Supplemental material: In a trajectory toward a healthy diet, meat consumption reduction needs specific diet changes: a graph-based analyses optimization study

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Supplemental Figure 1 Flow chart explaining the sampling of French participants from the third Individual and National Study on Food Consumption Survey (INCA3)

Supplemental Figure 2 Consumption of each type of meat in the target and initial diets by sex and considered population. Three different initial diets are considered by sex, corresponding to Low (first quintile), Mean, and High (fifth quintile) consumption of meat, with all initial consumptions adjusted to differ from target consumption by an integer number of portions (see Supplemental Method 2). The blue lines show the meat consumption observed in the population. Rather than adjusting the target diets, which could have altered their full nutritional adequacy, we rounded the difference between the initial and target diets and slightly adjusted the initial diets so that they differ from the target diets by the integer number of portions. Each histogram bar thus describes the adjusted meat consumption for each diet. They are composed of zero, one, or two portion (full-colored rectangle) step sizes (50 grams for red meat and poultry and 40 grams for processed meat) and the common remainder (hatched). Above the graphs are the number of portion increases or decreases needed to reach the target diet (i.e., a -1 means a decrease of one portion is needed).

Supplemental Figure 3 Best pathway identified for males based on their first quintile of meat dietary intake.

Supplemental Figure 4 Best pathway identified for males based on their fifth quintile of meat dietary intake.

Supplemental Figure 5 Best pathway identified for females based on their first quintile of meat dietary intake.

Supplemental Figure 6 Best pathway identified for females based on their fifth quintile of meat dietary intake.

Supplemental Figure 7 Changes in nutrient (as a percentage of the reference value) along the pathway from initial to target diets for males based on their first quintile of meat dietary intake

Three different initial diets are considered by sex: Low (first quintile), Mean, and High (fifth quintile) meat-eaters. The orange and red lines represent the reference dietary intake and the lower threshold of overt deficiency, ensuring ≤5% prevalence of iron-deficiency anemia, respectively.

Supplemental Figure 8 Changes in nutrient (as a percentage of the reference value) along the pathway from initial to target diets for males based on their mean dietary intake

Three different initial diets are considered by sex: Low (first quintile), Mean, and High (fifth quintile) meat-eaters. The orange and red lines represent the reference dietary intake and the lower threshold of overt deficiency, ensuring ≤5% prevalence of iron-deficiency anemia, respectively. The symbols show what would have happened if red meat (red triangle) or processed meat (pink diamond) had been reduced.

Supplemental Figure 9 Changes in nutrient (as a percentage of the reference value) along the pathway from initial to target diets for males based on their fifth quintile of meat dietary intake

Three different initial diets are considered by sex: Low (first quintile), Mean, and High (fifth quintile) meat-eaters. The orange and red lines represent the reference dietary intake and the lower threshold of overt deficiency, ensuring ≤5% prevalence of iron-deficiency anemia, respectively. The symbols show what would have happened if red meat (red triangle) or processed meat (pink diamond) had been reduced.

Supplemental Figure 10 Changes in nutrient (as a percentage of the reference value) along the pathway from initial to target diets for females based on their first quintile of meat dietary intake

Three different initial diets are considered by sex: Low (first quintile), Mean, and High (fifth quintile) meat-eaters. The orange and red lines represent the reference dietary intake and the lower threshold of overt deficiency, ensuring ≤5% prevalence of iron-deficiency anemia, respectively.

Supplemental Figure 11 Changes in nutrient (as a percentage of the reference value) along the pathway from initial to target diets for females based on their mean dietary intake

Three different initial diets are considered by sex: Low (first quintile), Mean, and High (fifth quintile) meat-eaters. The orange and red lines represent the reference dietary intake and the lower threshold of overt deficiency, ensuring ≤5% prevalence of iron-deficiency anemia, respectively. The symbols show what would have happened if red meat (red triangle) or processed meat (pink diamond) had been reduced.

Supplemental Figure 12 Changes in nutrient (as a percentage of the reference value) along the pathway from initial to target diets for females based on their fifth quintile of meat dietary intake

Three different initial diets are considered by sex: Low (first quintile), Mean, and High (fifth quintile) meat-eaters. The orange and red lines represent the reference dietary intake and the lower threshold of overt deficiency, ensuring ≤5% prevalence of iron-deficiency anemia, respectively. The symbols show what would have happened if red meat (red triangle) or processed meat (pink diamond) had been reduced.

Supplemental Figure 13 Similarity between the consumption profiles as defined using the hierarchical classification of the food groups consumed by the INCA3 individual participants and the diets throughout the trajectory, as assessed using the Diet Similarity Index (Mertens et al., 2021, 2020) **with the first quintile of meat consumption as initial diet for male**

Supplemental Figure 14 Changes in the Greenhouse gas emissions (CO2eq) along the pathway from initial to target diets by sex and considered population. Three different initial diets are considered by sex: Low (first quintile), Mean, and High (fifth quintile) meat-eaters.

Supplemental Figure 15 Changes in Water use (m3) along the pathway from initial to target diets by sex and considered population. Three different initial diets are considered by sex: Low (first quintile), Mean, and High (fifth quintile) meat-eaters.

Supplemental Table 1 Food group consumptions (g/d) by sex in the observed diets (Low (first quintile), Mean, and High (fifth quintile) meat-eaters) and target diets

Nuts: Nuts and seeds, Refined bread: Bread and refined bakery products, Whole bread: Whole meal and semi-refined bread and bakery products, Other whole starches: Other whole and semi-refined starches, Processed products: Processed starch-based products, Eggs: Eggs and egg-based dishes, Animal fats: Animal fats and assimilated fats, ALA vegetable fats: Vegetable fats rich in α-linoleic acid, Other Vegetable fats: Vegetable fats low in α-linoleic acid, Sauces: Sauces and fresh creams, SSB: Sugar-sweetened beverages, including fruit juices, Soups: Soups and bouillons, Substitutes: Substitutes for animal products

Supplemental Table 2 Food group consumption (g/d) for each consumption profile coming from the hierarchical classification of the food groups consumed by the INCA3 individual participants.

Nuts: Nuts and seeds, Refined bread: Bread and refined bakery products, Whole bread: Whole meal and semi-refined bread and bakery products, Other whole starches: Other whole and semi-refined starches, Processed products: Processed starch-based products, Eggs: Eggs and egg-based dishes, Animal fats: Animal fats and assimilated fats, ALA vegetable fats: Vegetable fats rich in α-linoleic acid, Other Vegetable fats: Vegetable fats low in α-linoleic acid, Sauces: Sauces and fresh creams, SSB: Sugar-sweetened beverages, including fruit juices, Soups: Soups and bouillons, Substitutes: Substitutes for animal products

Multi-criteria diet optimization under constraints

Target diets were identified using a multi-criteria optimization approach previously developed by our group (Dussiot et al., 2022a; Fouillet et al., 2022). We thus identified modeled target diets (i.e., modeled consumptions of 33 food groups) with minimal long-term health risk and a minimal departure from the observed diet (to consider cultural acceptability and inertia), under constraints to ensure adequate nutrient intakes and remain within current consumption limits.

This non-linear optimization problem was performed using the NLP solver of the OPTMODEL procedure of SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA.). Optimization was implemented at the population level but in males and females, separately.

Constraints

During diet optimization, the total energy intake was constrained to stay within ±5% of its observed value. Thirty-five nutritional constraints were applied to ensure adequate nutrient intake in the male and female populations (Method Table 1), based on the most recent reference values from the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) (ANSES, 2021b). We did not consider any constraints for vitamin D because its reference value is known to be much too high to be reached by a non-fortified diet alone (Dussiot et al., 2022b; Mariotti et al., 2021). As the absorption of iron and zinc is dependent on dietary factors, the requirements were based on bioavailable iron and zinc calculated from the dietary intake using equations that predict their absorption (Armah et al., 2013; Hallberg and Hulthén, 2000; Miller et al., 2007; "Scientific Opinion on Dietary Reference Values for zinc," n.d.), as detailed in a previous study by our group (Dussiot et al., 2022b). This previous study demonstrated that current recommendations regarding bioavailable iron and zinc are very constraining when trying to model healthier diets, these recommendations being much higher than current intakes (e.g., there is a current iron-deficiency anemia prevalence of 4.1% in French female) (Dussiot et al., 2022b). Therefore, like in this previous study, we used threshold values lower than current reference values. They correspond to a deficiency prevalence of 5% because such flexibility enables the identification of diets that are apparently healthier overall, with a better balance in disability-adjusted life-years (DALYs) due to less cardiometabolic disease, despite a higher prevalence of iron-deficiency anemia (Dussiot et al., 2022b). In addition, to take into account the slightly lower digestibility of plant *vs.* animal proteins regarding the nutritional constraint on protein requirement, a 5% penalty was applied to protein intake from plant protein food items, as previously described (De Gavelle et al., 2018). As the intake of individual amino acids is generally adequate when the protein intake is sufficient in a varied diet (de Gavelle et al., 2017), only protein requirements were considered in the model constraints. However, we have *a posteriori* verified that modeled diets also contained adequate intakes of indispensable amino acids by using a database of the amino acid composition of food groups.

Moreover, some acceptability constraints were applied to the food group consumption (Method Table 2). Acceptability constraints aimed to keep the food group intakes within the range of observed intakes by bounding each food group intake between its $5th$ and $95th$ percentile of observed consumption in males and females separately. For the unhealthy food groups (red meat, processed meat and sweetened beverages), more restrictive upper limits were defined as dietary constraints according to the French dietary guidelines. Another exception was made for some healthy food groups (legumes and milk) that had 95th percentile values slightly lower than TMREL values, and for which the upper limit has thus been raised to their TMREL values.

Objectives

The main optimization objective was to minimize the long-term health risk of the modeled diet, as assessed by the *HR* criterion. The *HR* criterion was set to target the dietary recommendations from the Global Burden of Diseases (GBD) based on epidemiological studies about the associations between the consumption of different food groups and the risk of chronic diseases (Murray et al., 2020). The *HR* criterion thus aimed to limit the consumption of three unhealthy food groups or categories (red meat, processed meat and sweetened beverages), while promoting six healthy food groups or categories (whole grain products, fruits, vegetables, legumes, nuts and seeds, and milk) until their TMREL values were reached. According to the most recent (2019) estimates from the GBD, TMREL values were 0 g/d for red meat, processed meat and sweetened beverages, and 150, 325, 300, 95, 14.5 and 430 g/d, respectively, for whole grain products, fruits, vegetables, legumes, nuts and seeds, and milk (Murray et al., 2020). According to the most recent (2019) estimates from the GBD, TMREL values were 3 mg/d for sodium, and 21.5 g/d, 1080 mg/d, 0.45 g/d and 8 % of total energy intake, respectively, for fibers, calcium, EPA/DHA and PUFA (Murray et al., 2020). In our study, the *HR* criterion was thus expressed and minimized as:

$$
\text{Min } HR = \sum_{i=1}^{3} \left(\frac{\text{Opt}(i)}{\text{Max}(i)} \times \frac{\text{DALYs}(i)}{\text{DALYs}(all)} \right) + \sum_{j=1}^{6} \left(\text{max} \left[\frac{\text{TMREL}(j) - \text{Opt}(j)}{\text{TMREL}(j)}; 0 \right] \times \frac{\text{DALYs}(j)}{\text{DALYs}(all)} \right) + \sum_{n=1}^{4} \left(\text{max} \left[\frac{\text{TMREL}(n) - \text{Opt}(n)}{\text{TMREL}(n)}; 0 \right] \times \frac{\text{DALYs}(n)}{\text{DALYs}(all)} \right) + \left(\text{max} \left[\frac{\text{Opt}(Na) - \text{TMREL}(Na)}{\text{TMREL}(Na)}; 0 \right] \times \frac{\text{DALYs}(Na)}{\text{DALYs}(all)} \right)
$$

Where i denotes the food groups to be decreased (red meat, processed meat and sweetened beverages), j denotes the food groups to be increased (whole grain products, fruits, vegetables, legumes, nuts and seeds, and milk), n denotes the nutrients to be increased (fibers, calcium, EPA/DHA, PUFA), Opt(i), Opt(i), Opt(n), and Opt(Na) are the optimized consumptions of food groups I and j and nutrients n and sodium (Na), respectively, Max(i) is the upper limit of consumption of food group i (in g/d), TMREL(j), TMREL(n), and TMREL(Na) are the TMREL values of food group j and nutrients n and Na, respectively (in g/d), DALYs(i), DALYs(j), DALYs(n), and DALYs(Na) are the disability-adjusted lifeyears associated with excessive or insufficient consumptions of food groups I and j and nutrients n and Na, respectively (in y), and DALYs(all) is the sum of all DALYs(i), DALYs(i), DALYs(n) and DALYs(Na). The Max(i) values used were the maximal recommended consumption of unhealthy foods in line with the French dietary guidelines (Mariotti et al., 2021): 71g/d for red meat, 25g/d for processed meat and 263 g/d (corresponding to the average portion size) for sweetened beverages intake. The TMREL and DALYs values used were issued from the most recent (2019) estimates from the GBD (Murray et al., 2020) adapted to our study context (by using sex-specific and French DALYs values, Method Table 3).

We also evaluated how the modeled diets deviated from current diets (*DD* criterion), in order to consider inertia to changes in food consumption, which is one way to account for social/cultural acceptability. The *DD* criterion was defined as the sum of the squares of the differences between observed and optimized food group consumption, standardized by their observed standard deviations, as previously explained (Dussiot et al., 2022b). *DD* was thus expressed and minimized as:

Min
$$
DD = \sum_{k=1}^{n} \left[\frac{Obs(k) - Opt(k)}{SD(k)} \right]^2
$$

Where k is the number of food groups (n=45), Obs(k) and Opt(k) are respectively the observed and optimized consumption of food group k (in g/d) and SD(k) is the current standard deviation of the consumption of food group k.

Supplemental Method 1, Table 1. Nutritional constraints applied in the optimization model in French males and females 1 .

¹ Lower and upper bounds of the nutritional constraints are based on the most recent nutrient reference values from the French Agency for Food, Environmental and Occupational Health and Safety (ANSES) (ANSES, 2021b).

² Lower bounds correspond to the Population Reference Intake (PRI) or lowest value of the macronutrient reference intake range. For vitamins B5, E, K1, copper, magnesium and manganese, lower bounds correspond to the 5th percentile of consumption. 3 Upper bounds correspond to the Tolerable Upper Intake Level (UL) or highest value of the macronutrient reference intake range. 4 Total energy intake was constrained to stay within ±5% of the current energy intake (2600 kcal for males and 2100 kcal for females).

⁵1 mg niacin equivalent (NE) is equal to 1 mg niacin or 60 mg tryptophan

⁶For vitamin D, a lower bound was not applied as the current reference value is too high to be reached through food intake alone. ⁷ For bioavailable iron and zinc, lower bounds were not based on current reference values but on lower threshold values ensuring ≤5% deficiency prevalence. During sensitivity analysis, we also used the values shown in parentheses, which consider more demanding requirements thus ensuring ≤1% deficiency prevalence. These latter values are closer to current reference values, although still lower (but nevertheless higher than the currently observed values for bioavailable iron in females).

 8 To account for the slightly lower average digestibility of plant protein, protein intake from plants was reduced by 5% when calculating total protein intake.

Atherogenic fatty acids, lauric and myristic and palmitic acids; DHA, docosahexaenoic acid; EI, energy intake; EPA, eicosapentaenoic acid.

Supplemental Method 1, Table 2. Dietary and acceptability constraints applied for the consumption of each food group in the optimization model in French males and females.

*These upper consumption limits correspond to coupled constraints for the groups mentioned (e.g., 71 g/d is the maximum intake for beef and veal, pork and other meats and offal grouped together).

¹In the dietary constraints, upper bounds were applied to the food groups for which the consumption needed to be limited, in line with the French dietary guidelines

(Mariotti et al., 2021).
²In the acceptability constraints, lower and upper consumption limits generally represented the 5th and 95th percentiles of consumption, respectively, of the food group in males and females, calculated using data from the third Individual and National Study on Food Consumption French Survey (INCA3), n=1125 (564 males, 561 females).

 3 For legumes and milk, the upper consumption limits in each sex were raised to their theoretical minimum-risk exposure level (TMREL) values as their 95th percentiles of consumption values were slightly lower (86 g/day and 43 g/day for legumes and 343 g/day and 322 g/day for milk in males and females, respectively).
⁴For fish, in order to take account of sustainable fish c consumption (ANSES, 2008), total fish consumption was limited to 39 g/day and oily fish consumption was limited to 26 g/day.

⁵For animal fats and assimilated fats and other foods, consumptions have been imposed constant and equal to the observed intakes in the modeled diets.
⁶For animal product substitutes, due to the very low value of the 9 females.
⁷For hot and alcoholic drinks, the upper bound was set at the prevailing consumption.

Supplemental Method 1, Table 3. Theoretical minimum-risk exposure level (TMREL) and disabilityadjusted life-years (DALYs) values used in the optimization model in French males and females.

¹According to the most recent (2019) estimates from the GBD, the TMREL values are 0 g/d for red meat, processed meat and sweetened beverages, and 150, 325, 95, 300, 14.5 and 430 g/d, respectively, for whole cereal products, fruits, legumes, vegetables, nuts and seeds, and milk (Murray et al., 2020). As these TMREL values are overall estimates corresponding to a mean energy intake of 2300 kcal (Murray et al., 2020), we used sex-specific values adapted to the particular energy intake of males and females in our French adult population (centered around 2600 kcal and 2100 kcal in males and females, respectively).

²We used the most recent (2019) French sex-specific DALYs values associated with excessive/insufficient consumption of unhealthy/healthy foods, available from the Global Health Data Exchange website [\(http://ghdx.healthdata.org/gbd-results-tool\)](http://ghdx.healthdata.org/gbd-results-tool).

Supplemental method 2 Rounding of the initial diet

For a portion size of x_{ps} , a target consumption of y_t , and a quantity q in the observed diet, the number of portions between the observed and target diet was calculated as follows:

number of portions = round-down
$$
\left(\frac{q - rest\left(\frac{y_t}{x_{ps}}\right)}{x_{ps}}\right)
$$

Round_down is the function rounding a number down to the closest integer.

If the number of portions was negative, it was rounded to 0. This method sets an integer number of portions to be modified (between observed and target), and so finally enables the construction of a graph with each node differing by one portion size, connecting observed and target diet.

For example, red meat portion size is 50 g/d and there is 54 g/d in the target diet for male. The high red meat intake for male is 108 g/d. Thus, the number of portions is:

number of portions = round-down
$$
\left(\frac{108 - remainder(54/50)}{50}\right)
$$

= round-down $\left(\frac{108 - 4}{50}\right)$
= round-down $\left(\frac{104}{50}\right)$
= 2

After adjustment, the quantity for the high meat intake initial diet of male is $104g/d$ (50 x 2 + 4), and the difference to the target diet is one portion (104-50=54g).

Supplemental Method 3: Calculation of the SecDiet

The SecDiet has been designed to assess the risk of nutrient deficiency due to insufficient intake of nutrients for an adult population. This score computes the probability for each nutrient of having a sufficient intake to avoid nutrient deficiency. This is calculated using the standard normal distribution of nutrient requirements, and taking into account the mean intake y, the day-to-day variability of intake SDy², the number of days of dietary record n, the inter-individual variability $SD_r²$ and the nutrient reference value r, as follows:

$$
F\left(\frac{y-r}{\sqrt{\text{SDr}^2 + \frac{\text{SDy}^2}{n}}}\right)
$$

F(x) is the function returning the probability that an observation from the standard normal distribution is lower than x. The probability for a nutrient ranges from 0 to 1, where 1 represents a 100 % probability that the usual intake is adequate.

The nutrients included as components in the SecDiet score and the associated threshold values are described in the table below

An extended description of the method is presented in Salomé et al. (Salomé et al., 2021b).

Supplemental Method 4: Agribalyse database

The environmental pressures associated with diets were estimated by matching INCA3 consumption data with the French database Agribalyse® 3.0.1 developed by the French Agency for the Environment and Energy Management (ADEME). This allowed for a connection to be made between the environmental and nutritional properties of foods for 2497 foods consumed in France (Colomb et al., 2015).

Environmental indicator estimations are based on the method of Life Cycle Assessment (LCA), whose scope is "from field to plate." The perimeter of the indicators covers each process of the value chain: production of raw materials, transport, transformation, packaging, distribution and retailing, food preparation by the consumer, and disposal of packaging. These processes are split into two phases 1) production and 2) post-farm. Of note for Agribalyse, losses and wastes (other than non-edible parts) at home, as well as transport from the retail to the household are not considered.

Overall, Agribalyse construction is based on the international LCA standards: ISO 14040 ("ISO 14040:2006(fr), Management environnemental — Analyse du cycle de vie — Principes et cadre," n.d.) and ISO 14044("ISO 14044:2006(fr), Management environnemental — Analyse du cycle de vie — Exigences et lignes directrices," n.d., p. 14044), LEAP guidelines ("Livestock Environmental Assessment and Performance (LEAP) Partnership - Food and Agriculture Organization of the United Nations," n.d.), and PEF (European Commission, 2018). The finalized indicators are provided per kg of product and are detailed per process.

For the agricultural phase of plant products, all upstream processes (notably input production), excluding storage or drying, are included except for ingredients in processed food. In the case of animal products, all operations including the phases of production, transport and storage of feed, fattening of animals, milking, construction and maintenance of buildings and machinery, have been considered. The scope chosen is consistent with those defined in GESTIM (Gac et al., 2011) and ecoinvent® (Nemecek and Kägi, 2007).

The LCI (life cycle inventory) data of AGRIBALYSE v3.0.1 covered the period 2005-2009, except for perennial crops (2000-2010). The variety of production systems was considered by applying coefficients based on the share of systems in national production. Imported products were also considered by applying coefficients. The allocation rules are varied and are based on international recommendations as described by the ISO 14040/14044 standards ("ISO 14040:2006(fr), Management environnemental — Analyse du cycle de vie — Principes et cadre," n.d.; "ISO 14044:2006(fr), Management environnemental — Analyse du cycle de vie — Exigences et lignes directrices," n.d.). In particular, allocations have been developed in order to distribute organic nitrogen fertilizers and mineral fertilizers (P and K) between crop sequences. Biophysical allocations were used for animal production (milk versus meat). The biophysical models used for animal production and allocations by type of productions are presented in the full report (Koch and Salou, 2020) according to the reference AFNOR-BPX 30-323 ("BP X30-323-5," n.d.)(AFNOR, 2011) and in compliance with the ISO 14044 standard ("ISO 14044:2006(fr), Management environnemental -Analyse du cycle de vie — Exigences et lignes directrices," n.d.) according to three rules in descending order: 1) allocation avoidance, 2) : biophysic allocation and 3) economic allocation.

A characterization method recommended by the European Commission (Environmental Footprint 3.0) translates the input and output flows of the inventory into impacts. For the background data (inputs in construction, raw materials, etc.) the ecoinvent[®] database is used to assess the indirect emissions (off-field emissions). The full methodology and methodological choices for the use of the ecoinvent® database have been described elsewhere (Koch and Salou, 2020).

The transition from commodities to consumed food results in two coefficients related to the edible food part, and economic allocations between co-products. The recipes are then disaggregated into ingredients. For feasibility reasons, a threshold of 95% of the ingredients covered was used. Similarly, for the origin of the ingredients, a threshold of 70% coverage was used followed by a standardization step. See (Asselin-Balençon et al., 2020) for the entire description of the methodology and methodological adoptions. Post-farm estimations are based on the PEF guidelines (European Commission, 2018)

A total of 14 midpoint indicators are available in Agribalyse: climate change, ozone depletion, particulate matters, ionizing radiation (effect on human health), ecotoxicity, photochemical ozone formation (effect on human health), acidification, terrestrial eutrophication, freshwater eutrophication, marine eutrophication, land use, water use, minerals and metals use, and fossil resources use.

Description of the environmental indicators

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