Original Research Article

# A linear programming based method for designing menus for controlled feeding trials 

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#### Abstract

Background: Controlled feeding trials are an important method to determine cause-effect relationships between dietary intake and metabolic parameters, risk factors, or health outcomes. Participants of a controlled feeding trial receive full-day menus during a prespecified period of time. The menus have to comply with the nutritional and operational standards of the trial. Levels of nutrients under investigation should differ sufficiently between intervention groups, and be as similar as possible for all energy levels within intervention groups. Levels of other key nutrients should be as similar as possible for all participants. All menus have to be varied and manageable. Designing these menus is both a nutritional and a computational challenge that relies largely on the expertise of the research dietician. The process is very time consuming, and last-minute disruptions are very hard to manage. Objective: This paper demonstrates a mixed integer linear programming model to support the design of menus for controlled feeding trials. Methods: The model is demonstrated for a trial that involved consumption of individualized, isoenergetic menus with either a low or a high protein content. Results: All menus generated by the model comply with all standards of the trial. The model allows for including tight ranges on nutrient composition, and complex design features. The model is very helpful in managing contrast and similarity of key nutrient intake levels between groups and energy levels, and in coping with many energy levels and nutrients. The model helps to propose several alternative menus and to manage last-minute disruptions. The model is flexible; it can easily be adapted to suit trials with other components or different nutritional requirements. Conclusions: The model helps to design menus in a fast, objective, transparent, and reproducible way. It greatly facilitates the design procedure for menus in controlled feeding trials and lowers development costs.


Keywords: mixed-integer linear programming, optimization, linearization, fully controlled dietary intervention, operations research

## Introduction

Controlled feeding trials are an important method to determine cause-effect relationships between dietary intake and metabolic parameters, risk factors, or health outcomes. They allow to investigate the effect of intake of specific nutrients, foods, or dietary patterns while controlling for potential confounding effects [1, 2]. The potential impact of controlled feeding trials is illustrated for example for the effect of trans fatty acids and cholesterol in the study of Mensink and Katan [3], for the effect of dietary patterns on blood pressure in the DASH-trial by Apple et al. [4], and for the effect of ultra processed diets on energy intake and weight gain by Hall et al. [5].

In controlled feeding trials, for a period of time participants are provided with specifically composed menus that meet the trial criteria. They have to consume everything that is provided and nothing more. The menus have a specific nutrient composition, contain specific foods and/or dietary pattern, and differ between control and intervention groups. In addition, individual energy and nutrient requirements of the participants are taken into account.

Designing the menus is both a nutritional and a computational challenge. On the one hand, all participants within a group have to receive the same foods. Moreover, the amounts of foods have to be in accordance with the individual energy requirements (referred to as energy level) of the participants. On the other hand, the menus have to differ between control and intervention groups in terms of nutrient

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composition, foods, and/or dietary pattern, in order to meet the criteria of the trial.

For designing the menus, research dieticians compose $n$-day menus that can be repeated throughout the duration of the trial. Food items are combined into so-called (meal) components, such as starch, vegetables, biscuits. Participants receive a serving of every component every day, but the actual food item per component per day will vary. For instance, a participant receives a daily serving of 100 gram of the starch component, which (in a 7-day menu) varies with frequencies 2 days rice, 2 days pasta, 3 days potatoes. This leads to two main design decisions: $F \sim$ how to compose the components (in other words: what
protein menu (Group 1) or a high protein menu (Group 2). A menu for one week was designed. The menu was repeated in the second week.

Key elements in the MILP model are decision variables that represent the two main design decisions $F$ and $X$, and the (mathematical) relations between these decision variables and the nutrient composition of the menu. These elements will be elaborated here, followed by a numerical toy example. The remainder of this section describes some functionality of the MILP model. The full mathematical formulation is provided in Supplementary Methods. The section ends with an outline of the solution approach and the implementation.

The following definitions are used.

| Indices |  |
| :--- | :--- |
| $e$ | Index for energy level, $e=1, \ldots, E$, with $E$ the number of energy levels |
| $f$ | Index for frequency of a food item in a component, $f=1, \ldots, \operatorname{maxx}_{i}$ with $\max _{i}$ the maximal frequency of food $i$ |
| $g$ | Index for group, $g=1,2$ |
| $i$ | Index for food item, $i=1, \ldots, I$, with $I$ the number of food items |
| $j$ | Index for nutrient, $j=1, \ldots, J$, with $J$ the number of nutrients |
| $k$ | Index for food component, $k=1, \ldots, K$, with $K$ the number of components |
| $k_{i}$ | Index of the component to which food $i$ belongs |
| Variables | Frequency of food item $i$ for group $g$ |
| $F_{i, g}$ | Amount of nutrient $j$ for energy level $e$ for group $g(\mathrm{~kJ} /$ day, $\mathrm{g} /$ day $)$ |
| $N M_{j, e, g}$ | Daily amount of food component $k$ for participants in energy level $e$ of group $g(\mathrm{~g}$ or pieces) |
| $X_{k, e, g}$ |  |
| Data | Amount of nutrient $j$ in food item $i(\mathrm{~kJ} / 100 \mathrm{~g}$ or $\mathrm{g} / 100 \mathrm{~g})$ |
| $c_{i, j}$ |  |

should be the frequency of food items within the components?), $X \sim$ how much of each component to serve per day. As all participants in a group get the same menu, decision $F$ has to be taken for every group. Decision $X$ has to be taken for every energy level in every group.

In the current manual design procedure, a nutrient calculation program and a spreadsheet application are used to keep track of the nutrient compositions of all menus. Frequencies $F$ of the food items in the components and daily amounts $X$ of components per energy level are adjusted manually to improve nutrient composition and amounts of foods until they meet the criteria of the trial. It is very hard to manually select all frequencies and amounts such that the nutrient composition and the composition of the menu comply with the objectives of the study for all energy levels of all groups. As a result, the design process is very time consuming, depends heavily on the experience and expertise of the research dietician, and last-minute disruptions (such as unavailability of a planned food) are very hard to manage.

For designing diets, Linear programming (LP) models have widely been used as tools [6]. To the best of our knowledge, LP has not yet been used to formulate menus for controlled feeding trials. LP models that contain integer variables are referred to as Mixed Integer Linear Programming (MILP) models [7]. This paper demonstrates a MILP model to support development of menus for controlled feeding trials.

## Methods

The case study ProBrain [8] is used to explain the MILP model and to demonstrate its performance by comparing the MILP menus with the manual menus that were actually used in the study. ProBrain consisted of a 14-day fully controlled dietary intervention that involved consumption of individualized, isoenergetic menus providing either a low

## Nutrient composition as function of the decision variables

The nutrient composition of the $n$-day menu for energy level $e$ of group $g$ can be calculated from the frequency $F_{i, g}$ of food $i$ and the daily amount $X_{k_{i}, e, g}$ of component $k_{i}$. The $n$-day amount of nutrient $j$ obtained from food $i$ for energy level $e$ of group $g$ equals $0.01 c_{i, j} F_{i, g} X_{k_{i}, e, g}$. The daily amount $N M_{j, e, g}$ of nutrient $j$ in energy level $e$ for group $g$ is then obtained by summing this expression over all food items $i$ and dividing by the number of days $n$ :
$N M_{j, e, g}=\sum_{i=1}^{I} 0.01 c_{i, j} F_{i, g} X_{k_{i}, e, g} / n$ for all $j, e, g$
Equation [1] is non-linear due to the multiplication of the two variables $F_{i, g}$ and $X_{k_{i}, e, g}$. As a consequence, a model that contains equation [1] cannot be solved with linear programming software. Supplementary Methods elaborates a two-step procedure that transforms equation [1] into an equivalent set of linear constraints. The linearized version of the model can be solved with standard linear programming software.

## Illustrative example

The following small numerical example illustrates the decision variables and shows how the nutrient composition is calculated from the decision variables. Suppose we are designing a four-day ( $n=4$ ) menu for a trial with two groups and two energy levels $(E=2)$. Assume there are five food items $(I=5)$ in two components $(K=2)$, see Table 1. Within the four-day period, participants of group $g=2$ get broccoli $(i=3)$ twice $\left(F_{3,2}=2\right)$, carrots $(i=4)$ once $\left(F_{4,2}=1\right)$, and spinach $(i=5)$ once $\left(F_{5,2}=1\right)$. Of vegetables $(k=2)$, the participants in energy level $e=1$ of group $g=2$ get $X_{2,1,2}=65 \mathrm{~g} /$ day, and the participants in energy level $e=2$ of group $g=2$ get $X_{2,2,2}=140 \mathrm{~g} /$ day. The amount of dietary

Table 1
Input and output of numerical example for average daily intake of dietary fiber.

| Input | Output |  |  |  |  |  |  |  | Dietary fiber contribution for $e=1, g=2$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| i. Food | k. Component | $c_{i, 6}$ | $F_{i, 1}$ | $F_{i, 2}$ |  | $X_{k, e, g}$ |  |  |  |
| 1. Rice | 1. Starch | 0.7 | 2 | 1 | $X_{1,1,1}=50$ | $X_{1,2,1}=100$ | $X_{1,1,2}=60$ | $X_{1,2,2}=110$ | 0.4 |
| 2. Pasta | 1. Starch | 1.4 | 2 | 3 |  |  |  |  | 2.5 |
| 3. Broccoli | 2. Vegetables | 2.7 | 1 | 2 |  |  |  |  | 3.5 |
| 4. Carrots | 2. Vegetables | 2.9 | 1 | 1 | $X_{2,1,1}=75$ | $X_{2,2,1}=150$ | $X_{2,1,2}=65$ | $X_{2,2,2}=140$ | 1.9 |
| 5. Spinach | 2. Vegetables | 3.3 | 2 | 1 |  |  |  |  | 2.1 |
|  |  |  |  |  |  |  |  |  | $N M_{6,1,2}=2.6$ |

$c_{i, 6}$ the amount of fiber in 100 g of food $i ; F_{i, g}$ the frequency of food $i$ in the four-day menu for group $g ; X_{k, e, g}$ the daily amount of component $k$ for energy level $e$ of group $g$; $N M_{6,1,2}$ the average daily intake of fiber.
fiber $(j=6)$ in broccoli $(i=3)$ is $c_{3,6}=2.7 \mathrm{~g} / 100 \mathrm{~g}$. The amount of fiber $(j=6)$ that participants in energy level $e=1$ of group $g=2$ get from broccoli is $0.01 c_{3,6} F_{3,2} X_{2,1,2}=0.01 \cdot 2.7 \cdot 2 \cdot 65=3.5 \mathrm{~g}$. The average daily fiber intake for energy level $e=1$ of group $g=2$ is calculated from the fiber contributions of all five food items: $N M_{6,1,2}=(0.4+2.5+\ldots+2.1)$ / $4=2.6 \mathrm{~g} / \mathrm{day}$.

## Components - properties

The study distinguishes 24 components, see Table 2. This section describes the properties that are shown as columns in Table 2. Supplementary Methods elaborates the properties of the individual components and the relations between the components. A full list of all foods (including their nutrient composition, serving size, and some other properties) is provided in Supplementary Table 1.

## Daily amount $X_{k, e, g}$ - continuous or integer variables

Components such as starch and salad dressing can be served in any number of grams. Therefore, their daily amounts $X_{k, e, g}$ are modelled as continuous variables. For instance, $X_{2,4,1}=100$ indicates that of component vegetables ( $k=2$ ) participants of energy level $e=4$ of group $g=1$ get $100 \mathrm{~g} /$ day.

Components such as bread and fruit are served in slices and pieces. Their daily amounts $X_{k, e, g}$ are modelled as integer variables. For instance, $X_{11,3,2}=5$ indicates that participants of energy level 3 of group 2 get 5 slices of bread ( $k=11$ ) per day.

## Lower bounds and upper bounds

Lower and upper bounds for the daily amount $X_{k, e, g}$ of component $k$, for energy level $e$ of group $g$, either in grams or in slices/pieces.

Table 2
Properties of components used in the MILP model.

| Component | Unit | $X_{k, e, g}$ | Lower bound | Upper bound | Synchronize $_{k}$ | Non-decreasing $k$ | All_days_same ${ }_{\text {k }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 1. Starch | gram | continuous | 50 | 250 | 1 | 1 |  |
| 2. Vegetables | gram | continuous | 100 | 250 | 1 | 1 |  |
| 3. Meat_continuous | gram | continuous | 50 | 150 |  | 1 |  |
| 4. Meat_integer | piece | integer | 0 | 4 |  | 1 |  |
| 5. Dessert | gram | continuous | 100 | 250 |  | 1 |  |
| 6. Sauce_basis | gram | continuous | 15 | 125 |  |  | 1 |
| 7. Sauce flavor | gram | continuous | 15 | 125 |  |  |  |
| 8. Salad_vegetables | gram | integer | 1 | 1 | 1 |  |  |
| 9. Salad_dressing | gram | continuous | 15 | 30 |  |  |  |
| 10. Salad_fat | gram | continuous | 0 | 10 |  |  |  |
| 11. Bread | slice | integer | 1 | 12 |  | 1 | 1 |
| 12. Margarine | cup | integer | 1 | 10 |  |  | 1 |
| 13. Top_sweet | slice | integer | 1 | 6 |  |  |  |
| 14. Top_cheese | slice | integer | 1 | 9 |  |  | 1 |
| 15. Top_meat | slice | integer | 1 | 9 |  |  |  |
| 16. Milk | glass | integer | $0 ; 1$ * | 3 |  |  | 1 |
| 17. Fruitl | piece | integer | 1 | 1 |  |  |  |
| 18. Fruit2 | piece | integer | 0 | 1 |  |  |  |
| 19. Fruit3 | piece | integer | 0 | 1 |  |  |  |
| 20. Biscuits | piece | integer | 1 | 5 |  |  |  |
| 21. Drinks | glass | integer | 0 | 1 |  |  | 1 |
| 22. Snack_carbs | piece | integer | 1 | 1 |  |  |  |
| 23. Snack_protein | piece | integer | 0; 1* | 1 |  |  |  |
| 24. Free choice items | piece | integer | 18 | 35 |  |  | 1 |

$X_{k, e, g}$ is the daily amount of component $k$ for energy level $e$ of group $g$. Lower and upper bounds are in grams for continuous $X_{k, e, g}$ and in number of pieces for integer $X_{k, e, g}$. Synchronize $_{k}=1$ indicates that participants in groups 1 and 2 get the same food for component $k$; non-decreasing ${ }_{k}=1$ indicates that the amounts of component $k$ should be non-decreasing with increasing energy level; all_days_same ${ }_{k}=1$ indicates that throughout the trial the same food needs to be selected for component $k$.

* 0 for group 1 and 1 for group 2.


## Synchronize ${ }_{k}$

For the sake of manageability (by kitchen and staff), components starch, vegetables and salad_vegetables are synchronized. For the practice of the trial, this means that every day only one type of starch/ vegetables/salad_vegetables is prepared, which is served to all participants in both groups. For the model, this means that the frequencies of the foods for group 1 are identical to those of group 2.

## Non-decreasing $k$

The amounts of starch/vegetables/meat/bread are non-decreasing with increasing energy level. In other words: no participant can have a smaller amount of these components than a participant of a lower energy level. This ensures that the nutrient sources are comparable across the energy intake levels.

## All_days_same ${ }_{k}$

For the sake of manageability, throughout the trial the same type of sauce_basis, bread, margarine, ..., free choice items is provided. For the model, this means that only one item per food component is selected.

## Solution approach

Solving the model for a case with 2 groups and more than 2 or 3 energy levels can take prohibitively much computation time. This is caused by the large number of integer and binary variables in the model. In such cases, solutions can be generated via a two-step approach:

Step 1. The model is solved for all groups, with only the lowest and the highest energy level included.
Step 2. The frequencies $F_{i, g}$ that were found in step 1 are used as input in Step 2. The model is solved for all energy levels and groups.

## Data, software, implementation

All input data for the MILP model was stored in one MS Excel file, including three sheets:

1. Components including properties as shown in Table 2.
2. Food items including properties as shown in Supplementary Table 1.
3. Ranges for key nutrients and other menu-related restrictions.

Energy and nutrient composition were derived from the Dutch food composition database [9] and values for composite foods were calculated using the nutrient calculation program Compl-eat [10]. The MILP model was implemented in Fico Xpress-IVE [11], which used the Excel file as input. The model's output was stored in the Excel file and available for further use during the trial. The Excel file and the Fico Xpress-IVE source code are available as online Supplementary Material.

## Results

The MILP model was used to generate menus for ProBrain. These menus will be referred to as 'MILP menus'. The MILP menus will be compared with the menus that were actually used in ProBrain [8], which will be referred to as 'manual menus'.

The target nutrient in ProBrain is protein. Protein should be exchanged with carbohydrates, and fat content should differ as little as possible between all energy levels and groups. Energy levels range from $7 \mathrm{MJ}(e=1)$ to $14 \mathrm{MJ}(e=8)$ per day. In the original manual menus, protein content in all energy levels of group 1 and 2 was designed to be $4.5-5.0 \mathrm{en} \%$ and $16.0-16.5 \mathrm{en} \%$, respectively. In order to demonstrate the power of the MILP model, the protein content of the MILP
menus was defined more precisely at $4.7-4.8 \mathrm{en} \%$ and $16.2-16.3$ en $\%$ in all energy levels of group 1 and 2 , respectively. The model was run with an objective function that minimized the difference in fat intake between all energy levels and groups, subject to the constraint that protein intake was within the target range. Runtime of the MILP model was less than 5 minutes.

Table 3 shows the daily amounts of all food components per group and energy level for both the MILP and manual menus, and Table 4 shows the nutrient compositions of the menus. The frequencies of the foods within the components are listed in Supplementary Table 2.

The results demonstrate that the MILP model generated menus that comply with all constraints for all energy levels of all groups.

## Discussion

This study describes a MILP model for generating full-day menus for a controlled feeding trial with a specific aim and key nutrients. The output of the MILP model is a list of the frequencies of the food items (per group), and a list that specifies the daily amount per component for every energy level of every group. The research dietician then decides which combination of foods should be consumed on the same day, for instance, the research dietician decides whether carrots should be combined with potatoes or with rice. The modelling approach can easily be adapted for trials with partial menus, another aim, different cultural eating habits, and other key nutrients; foods and components can be removed, added, or changed, and the modeller can adjust the dietary reference values.

In many ways, the MILP menus comply better with the study criteria than the manual menus:

- The MILP model generates menus with tighter ranges on macro nutrient intake than the manual procedure.
- The MILP model generates menus that comply with all constraints for every energy level of every group. In the manual design procedure, for the 7MJ and 8 MJ group the nutrient requirements could only be met by reducing the number of free choice items and sweet toppings.
- The MILP model generates menus with margarine and milk in cups and glasses, respectively, which is preferred from the perspective of practical manageability, but which was not attainable in the manual design procedure.

The accuracy of both the manual and the MILP-based design method is limited by the accuracy of the food composition data. Chemical analysis of duplicate composites of the diet should be undertaken to report nutrient levels.

In 2021, the MILP-based design procedure has successfully been used to design the menus of controlled feeding trial VD2O (https://www .trialregister.n1/trial/9542), which studies the short-term effects of vegan diets on daily muscle protein synthesis rates as compared to omnivorous diets in older adults assessed by D2O. It was experienced that the model developed for ProBrain could very easily be adapted to fit the setup and criteria of VD2O. Key in VD2O is that the distribution of protein intake over six daily eating moments should be as similar as possible for all participants. In the MILP model, this challenging requirement was easily modelled via an extra set of constraints. Adjusting the set of components to the design of VD2O was straight-forward, as was excluding non-vegan food items from vegan menus. Running the model in slightly different ways generated a set of alternative menus, thus providing the research dietitian with several menu options. This was experienced as very valuable. Moreover, it was easy to answer what-if questions, such as 'What if we add meat replacers X and Y to the food list; will they actually be selected and will they help to level the protein intake?' and to investigate

Table 3
Daily amounts of the components (MILP menus and manual menus).

| Component (unit) | Group 1 (low-protein) |  |  |  |  |  |  |  | Group 2 (high-protein) |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|  | MJ | MJ | MJ | MJ | MJ | MJ | MJ | MJ | MJ | MJ | MJ | MJ | MJ | MJ | MJ | MJ |
| MILP |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 1. Starch (g) | 52 | 65 | 100 | 105 | 110 | 121 | 126 | 150 | 81 | 150 | 159 | 178 | 195 | 250 | 250 | 250 |
| 2. Vegetables (g) | 100 | 100 | 100 | 100 | 100 | 103 | 103 | 103 | 100 | 107 | 107 | 107 | 107 | 224 | 224 | 250 |
| 3. Meat_continuous (g) | 50 | 50 | 50 | 50 | 51 | 51 | 51 | 51 | 71 | 100 | 125 | 135 | 135 | 140 | 150 | 150 |
| 4. Meat_integer (pieces) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 3 | 3 | 4 | 4 | 4 | 4 |
| 5. Dessert (g) | 101 | 101 | 104 | 104 | 104 | 104 | 104 | 114 | 100 | 100 | 100 | 100 | 100 | 175 | 175 | 194 |
| 6. Sauce_basis (g) | 15 | 24 | 15 | 47 | 55 | 24 | 19 | 22 | 40 | 58 | 72 | 68 | 97 | 115 | 125 | 119 |
| 7. Sauce flavor (g) | 15 | 24 | 15 | 47 | 55 | 24 | 19 | 22 | 40 | 58 | 72 | 68 | 97 | 115 | 125 | 119 |
| 8. Salad_vegetables (bowls) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 9. Salad_dressing (g) | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 |
| 10. Salad fat (g) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 11. Bread (slices) | 3 | 4 | 6 | 6 | 7 | 9 | 11 | 12 | 5 | 5 | 5 | 7 | 7 | 8 | 8 | 9 |
| 12. Margarine (cups) | 2 | 2 | 4 | 4 | 4 | 6 | 7 | 9 | 4 | 4 | 4 | 5 | 5 | 5 | 5 | 7 |
| 13. Top_sweet (slice) | 1 | 1 | 3 | 3 | 3 | 4 | 5 | 5 | 1 | 1 | 1 | 2 | 3 | 2 | 1 | 2 |
| 14. Top_cheese (slice) | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 1 | 1 | 1 | 2 | 1 | 2 | 2 | 2 |
| 15. Top_meat (slice) | 1 | 2 | 2 | 2 | 3 | 3 | 4 | 5 | 3 | 3 | 3 | 3 | 3 | 4 | 5 | 5 |
| 16. Milk (glass) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 2 |
| 17. Fruitl (piece) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 18. Fruit2 (piece) | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 |
| 19. Fruit3 (piece) | 1 | 1 | 0 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 20. Biscuits (piece) | 4 | 5 | 4 | 4 | 5 | 5 | 5 | 2 | 1 | 2 | 3 | 1 | 1 | 1 | 4 | 1 |
| 21. Drinks (glass) | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 |
| 22. Snack_carbs (piece) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 23. Snack protein (piece) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 24. Free choice items (piece) | 18 | 20 | 23 | 25 | 28 | 30 | 33 | 35 | 18 | 20 | 23 | 25 | 28 | 30 | 33 | 35 |
| Manual |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 1. Starch (g) | 95 | 100 | 110 | 110 | 130 | 140 | 170 | 180 | 40 | 50 | 50 | 50 | 70 | 90 | 110 | 130 |
| 2. Vegetables (g) | 125 | 150 | 150 | 150 | 150 | 150 | 200 | 200 | 90 | 90 | 100 | 120 | 140 | 150 | 175 | 190 |
| 3. Meat_continuous (g) | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 25 | 145 | 145 | 145 | 145 | 145 | 160 | 185 | 185 |
| 4. Meat_integer (pieces) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| 5. Dessert (g) | 85 | 100 | 110 | 120 | 130 | 140 | 150 | 160 | 90 | 120 | 130 | 130 | 140 | 140 | 180 | 180 |
| 6. Sauce_basis (g) | 30 | 32.5 | 40 | 44 | 45 | 49 | 50 | 52.5 | 10 | 10 | 15 | 15 | 20 | 20 | 25 | 25 |
| 7. Sauce flavor (g) | 30 | 32.5 | 40 | 44 | 45 | 49 | 50 | 52.5 | 10 | 10 | 15 | 15 | 20 | 20 | 25 | 25 |
| 8. Salad_vegetables (bowls) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 9. Salad_dressing (g) | 12 | 15 | 17 | 25 | 26 | 27 | 29 | 30 | 5 | 5 | 10 | 10 | 15 | 15 | 18 | 18 |
| 10. Salad_fat (g) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 11. Bread (slices) | 4 | 5 | 5 | 6 | 7 | 8 | 8 | 9 | 4 | 4 | 5 | 6 | 7 | 8 | 8 | 9 |
| 12. Margarine (cups) | 20 | 25 | 25 | 30 | 35 | 40 | 45 | 50 | 15 | 20 | 25 | 30 | 30 | 35 | 40 | 45 |
| 13. Top_sweet (slice) | 2 | 3 | 3 | 4 | 4 | 5 | 5 | 6 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 14. Top_cheese (slice) | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 1 | 2 | 3 | 3 | 4 | 4 | 4 | 4 |
| 15. Top_meat (slice) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 3 | 4 | 4 |
| 16. Milk (glass) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 125 | 200 | 200 | 250 | 300 | 333 | 333 | 500 |
| 17. Fruitl (piece) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 18. Fruit2 (piece) | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 19. Fruit3 (piece) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 20. Biscuits (piece) | 1 | 1 | 2 | 2 | 2 | 2 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 21. Drinks (glass) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 22. Snack_carbs (piece) | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 23. Snack protein (piece) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 24. Free choice items (piece) | 19 | 21 | 22 | 23 | 28 | 30 | 32 | 33 | 12 | 14 | 18 | 22 | 24 | 26 | 32 | 32 |

trade-offs between various design features, such as 'How does synchronizing desserts affect the distribution of protein over eating moments?'.

The MILP-based design method requires a close cooperation between a research dietician and an expert in MILP modeling (referred to as the modeler). In a typical MILP-supported design procedure, the research dietician specifies the components list, the food list, and the ranges for the key nutrients. The modeler implements the MILP model
defined in Supplementary Methods in the software of his/her choice and tailors its functionality to the wishes of the research dietician. The modeler uses the MILP model to generate an initial menu. The research dietician indicates which changes are needed: add/remove foods to/ from food list, change input parameters (for instance maximal frequencies of foods, synchronize components), change functionality of the model (for instance link the amounts of two components). The

Table 4
Nutrient content of the menus (MILP menus and manual menus).

|  | Group 1 (low-protein) |  |  |  |  |  |  | Group 2 (high-protein) |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| MILP |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 1. Energy (MJ) | 7.0 | 8.0 | 9.0 | 10.0 | 11.0 | 12.0 | 13.0 | 14.0 | 7.0 | 8.0 | 9.0 | 10.0 | 11.0 | 12.0 | 13.0 | 14.0 |
| 2. Protein (en\%) | 4.8 | 4.7 | 4.8 | 4.8 | 4.7 | 4.8 | 4.8 | 4.8 | 16.3 | 16.2 | 16.3 | 16.3 | 16.2 | 16.3 | 16.2 | 16.3 |
| 3. Fat (en\%) | 31.1 | 31.1 | 31.1 | 31.1 | 31.1 | 31.1 | 31.1 | 31.1 | 31.1 | 31.1 | 31.1 | 31.1 | 31.1 | 31.1 | 31.1 | 31.1 |
| 4. Saturated fat (en\%) | 9.5 | 9.1 | 8.9 | 9.3 | 8.5 | 8.8 | 8.7 | 8.6 | 10.0 | 10.0 | 10.0 | 9.9 | 9.9 | 9.8 | 10.0 | 9.9 |
| 5. Carbohydrates (en\%) | 60.6 | 60.9 | 60.8 | 61.0 | 61.0 | 61.1 | 61.0 | 61.3 | 48.4 | 48.8 | 48.7 | 48.8 | 49.0 | 48.7 | 48.7 | 48.7 |
| 6. Dietary fiber ( $\mathrm{g} / \mathrm{MJ}$ ) | 4.3 | 4.5 | 4.7 | 4.4 | 4.7 | 4.5 | 4.7 | 4.6 | 3.4 | 3.3 | 3.2 | 3.3 | 3.1 | 3.5 | 3.4 | 3.4 |
| 7. Alcohol (en\%) | 1.3 | 1.3 | 1.3 | 1.3 | 1.3 | 1.3 | 1.3 | 1.3 | 1.6 | 1.5 | 1.6 | 1.5 | 1.6 | 1.5 | 1.6 | 1.5 |
| Manual |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 1. Energy (MJ) | 7.0 | 8.0 | 9.0 | 10.0 | 11.0 | 12.0 | 13.0 | 14.0 | 7.1 | 8.0 | 9.0 | 10.0 | 11.0 | 12.0 | 13.0 | 14.0 |
| 2. Protein (en\%) | 5.1 | 5.0 | 4.7 | 4.6 | 4.7 | 4.7 | 4.7 | 4.7 | 16.9 | 16.8 | 16.4 | 16.2 | 16.3 | 16.3 | 16.3 | 16.3 |
| 3. Fat (en\%) | 34.5 | 34.2 | 34.3 | 34.3 | 34.6 | 34.4 | 34.4 | 34.4 | 33.3 | 33.6 | 34.2 | 34.3 | 33.7 | 33.9 | 34.1 | 34.1 |
| 4. Saturated fat (en\%) | 10.0 | 9.9 | 9.8 | 9.7 | 10.1 | 10.0 | 9.9 | 9.9 | 13.3 | 14.0 | 14.3 | 14.2 | 14.0 | 14.0 | 13.9 | 14.0 |
| 5. Carbohydrates (en\%) | 57.0 | 57.5 | 57.6 | 57.9 | 57.4 | 57.8 | 57.7 | 57.8 | 46.5 | 46.6 | 46.3 | 46.3 | 46.7 | 46.4 | 46.2 | 46.3 |
| 6. Dietary fiber ( $\mathrm{g} / \mathrm{MJ}$ ) | 4.0 | 4.1 | 4.1 | 4.1 | 4.1 | 4.1 | 4.2 | 4.2 | 2.7 | 2.5 | 2.6 | 2.7 | 2.8 | 2.8 | 2.7 | 2.8 |
| 7. Alcohol (en\%) | 1.4 | 1.4 | 1.3 | 1.2 | 1.3 | 1.3 | 1.3 | 1.2 | 0.9 | 0.9 | 1.0 | 1.2 | 1.1 | 1.1 | 1.3 | 1.2 |

modeler adapts and re-runs the model. This loop is repeated until the research dietician is satisfied.

## Conclusion

This study presents a MILP model that supports development of menus for controlled feeding trials. The results suggest that the MILP model makes the development process faster and more transparent than the manual design procedure. The model allows for including tight nutrient ranges and complex design features. The model is very helpful in managing contrast and similarity of key nutrient intake levels between groups and energy levels, and in coping with many energy levels and nutrients. Moreover, the model is flexible; it can easily be adapted to suit trials with other components, foods, or different nutritional requirements. The model helps to greatly facilitate the design procedure for menus in controlled feeding trials, and to lower the development costs.

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## Data availability

Data described in the manuscript, code book, and analytic code will be made publicly and freely available without restriction as online supplementary material.

## Conflict of interest

The authors declare no conflict of interest.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https ://doi.org/10.1016/j.ajcnut.2022.11.006.

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[^0]:    Abbreviations: LP, Linear Programming; MILP, Mixed-Integer Linear Programming.

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