2**). The total weight of the formulation from ingredients included in the database was set at 96 g to allow for 4 g ingredients from a micronutrient premix and stabilizer/emulsifier. A constraint on the fraction of the formulation sourced from locally available ingredients (where "local" was defined as a product available in the country in quantities sufficient for medium-scale production) was also included (Supplemental Table 2).

For Ethiopia, local ingredients and a set of imported ingredients with unique nutrient properties were selected as candidate ingredients (**Supplemental Table 3**). Candidate imported ingredients included animal proteins (e.g., dried milk ingredients and dried eggs), high-MUFA or -PUFA ingredients (e.g., olive oil and canola oil), and specialty ingredients particularly high in $n-3$ fatty acids (e.g., fish oil and fish oil powder). Common nutritional paste ingredients (e.g., soybeans and nonfat dry milk) and functional ingredients (e.g., palm oil) were also included as imported ingredients if they were not available in Ethiopia (Supplemental Table 3).

Many iterations were run using the LP tool for Ethiopia to establish proof-of-concept for the tool, to learn about the capabilities of the tool, and to identify formulations that were acceptable in terms of viscosity, taste, and feasibility of preparation in the laboratory (Figure 1; Supplemental Table 2). The multiple iterations tested different combinations of ingredients, nutrients, and quality constraints. Examples of iterations were as follows: *1*) including and excluding calcium, phosphorus, and/or bioavailable phosphorus constraints (because these can be added in a micronutrient premix); *2*) including, excluding, and varying the level of the local ingredient constraint; and *3*) including, excluding, and varying the food-quality constraints. In addition, the candidate ingredient list was varied from iteration to iteration for experimental purposes to see what ingredients were selected when one candidate ingredient was excluded (Supplemental Table 2). Each of the formulations was assessed for feasibility of mixing in the laboratory and predicted feasibility of mixing in full-scale production. Qualitative questions, such as "Can this formulation be mixed with a counter-top mixer? A food processor? A blender?" and "Is it predicted that this product can be mixed in a bakery mixer? Ribbon blender? Other mixing equipment?" were answered for each formulation. Other factors assessed qualitatively were antinutrient contribution, anticipated ingredient interactions, and sensory prediction. On the basis of these assessments, 32 formulations were prepared in the laboratory. All 32 prepared formulations were then tasted informally by individuals familiar with RUTF. Basic tastes were rated informally on a 9-point hedonic scale, and a just-about-right scale was used to rate sweetness, saltiness, viscosity, and texture by an untrained panel of adults with experience working in food aid projects in sub-Saharan Africa.

The 4 most promising formulations were chosen for pilot-level scale-up (**Table 2**, Figure 1). The users of the LP tool will be individuals with food, food technology, and nutrition experience

TABLE 1
Default least-cost optimization model constraints

Constraint	Instruction to user	Default value
Food ingredient weight	Enter total weight, g	96
Local ingredients[1]	Enter minimum percentage of ingredient weight sourced from locally available ingredients	
From UNICEF RUTF[2] requirements		
Energy	Enter minimum total energy, kcal	520
	Enter maximum total energy, kcal	550
Total protein	Enter minimum target percentage of energy from protein, %	0.1
	Enter maximum target percentage of energy from protein, %	0.12
	Enter minimum target percentage of weight from protein, %	0.13
	Enter maximum target percentage of weight from protein, %	0.16
Lipid	Enter minimum target percentage of energy from lipids, %	0.45
	Enter maximum target percentage of energy from lipids, %	0.6
	Enter minimum target percentage of weight from lipids, %	0.26
	Enter maximum target percentage of weight from lipids, %	0.36
n−6 Fatty acids	Enter minimum target percentage of energy from n−6 fatty acids, %	0.03
	Enter maximum target percentage of energy from n−6 fatty acids, %	0.1
n−3 Fatty acids	Enter minimum target percentage of energy from n−3 fatty acids, %	0.003
	Enter maximum target percentage of energy from n−3 fatty acids, %	0.025
Carbohydrate	Enter minimum target percentage of product weight from carbohydrates, %	0.41
	Enter maximum target percentage of product weight from carbohydrates, %	0.58
Sodium	Enter maximum sodium content, mg	290
Calcium	Enter minimum calcium content, mg	0
	Enter maximum calcium content, mg	600
Phosphorus	Enter minimum phosphorus content, mg	0
	Enter maximum phosphorus content, mg	600
Bioavailable phosphorus[3]	Enter minimum bioavailable phosphorus content, mg	0
	Enter maximum bioavailable phosphorus content, mg	600
Dairy protein[4]	Enter minimum percentage of protein from dairy sources, %	0.5
Fiber content	Enter maximum percentage of ingredient weight from fiber, %	0.05
Additional quality constraints		
Sugar	Enter minimum percentage of ingredient weight from sugar	
Groundnuts	Enter minimum percentage of ingredient weight from groundnuts	
Dairy sugar[4]	Enter maximum percentage of sugar from dairy sources	

[1]Local ingredients are defined as those available in the country in quantities sufficient for medium-scale production.
[2]RUTF, ready-to-use therapeutic food.
[3]Bioavailable phosphorus was estimated by multiplying plant ingredients by 0.3 (19).
[4]Ingredients were classified as dairy ingredients in the database.

and individuals with a basic understanding of RUTF and spreadsheet-based optimization programs. After further testing by individuals not a part of the research team, the tool will be available for public use, and a detailed user's manual will accompany it.

Preparation of the formulations

Formulations were prepared in the Principal Investigator's food-preparation laboratory at Washington University in St. Louis. Grains and legumes that had to be extruded were instead cooked and dried to mimic extrusion processing. A portion of the oil in the formulation and all of the powdered lipid emulsifier (2% wt:wt) were melted to 64°C on a stirring hot plate. This mixture and the remaining oil and seed and/or legume ingredients at room temperature (22°C) were added to a food processer (RobotCoupe Blixer 4V) and mixed for 1 min at 300 rpm. The remaining (dry) ingredients, including 2% wt:wt of a generic micronutrient premix, were mixed with the liquid/oil ingredients for 2 min at 300 rpm with a scrape-down step after 1 min; additional mixing in 1-min intervals and at higher speeds was done as necessary, depending on the ingredients included in the formulation. The final temperature was between 35 and 45°C. Prepared formulations were stored in plastic, air-tight containers and allowed to cool to 22°C for subsequent analysis.

Analysis of formulations

After 24 h, water activity and pH were measured at 22°C, and an informal sensory analysis was conducted. Laboratory

TABLE 2
Weight of linear programming tool-selected ingredients and ingredient cost for 4 Ethiopia formulations and the current RUTF formulation[1]

Ingredient name	Fish/ pumpkin seed	Peanut/pea/ pumpkin seed	Oat/ peanut	Millet	Current RUTF
Cereal/grain, g					
Maize, white, flour of whole grain	—	3.3	—	—	–
Millet, pearl, whole grain, raw	—	—	—	17.8	–
Oats		—	1.9	—	–
Teff	3.6	—	—	—	—
Fish, dried, average, includes small bones, g	4.9	—	—	—	—
Legume, g					
Groundnut, shelled, dried, raw	—	10.0	10.0	—	27.0
Peas	—	7.7	—	—	—
Soybeans	—	—	6.5	12.7	—
Milk, acid whey powder, g	—	—	14.4	8.9	—
Oil, g					
Canola, rapeseed	2.9	1.1	11.6	—	—
Palm	22.8	22.8	15.5	25.3	15.8
Soybean	1.0	0.2	—	4.4	2.9
Seed, pumpkin, g	13.6	9.3	—	—	—
Sugar, g					
Brown	—	7.7	—	20.0	—
White	25.0	12.3	20.0	—	26.0
Milk, g					
Whey protein concentrate 34[2]	22.3	21.4	10.5	—	—
Whey protein concentrate 80[2]	—	—	5.5	6.9	—
Dry, nonfat, regular, without added vitamin A and vitamin D	—	—	—	—	25.0
Total, g	96.0	96.0	96.0	96.0	96.75
Ingredient cost, $/96 g	0.119	0.115	0.125	0.104	0.210

[1]RUTF, ready-to-use therapeutic food.
[2]Number indicates percentage protein in the whey protein ingredient.

analysis was performed by an accredited outside laboratory for protein [combustion; Association of Official Analytical Chemists (AOAC) 990.03; AOAC 993.15], lipid (acid hydrolysis; AOAC 954.02), moisture (vacuum oven; AOAC 925.09), ash (AOAC 942.05), carbohydrate [calculated by difference (23)], and total energy (bomb calorimeter; Parr Instruments). The relative difference between the LP tool calculated values, and the laboratory-analyzed values were calculated according to Dibari et al. (6).

RESULTS

From the 476 potential candidate ingredients, 204 were included for the Ethiopia database (Supplemental Figure 1). In the context of Ethiopia, 83 ingredients were excluded because the 6-mo shelf stability was unlikely (e.g., fruit and vegetables and raw meats); for 38 other ingredients, nutrient data could not be found, which suggested that these were rare ingredients (Supplemental Figure 1). Of the 204 final database ingredients, local price analysis identified 30 Ethiopian ingredients meeting the criterion of being locally available. An additional 31 imported ingredients were included. In total, 125 iterations using the LP tool were performed (Figure 1) with varying constraints and ingredient exclusions for experimental interest. On the basis of these findings, adjustments to the LP tool were made to reduce the number of iterations for future users. Adjustments to the LP tool included adding individual ingredient constraints so that specific ingredients, such as the often-acceptable peanuts or palm oil—a solid fat with reduced oil separation—could be included in formulations if desired. Depending on the constraints set and the set of candidate ingredients, the LP tool selected a variety of cereals and legumes and a variety of dairy ingredients and fish as the optimal combination of ingredients (Table 2). The minimum calcium, phosphorus, and bioavailable phosphorus constraints were set at either 0 or 300 mg/100 g, and the quality constraints of sugar and groundnuts ranged from 20% to 25% and 0% to 10%, respectively. The range of sugar was selected to be equal to or somewhat lower than current peanut RUTF formulation and similar to that used by Dibari et al. (6). For experimental purposes, butter, dried-egg ingredients, a specialty calcium rice chelate, Niger seed, millet, soybeans, reduced lactose whey, acid whey, and dried fish were excluded from the set of candidate ingredients in some iterations (Supplemental Table 2). A lactose constraint was included in some optimization models as a way to limit total dairy ingredients, because on organoleptic testing it was determined that dairy confers an adverse taste.

A total of 32 formulations were selected for preparation based on their predicted production feasibility and organoleptic acceptability. All formulations formed pastes or semiliquid colloidal suspensions. Four formulations were chosen for further analysis based on palatability and a variety of ingredients: fish/pumpkin seed, peanut/pea/pumpkin seed, oat/peanut, and millet RUTF (Table 2). Note that, for simplicity, only one variety of fish was included as a candidate ingredient, and the nutrient

TABLE 3
Nutrient composition (per 100 g) of linear programming tool-selected formulations for Ethiopia

	Fish/pumpkin seed			Peanut/pea/pumpkin seed			Oat/peanut			Millet		
	Tool calculated	Laboratory analyzed	Relative difference, %	Tool calculated	Laboratory analyzed	Relative difference, %	Tool calculated	Laboratory analyzed	Relative difference, %	Tool calculated	Laboratory analyzed	Relative difference, %
Energy, kcal	520	592	14	520	603	16	520	596	15	520	592	13.8
Lipid, g	34.3	36.3	5.8	34.5	36.3	5.1	34.2	34.9	1.9	33.9	33.4	−1.4
Protein, g	15.0	14.9	−0.7	15.0	14.9	−0.8	15.0	15.4	2.7	13.0	13.5	4.0
Carbohydrate, g[1]	41.0	41.8	2.0	41.0	43.9	7.1	41.0	44.4	8.4	41.7	48.2	15.7
Water, g	2.9	2.5	−13.8	3.0	1.0	−67.1	2.3	1.3	−43.5	2.8	1.5	−46.4
Ash, g	2.7	4.5	66.7	2.2	3.9	75.2	3.0	4.0	33.7	2.2	3.3	51.4
Energy calculated, kcal[2]	—	554	6	—	562	8	—	553	6	—	548	5

[1]Calculated and laboratory-analyzed nutrient composition from one replication analyzed by an outside accredited laboratory. Carbohydrate calculated for laboratory-analyzed samples [ash, lipid, protein, and water (g) subtracted from 100 g (23)].

[2]Energy calculated from laboratory-analyzed protein, carbohydrate, and lipid. Energy (kcal) = (g protein × 4) + (g carbohydrate × 4) + (g lipid × 9) (23); relative difference comparison was between the laboratory-analyzed calculated energy value and the tool calculated energy value.

information was taken from an average fish nutrient data source as opposed to the specific fish species. When the LP tool is used in the future, the best nutrient data for the specific species of fish might well be used. These formulations contain more ingredients than the current RUTF. The nutrient content of each formulation, as calculated by the LP tool, falls within the specified ranges (e.g., **Table 3** and **Table 4**). The macronutrient contents (lipid, protein, and carbohydrate) were similar to the calculated macronutrient values, with <10% difference except for carbohydrate in the millet RUTF (Table 3). All of the macronutrients fell within specifications (22) (Supplemental Table 1).

Total energy, as determined by bomb calorimetry, was consistently greater than the LP tool-predicted energy content; however, all energy measured by this method is not bioavailable (Table 3). The concentrations of ash and water vary, but these values were not confirmed in the nutrient database and were not used in the optimization step and, thus, should not be predicted by the LP tool. It is counterproductive to use these values in optimization unless the correct values are known; moisture content (water) can vary dramatically depending on the original extent of drying and storage conditions, and ash can vary depending on crop growing conditions. The 4 chosen formulations were less expensive than the standard international RUTF formula when total ingredient price was calculated by using the LP tool (Table 2).

DISCUSSION

The LP tool successfully identified new RUTF formulations that were feasible to prepare and found acceptable on preliminary organoleptic screening. This novel, robust LP tool—developed by using insight from the fields of food science, nutrition, and economics—proved to be a functional and reliable method to compose new RUTF formulations that meet international specifications when applied to Ethiopia.

The primary limitation of this work was the accuracy of the assumptions that were made in creating the candidate nutrient database and in identifying prices for candidate ingredients and their transport and processing. This limitation was mitigated by use of validated databases and authoritative sources. We will continue to investigate the validity of our assumptions and update the LP tool accordingly.

Even if the LP tool is constructed with the best information, a successful RUTF formulation requires several subsequent steps. A nutrient analysis is required on final formulations, as are acceptability trials with target consumers—children. Ingredient prices need to be verified for the target market. Formulation-specific fixed production costs, such as quality-control expenses, need to be assessed. A micronutrient premix needs to be custom designed, taking into consideration the micronutrients in the selected ingredients. A standardized micronutrient premix could be investigated that is suitable for addition to various formulations of local RUTF. The LP tool suggests possible formulations for RUTF, but any possible formulation requires acceptability and effectiveness testing before its wide-scale adoption.

LP has been used previously for dietary recommendations and food formulation. LP has been used to investigate whether local foods are adequate to meet nutrient requirements for

TABLE 4
Nutrient composition of linear programming tool-selected formulations for Ethiopia[1]

	Fish/pumpkin seed	Peanut/pea/ pumpkin seed	Oat/peanut	Millet	Minimum[2]	Maximum[3]
Locally available weight, g	50.0	51.5	50.0	50.5		
Dairy protein, g	7.8	7.5	9.7	6.5		
Fiber, g	1.2	3.7	1.7	2.9		5.0
Calcium, mg	300.0	139.9	416.2	281.9	300.0	600.0
Phosphorus, mg	391.3	300.0	365.2	275.4	300.0	600.0
Bioavailable phosphorus, mg	268.3	170.7	300.0	185.4		
n−3 Fatty acids, % of total energy	0.7	0.3	2.0	0.9	0.3	2.5
n−6 Fatty acids, % of total energy	10	10	10	10	3	10
pH	6.18	6.10	6.19	6.23		
Water activity	0.42	0.33	0.19	0.17		0.6

[1]Values are calculated nutrient composition and other parameters. RUTF, ready-to-use therapeutic food.
[2]Minimum value from UNICEF RUTF requirements.
[3]Maximum value from UNICEF RUTF requirements.

treatment of SAM and to identify limiting nutrients in local diets (24–26). It has also been used to design fortified complementary and therapeutic foods and complementary diets (6, 17, 27, 28), to assess the economic value of supplemental foods (29) and to assess the affordability of diets that meet nutrient intake recommendations (30). The objectives of these linear programs were to minimize total energy, minimize cost, or maximize the concentration of a certain nutrient in the food or diet. Our LP tool uses a larger database so that more candidate ingredients may be considered and more ingredient characteristics can be assessed, thus combining the previous LP research and attempted RUTF design approaches (4–9) into one comprehensive, robust tool.

The 4 Ethiopian formulations identified by our method differed in their ingredients and ingredient processing, both of which affect the appropriateness of each formulation in a given circumstance. The inclusion of peanuts was a constraint in the peanut/pea/pumpkin seed and oat/peanut RUTF formulations. This constraint was chosen because, to date, all RUTFs that have been shown to have clinical effectiveness in recovering children from SAM have contained 25% peanuts, and to the Western palate a small amount of peanut increases acceptability.

All 4 formulations meet the Joint UN agency requirement that ≥50% of the protein comes from dairy (1); however, for the oat/peanut RUTF, the model selected 3 different dairy ingredients to meet this requirement. Use of multiple dairy ingredients may not be possible for some production locations that import dairy products because of quality-control, import, and transport expenses.

Processing of the ingredients differs between the 4 Ethiopian RUTF formulations. In these formulations, high-lipid ingredients such as pumpkin seeds and peanuts require roasting, whereas ingredients with fewer lipids such as peas, oats, and millet can be extrusion processed, so ingredient processors using these cooking methods must be available. All ingredients could theoretically be roasted; however, extrusion cooking results in higher product quality and is cost-effective compared with other ingredient processing methods (31).

Finally, these formulations all use some imported ingredients to meet nutritional constraints and reduce the cost of RUTFs. The functionality of the LP tool allows the user to exclude or limit ingredients, including imported ingredients. Likewise, ingredients can be limited or excluded based on cultural practices, such as vegetarianism.

The LP tool is unique because of its comprehensive ingredient and nutrient database. Multiple sources were searched for macronutrient staples in different areas of the developing world to populate the ingredient database. The user of the LP tool can customize the tool by selecting ingredients available in his or her region and assigning prices. The LP tool may be adapted to create new formulations of other foods, such as supplementary foods, local foods, or foods high in a particular nutrient, by altering the optimization problem, constraints, or candidate ingredient list. For example, the LP tool can be used to maximize a specific nutrient (e.g., bioavailable phosphorus) or to maximize locally sourced ingredients—both subject to product weight, nutrient content, quality, and total cost constraints.

This research shows that the LP tool and nutrient database are reliable for predicting macronutrient content for the specific formulations selected in this Ethiopian context. The user may add ingredients to the database provided that he or she enters the nutrient and price data and alters data if new information is discovered. Although this is not the first attempt to use LP to formulate new RUTFs, our work is unique in that we assembled a large candidate ingredient and food composition database that will allow quick and efficient utilization of the LP tool to create new RUTF formulations for many settings with input of local prices of chosen ingredients. Furthermore, the tool will be available publicly, free of charge. International agencies and local governments have requested that food-aid products include more local ingredients, particularly in Asia; this LP tool and RUTF formulation process will facilitate their inclusion of such by identifying cost-effective and safe ingredients in combinations that meet international specifications. By providing a method to create RUTFs deemed more acceptable to the many diverse malnourished populations of the world, the benefits of therapy can be more widely realized. The next step will be to use the LP tool for a variety of countries, to determine how frequently a more cost-effective RUTF can be identified, and to use the LP tool to increase the numbers of children with SAM that receive effective therapy. The dissemination and use of this LP tool could spark innovation in the local production of RUTF. Future work should assess both the accuracy of the LP tool when high-quality RUTF production is scaled up in a production facility and the investment required to do so.

We thank Kassahun Aberra Endeshaw, Ellen Murray, and Bethany Whisenhunt for assistance with data collection and interpretation.

The authors' responsibilities were as follows—KNR, KPA, SAV and MJM: conceptualized and designed the study; KNR, KPA, and SAV: developed the LP tool; KNR, MIO, and EDC: prepared the foods; KNR, KPA, SAV, and MJM: analyzed and interpreted the data and wrote the first draft of the manuscript; and MJM: had primary responsibility for the final content. The sponsors of the study had no role in the study design, study implementation, data collection, data analysis, data interpretation, or writing of the report. No known disclosures or conflicts of interest were reported, and all ethical standards of the institutions were followed.

REFERENCES

1. WHO. Community-based management of severe acute malnutrition. Geneva (Switzerland): World Health Organization/World Food Programme/United Nations System Standing Committee on Nutrition/The United Nations Children's Fund; 2007.
2. WHO. Updates on the management of severe acute malnutrition in infants and children. Geneva (Switzerland); World Health Organization/ World Food Programme/United Nations System Standing Committee on Nutrition/The United Nations Children's Fund; 2013. p. 1–123.
3. UNICEF. Ready-to-use therapeutic food: current outlook. Copenhagen (Denmark): United Nations Children's Fund Supply Division, 2013.
4. Collins S, Henry J. Alternative RUTF formulations. Field Exchange 2004;102:35–7.
5. Lagrone L, Cole S, Schondelmeyer A, Maleta K, Manary MJ. Locally produced ready-to-use supplementary food is an effective treatment of moderate acute malnutrition in an operational setting. Ann Trop Paediatr 2010;30:103–8.
6. Dibari F, Diop EHI, Collins S, Seal A. Low-cost, ready-to-use therapeutic foods can be designed using locally available commodities with the aid of linear programming. J Nutr 2012;142:955–61.
7. Nga TT, Nguyen M, Mathisen R, Hoa DT, Minh NH, Berger J, Wieringa FT. Acceptability and impact on anthropometry of a locally developed ready-to-use therapeutic food in pre-school children in Vietnam. Nutr J 2013;12:120.
8. Bahwere P, Sadler K, Collins S. Acceptability and effectiveness of chickpea sesame-based ready-to-use therapeutic food in malnourished HIV-positive adults. Patient Prefer Adherence 2009;3:67–75.
9. Nabuuma D, Nakimbugwe D, Byaruhanga YB, Saalia FK, Phillips RD, Chen J. Formulation of a drinkable peanut-based therapeutic food for malnourished children using plant sources. Int J Food Sci Nutr 2013; 64:467–75.
10. Dibari F. Linear programming to design low cost, local RUTF. Field Exchange 2012;43:36–7.
11. WHO/FAO. Microbial safety of ready-to-use lipid-based therapeutic and supplementary foods. Rome (Italy): FAO/WHO; 2012. p. 28.
12. Ray B. Fundamental food microbiology. 3rd ed. Boca Raton (FL): CRC Press; 2003.
13. Leistner L. Basic aspects of food preservation by hurdle technology. Int J Food Microbiol 2000;55:181–6.
14. Nelson KA, Labuza TP. Water activity and food polymer science: implications of state on Arrhenius and WLF models in predicting shelf life. J Food Eng 1994;22:271–89.
15. Beuchat LR. Pathogenic microorganisms associated with fresh produce. J Food Prot 1995;59:204–16.
16. Scallan E, Hoekstra RM, Angulo FJ, Tauxe RV, Widdowson M-A, Roy SL, Jones JL, Griffin PM. Foodborne illness acquired in the United States—major pathogens. Emerg Infect Dis 2011;17:7–15.
17. Skau JK, Bunthang T, Chamnan C, Wieringa FT, Dijkhuizen MA, Roos N, Ferguson EL. The use of linear programming to determine whether a formulated complementary food product can ensure adequate nutrients for 6- to 11-month-old Cambodian infants. Am J Clin Nutr 2014; 99:130–8.
18. Luenberger DG, Yinyu Y. Linear and non-linear programming. 3rd edition. New York: Springer Science + Business Media, LLC; 2008.
19. WHO. Technical note: supplementary foods for the management of moderate acute malnutrition in infants and children 6-59 months of age. Geneva (Switzerland): WHO; 2012.
20. Abrams SA, Atkinson SA. Calcium, magnesium, phosphorus and vitamin D fortification of complementary foods. J Nutr 2003;133(Suppl): 2994S–9S.
21. Michaelsen KF, Hoppe C, Roos N, Kaestel P, Stougaard M, Lauritzen L, Mølgaard C, Girma T, Friis H. Choice of foods and ingredients for moderately malnourished children 6 months to 5 years of age. Food Nutr Bull 2009;30(Suppl):S343–404.
22. UNICEF. Technical Requirements of Ready-to-Use Therapeutic Foods, RFP-DAN-2013-501715 (2013).
23. FDA. Nutrition Labeling of Food, 21 C.F.R. Sect. 101.9 (2013).
24. Ferguson EL, Darmon N, Fahmida U, Fitriyanti S, Harper TB, Premachandra IM. Design of optimal food-based complementary feeding recommendations and identification of key "problem nutrients" using goal programming. J Nutr 2006;136:2399–404.
25. Ferguson EL, Briend A, Darmon N. Can optimal combinations of local foods achieve the nutrient density of the F100 catch-up diet for severe malnutrition? J Pediatr Gastroenterol Nutr 2008;46:447–52.
26. Darmon N, Ferguson E. Linear and nonlinear programming to optimize the nutrient density of a population's diet: an example based on diets of preschool children in rural Malawi. Am J Clin Nutr 2002;75: 245–53.
27. Briend A, Darmon N, Ferguson E, Erhardt JG. Linear programming: a mathematical tool for analyzing and optimizing children's diets during the complementary feeding period. J Pediatr Gastroenterol Nutr 2003;36:12–22.
28. Santika O, Fahmida U, Ferguson EL. Development of food-based complementary feeding recommendations for 9- to 11-month-old peri-urban Indonesian infants using linear programming. J Nutr 2009;139: 135–41.
29. Briend A, Ferguson E, Darmon N. Local food price analysis by linear programming: a new approach to assess the economic value of fortified food supplements. Food Nutr Bull 2001;22:184–9.
30. Baldi G, Martini E, Catharina M, Muslimatun S, Fahmida U, Jahari AB, Hardinsyah, Frega R, Geniez P, Grede N, et al. Cost of the Diet (CoD) tool: first results from Indonesia and applications for policy discussion on food and nutrition security. Food Nutr Bull 2013;34: S35–42.
31. Harper JM. Food extrusion. CRC Crit Rev Food Sci Nutr 1978;11: 155–215.