**Appendix 1 – Mathematical formulation of models**

The mathematical formulation of non-fasting diet model (Model 1) as explained textually below. The adaptations made to this model to formulate the continuous fasting and intermittent fasting models are also given below.

**Basic model (Model 1 – non-fasting)**

#### Outline

The model used in this research aims to optimize the nutrient intake of each individual diet while restricted by palatability constraints. With the set of available foods, no diet can be formulated that complies with all constraints. Therefore, the model is formulated according to the linear goal programming approach as described by Gerdessen & De Vries (2015). This approach aims to find a so-called Pareto-optimal solution, which is a solution in which the adequacy of a nutrient intake cannot be improved without worsening the adequacy of another nutrient intake. The approach of Gerdessen & De Vries (2015) finds the Pareto-optimal diet by quantifying the extent to which the diet violates the constraints, after which a function of these violations is minimised. This function of violations is called the achievement function. It is assumed that the adequacy of a diet is determined by the adequacy of the bottleneck nutrient, which has the largest unwanted nutrient intake deviation.

#### Nutrient intake constraints – adequacy curves

To determine the largest unwanted nutrient intake deviation, nutritional constraints are formulated via adequacy curves, as introduced in Gerdessen & De Vries (2015). As an example, the adequacy curve of calcium is shown in figure 1. The four characteristic points of an adequacy curve are defined as follows: A is the lower intake level (LL) below which an intake could lead to risk in most individuals; B is the Estimated Average Requirement (EAR) that meets the nutrient needs of half of the healthy individuals; C is the Recommended Daily Amount (RDA) which is sufficient for nearly all people; D is the upper intake level (UL) that is unlikely to pose a risk of adverse health effects (Gerdessen & De Vries, 2015). A nutrient intake is considered fully adequate if it is between the EAR and the RDA (adequacy equals 1), and fully inadequate if it is below the LL or above the UL (adequacy equals 0). Between the LL and the EAR a linear increase of the adequacy is assumed, and between the RDA and the UL a linear decrease. For instance, the adequacy of a calcium intake of 820 mg is estimated to be 0.6. The nutrient reference values used are shown in table 1.

Mathematically, the adequacy of each nutrient is calculated by the following constraints:

**Decision variables**

*NIAj*  Nutrient Intake Absolute; Quantity of nutrient *j* consumed in optimal diet in absolute values (for instance kcal or grams, dependent on the nutrient *j*)

*ndEARj* negative deviation EAR; the normalized negative intake deviation of nutrient *j* with regard to the EAR

*pdEARj* positive deviation EAR; the normalized positive intake deviation of nutrient *j* with regard to the EAR

*ndRDA*j negative deviation RDA; the normalized negative intake deviation of nutrient *j* with regard to the RDA

*pdRDAj* positive deviation RDA; the normalized positive intake deviation of nutrient *j* with regard to the RDA

**Indices**

*j* (1..J) nutrients

**Parameters**

*llj*  Lower Limit intake level of nutrient *j*

*earj*  Estimated Average Requirement intake level of nutrient *j*

*rdaj*  Recommended Daily Amount intake level of nutrient *j*

*ulj* Upper Level intake level of nutrient *j*

**Mathematical formulation**

|  |  |  |
| --- | --- | --- |
|  |  | (1a) |
|  |  | (2a) |
|  |  |  |
|  |  | (3) |
|  |  | (4) |

Constraints (1a) and (2a) normalize the negative or positive deviations (*ndEARj* or *pdEARj*) of the nutrient intake *NIAj* from the EAR. Note that a negative nutrient intake deviation from the EAR, so a nutrient intake that is lower than the EAR, is unwanted. These constraints determine the adequacy of a nutrient intake. For instance, for a calcium intake of 820 mg as shown in figure 1 the *ndEARj* is calculated as follows: 820 + (900-700)\**ndEARj* – (900-700)\**pdEARj* = 900. As the sum of the deviations (*ndEARj* and the *pdEARj*) is minimized in the achievement function as explained below, this means that in this case the *ndEARj* = 0.4 and the *pdEARj* = 0. The adequacy of a calcium intake of 820 mg is therefore 1 - 0.4 = 0.6. Note that only *ndEARj* has an upper bound of 1 (constraint 2a); *pdEARj* can be as large as needed.

Constraints (3) and (4) normalize the negative or positive deviations (*ndRDAj* or *pdRDAj*) of the nutrient intake *NIAj* from the RDA. Note that a positive nutrient intake deviation from the RDA, so a nutrient intake that is higher than the RDA, is unwanted. However, in this research, nutrient intakes below the EAR are prioritised over nutrient intakes above the RDA. Therefore, nutrient intakes above the RDA but below the UL are not considered to impact nutrient adequacy.

#### Achievement function

The achievement function as defined in the model is formulated as follows:

minimize(*MAXDEV + 0.001\*SUMDEV*)

In this research, an optimal diet is defined as a diet that minimises the bottleneck nutrient intake, which is the largest unwanted nutrient intake deviation of the micronutrients (*MAXDEV*). An unwanted nutrient intake is an intake that is below the EAR or above the RDA, as seen in Figure 1. Hence, the model aims to keep the nutrient intake levels between the EAR and RDA. Note that before optimizing a diet, it is not known which nutrient becomes the bottleneck nutrient. A small fraction of the sum of the total nutrient intake deviations (*SUMDEV*) is added to the achievement function as a tie-breaking term to make sure that of the alternatives that have the lowest maximum deviation (*MAXDEV*), the alternative that has the lowest sum of unwanted deviations (*SUMDEV*) is picked by the model.

The *MAXDEV* and *SUMDEV* are calculated as follows:

**Decision variables (in addition to those mentioned in previous section)**

*MAXDEV* Largest unwanted nutrient intake deviation

*SUMDEV* Sum of the total nutrient intake deviations

**Mathematical formulation**

|  |  |  |
| --- | --- | --- |
|  |  | (5a) |

|  |  |  |
| --- | --- | --- |
|  |  | (6) |

Constraints (5) calculate the maximum unwanted nutrient intake deviation (*MAXDEV*). In other words, the *MAXDEV* is the deviation from the EAR of the bottleneck nutrient intake. Only the micronutrients of interest (moi) are considered for calculating the *MAXDEV*. In this research, the micronutrients of interest are protein, calcium, iron, zinc, vitamin A, thiamine, riboflavin, niacin, vitamin B6, folate, vitamin B12, and vitamin C. Note that protein is not a micronutrient, but is considered in determining the MAXDEV.

Constraints (6) calculate the sum of nutrient intake deviations (*SUMDEV*). Recall that the *SUMDEV* is added to the achievement function as a tie-breaking term. The unwanted nutrient intake deviations are the intakes of the micronutrients of interest (moi) below the EAR (*ndEARj*) and above the RDA (*pdRDAj*). In the first part of the equation, extra weight is assigned to these deviations. The second part of the equation sums both negative and positive deviations of both the EAR and the RDA (*ndEARj*, *pdEARj*, *ndRDAj*, *pdRDAj*).

#### Food consumption constraints

The mathematical formulation of the constraints that limit the deviation of food consumption from the current diet in the model are as follows:

**Decision variables**

*Xi*  Quantity of regular food item *i* in optimal diet (in grams)

*QFGg*  Quantity Food Group; Quantity of food items of food group *g* consumed in optimal diet (in grams)

*QSGs*  Quantity Sub Group; Quantity of food items of food subgroup *s* consumed in optimal diet (in grams)

*NIAj*  Nutrient Intake Absolute; Quantity of nutrient *j* consumed in optimal diet in absolute values (for instance kcal or grams, dependent on the nutrient j)

**Indices**

*p* (1..P) persons. The model computes an optimal diet for one fixed person *p* at a time, but is executed in a loop. Therefore, this index is solely used to retrieve the current consumption data (*qipip*) of the person for whom an optimal diet is computed at that time.

*i*  (1..I) regular food items

*j* (1..J) nutrients

*g* (1..G) Each food group *g* consists of several food subgroups *s*, which consist of food items *i*. For instance, *g=7* (*Fruits*) consists of subgroups *s=7.1*, *s=7.2* and *s=7.3*.

*s* (1..S) Each food subgroup *s* belongs to a food group *g* and consists of several *i*. For instance, *s=7.3* (*Other Fruits)* belongs to *g=7* (*Fruits*) and consists of *i=2* (*Banana)*, *i=174* (*Avocado)*, and *i=257* (*Watermelon)*.

**Parameters**

*cijij* Composition Item Nutrient; Food composition database with the quantity of nutrient *j* in 100 grams of each food item *i* (nutrients *j* are expressed in their common absolute units such as kcal, gram, or miligram; e.g. *j=1* is energy in kcal)

*qipip* Quantity Item Person; Quantity of food item *i* consumed by person *p* (in grams). Note that this parameter is only used to retrieve the data on the current food consumption of person *p* from the data file.

*qgg* Quantity Group; Quantity of food items consumed in food group *g* (in grams). This parameter is calculated by summing the amount of food items consumed by a person in a food group (*qipip*) for each food group, like this;

*qss* Quantity Subgroup; Quantity of food items consumed in food subgroup *s* (in grams). This parameter is calculated by summing the amount of food items consumed by a person in a food subgroup (*qipip*) for each food group, like this;

*ckal* Current energy in Kcal; This parameter is calculated by summing the amount of kcal consumed by a person in all food items, like this;

*gdev* Group Deviation; Allowed deviation of food group consumption in the optimal diet from the current diet (in a percentage)

*sgdev* Subgroup Deviation; Allowed deviation of food subgroup consumption in the optimal diet from the current diet (in a percentage)

*kcaldev* Kcal Deviation; Allowed deviation of kcal consumption in the optimal diet from the current diet (in a percentage)

**Mathematical formulation**

|  |  |  |
| --- | --- | --- |
| Food group level constraints: |  |  |
|  |  | (7) |
|  |  | (8a) |
|  |  | (9a) |
|  |  |  |
| Food subgroup level constraints: |  |  |
|  |  | (10) |
|  |  | (11a) |
|  |  | (12) |
|  |  |  |
| Energy level constraints: |  |  |
|  |  | (13) |
|  |  | (14) |

Constraints (7), (8) and (9) limit the deviation of food group consumption from the current diet. Constraints (7) calculate the total amount of food items consumed in a food group in the optimal diet (*QFGg*) for each food group. This is done by summing the amount of regular food item *i* in grams in the optimal diet (*Xi*) of food group *g*. Constraints (8) and (9) make sure that the quantity of food items in group g in the optimal diet (*QFGg*) deviates no more than *gdev* from the amount of food items consumed in group g in the current diet (*qgg*). In this research this deviation may be at most 10% (*gdev*=0.10), so *QFGg* lies between 0.9\**qgg* and 1.1\**qgg*. Constraints (10), (11) and (12) work the same way as constraints (7), (8), and (9) respectively, but limit the deviation of food subgroup consumption instead of food group consumption. In this research the subgroup consumption deviation may be at most 15% (*sgdev*=0.15), so *QSGs* lies between 0.85\**qss* and 1.15\**qss*.

Constraints (13) and (14) limit the deviation of energy intake from the current diet. *NIAj*=*1* is the energy intake in kcal in the optimised diet, which can deviate no more than *kcaldev* from the current kcal intake (*ckcal*). In this research, the energy intake deviation may be at most 5% (*kcaldev*=0.05), so *NIAj*=1 lies between 0.95\**ckal* and 1.05\**ckal*.

## Incorporating GBD recommendations

The consumption data show that some food groups (Nuts and seeds, Milk and dairy, Fish and shellfish, Meat and eggs, and Fruits) are barely consumed by the sample population, as stated before in (reference Handling barely consumed food groups). To still include food items of these food groups in some of the model runs, a lower and upper bound are set for the number of grams of each of these barely consumed food groups. These bounds are based on the recommendations of the Global Burden of Disease(24). As shown in (table 1) and as stated before in the main text, model runs are set up in which the lower bound is set to 0%, 50%, or 75% and the upper bound to 50%, 75%, or 100% of the number of grams of the GBD recommendations, respectively. There are no additional constraints on the division of these recommended grams on sub group level. Furthermore, a model run is set up in which no GBD recommendations are applied.

In order to incorporate these bounds, the following parameters and constraints are added to the model:

**Parameters**

*fg\_con\_ming* Food group consumption minimum; Quantity of food group *g* that should at least be included in the optimized diet (in grams)

*fg\_con\_maxg* Food group consumption maximum; Quantity of food group *g* that should at most be included in the optimized diet (in grams)

*sg\_con\_maxs* Subgroup consumption minimum; Quantity of subgroup *s* that should at most be included in the optimized diet (in grams)

**Mathematical formulation**

|  |  |  |  |
| --- | --- | --- | --- |
| Food group level constraints: |  | |  |
|  |  | | (7) |
|  |  | | (8a) |
|  |  | | (9a) |
|  |  | |  |
|  |  | | (8b) |
|  |  | | (9b) |
|  |  | |  |
| Subgroup level constraints: | |  |  |
|  | |  | (10) |
|  | |  | (11a) |
|  | |  | (12) |
|  | |  |  |
|  | |  | (11b) |

Constraints (8b) are strict lower bounds that ensure that the number of grams of the minimum food group requirement set (*fg\_con\_ming*) are included in the optimized diet (*QFGg*), for each food group g for which the GBD recommendations are used. These GBD food groups are Nuts and seeds, Milk and dairy, Fish and shellfish, Meat and eggs, and Fruits. Constraints (9b) are the strict upper bounds. Constraints (11b) apply similar strict upper bounds (*sg\_con\_maxs*) on subgroup level.

**Fasting models**

**Model 2 - Continuous Fasting**

For the continuous fasting model, three sets of constraints are added to the basic model:

|  |  |  |
| --- | --- | --- |
| Food group level constraints: |  |  |
|  |  | (15) |
|  |  |  |
| Subgroup level constraints: |  |  |
|  |  | (16) |
|  |  |  |
| Food item level constraints: |  |  |
|  |  | (17) |

Constraints (15), (16), and (17) make sure that no animal-based food groups, subgroups, and food items, respectively, are included in the optimized diets. An example of an animal-based food item that does not belong to an animal-based food group or subgroup is honey. In this model, vitamin B12 and calcium are excluded from the *SUMDEV* and *MAXDEV* in the achievement function.

**Model 3 - Intermittent fasting**

The intermittent fasting model calculates optimized diets on a weekly basis. For the two fasting days, food consumption constraints as in the continuous fasting model are used. For the five non-fasting days, food consumption constraints as in the non-fasting model are used. Therefore, the food consumption constraints are formulated as follows:

**Decision variables**

*Xi,d* Quantity of regular food item *i* in optimal diet (in grams) on a non-fasting day (*d*=1) or fasting day (*d*=2)

**Indices**

*d*non-fasting day *d*=1, or fasting day *d*=2.

**Mathematical formulation**

|  |  |  |
| --- | --- | --- |
| Food group level: |  |  |
|  |  | (18) |
| Non-fasting days: |  |  |
|  |  | (19) |
|  |  | (20) |
| Fasting days: |  |  |
|  |  | (21) |
|  |  | (22) |
|  |  | (23) |
|  |  |  |
| Subgroup level: |  |  |
|  |  | (24) |
| Non-fasting days: |  |  |
|  |  | (25) |
|  |  | (26) |
| Fasting days: |  |  |
|  |  | (27) |
|  |  | (28) |
|  |  | (29) |
|  |  |  |
| Energy level constraints: |  |  |
|  |  | (30) |
|  |  | (31) |

In this model, calcium and vitamin B12 requirements are considered on a weekly basis. In that way, inadequate calcium and vitamin B12 intakes on fasting days can be compensated on non-fasting days. To do this, the computation of the *MAXDEV* is adapted. Before, one nutrient intake for each nutrient was used to compute the nutrient intake deviations from the EAR. In the intermittent fasting model, a differentiation is made between nutrient intakes on non-fasting days, fasting days, and average nutrient intakes on a weekly basis (for calcium and vitamin B12). The intermittent fasting model aims to find an optimized diet in which the largest deviation from the EAR of these three nutrient intake types is as small as possible.

The constraints formulated to compute these deviations and the *MAXDEV* are formulated as follows:

**Decision variables**

*nfNIAj* Non-fasting Nutrient Intake Absolute; Quantity of nutrient *j* consumed in optimal diet in absolute values (for instance kcal or grams, dependent on the nutrient *j*) on non-fasting days.

*fNIAj* Fasting Nutrient Intake Absolute; Quantity of nutrient *j* consumed in optimal diet in absolute values (for instance kcal or grams, dependent on the nutrient *j*) on fasting days.

*avgNIAj* Average Nutrient Intake Absolute; Quantity of nutrient *j* consumed in optimal diet in absolute values (for instance kcal or grams, dependent on the nutrient *j*) on average per week (5 non-fasting days and 2 fasting days)

nf\_*ndEARj* non-fasting negative deviation EAR; the normalized negative intake deviation of nutrient *j* with regard to the EAR

*nf\_pdEARj* non-fasting positive deviation EAR; the normalized positive intake deviation of nutrient *j* with regard to the EAR

*f\_ndEARj*  fasting negative deviation EAR; the normalized negative intake deviation of nutrient *j* with regard to the EAR

*f\_pdEARj*  fasting positive deviation EAR; the normalized positive intake deviation of nutrient *j* with regard to the EAR

*avg\_ndEARj*  average negative deviation EAR; the normalized negative intake deviation of nutrient *j* with regard to the EAR

*avg\_pdEARj*  average positive deviation EAR; the normalized positive intake deviation of nutrient *j* with regard to the EAR

**Mathematical formulation**

|  |  |  |
| --- | --- | --- |
|  |  | (1b) |
|  |  | (2b) |
|  |  |  |
|  |  | (1c) |
|  |  | (2c) |
|  |  |  |
|  |  | (1d) |
|  |  | (2d) |

|  |  |  |
| --- | --- | --- |
|  |  | (5b) |
|  |  | (5c) |
|  |  | (5d) |

Constraints (1b) – (2d) operate in the same way as Constraints (1a) and (2a) as explained before. However, in this case a differentiation is made between nutrient intakes on non-fasting days, fasting days, and average nutrient intakes per week.

Constraints (5b) – (5d) compute the *MAXDEV*. In Constraints (5c), on fasting days, calcium and vitamin B12 are not considered for the calculation of the MAXDEV. Instead, calcium and vitamin B12 intakes are considered on a weekly basis in Constraints (5d). Thus, a lack of calcium and vitamin B12 intake on fasting days can be compensated on non-fasting days.

## Model runs

Model runs were set up for each combination of model (3 models) and GBD recommendations applied (4 scenarios). In total, 3\*4=12 model runs were conducted as shown in table 6.

Table 6 Model runs conducted in this research

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **GBD recommendations used (lower-upper bound)** | | | |
| **Model used** | Not used | 0-50% | 50-75% | 75-100% |
| 1-Non-fasting | run 1 | run 2 | run 3 | run 4 |
| 2-Continuous fasting | run 5 | run 6 | run 7 | run 8 |
| 3-Intermittent fasting | run 9 | run 10 | run 11 | run 12 |