



**HAL**  
open science

## Modeled healthy eating patterns are largely constrained by currently estimated requirements for bioavailable iron and zinc – a diet optimization study in French Adults

Alison Dussiot, H el ene Fouillet, Juhui Wang, Marion Salom e, Jean-Fran ois Huneau, Emmanuelle Kesse-Guyot, Fran ois Mariotti

### ► To cite this version:

Alison Dussiot, H el ene Fouillet, Juhui Wang, Marion Salom e, Jean-Fran ois Huneau, et al.. Modeled healthy eating patterns are largely constrained by currently estimated requirements for bioavailable iron and zinc – a diet optimization study in French Adults. *The American Journal of Clinical Nutrition*, 2022, 115 (3), p. 958-969. 10.1093/ajcn/nqab373 . hal-03442190v2

**HAL Id: hal-03442190**

**<https://hal.science/hal-03442190v2>**

Submitted on 25 Nov 2021

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destin ee au d ep ot et  a la diffusion de documents scientifiques de niveau recherche, publi es ou non,  emanant des  tablissements d'enseignement et de recherche fran ais ou  trangers, des laboratoires publics ou priv es.

**Modeled healthy eating patterns are largely constrained by currently estimated requirements for bioavailable iron and zinc – a diet optimization study in French Adults.**

**Alison Dussiot<sup>1</sup>, H  l  ne Fouillet<sup>1</sup>, Juhui Wang<sup>1</sup>, Marion Salom  <sup>1</sup>, Jean-Fran  ois Huneau<sup>1</sup>,  
Emmanuelle Kesse-Guyot<sup>2</sup>, Fran  ois Mariotti<sup>1</sup>**

<sup>1</sup> Universit   Paris-Saclay, AgroParisTech, INRAE, UMR PNCA, 75005, Paris, France

<sup>2</sup> Sorbonne Paris Nord University, Inserm, INRAE, Cnam, Nutritional Epidemiology Research Team (EREN),  
Epidemiology and Statistics Research Center – University of Paris (CRESS), 93017, Bobigny, France

**Corresponding author:** Professor Fran  ois Mariotti, 16 rue Claude Bernard, 75005 Paris, France,  
francois.mariotti@agroparistech.fr

**Short title:** Healthy eating pattern and absorbed iron and zinc

#### **Financial support**

This research received no external funding.

#### **Conflict of Interest**

None.

#### **List of abbreviations**

ANSES, French Agency for Food, Environmental and Occupational Health & Safety;

DALYs, Disability Adjusted Life Years;

FBDG, Food-based dietary guidelines;

Flex, Flexible model;

NFlex, Non-Flexible model

Data described in the manuscript, code book, and analytic code will be made available upon request pending application and approval.

## Abstract

1 Background: Healthier dietary patterns involve more plant-based foods than current Western diets rich in  
2 animal products containing high levels of bioavailable iron and zinc. Little consideration is given to the  
3 bioavailability of iron and zinc when studying healthy eating patterns.

4 Objectives: Our aim was to determine whether currently estimated requirements for bioavailable iron and  
5 zinc limit the identification of healthier dietary patterns.

6 Methods: Using dietary data from a representative French survey and multi-criteria non-linear  
7 optimization, we identified diets that maximize health criteria based on Food-Based Dietary Guidelines  
8 and concomitantly depart only minimally from the observed diet, while complying with all nutrient  
9 reference values either strictly (non-flexible optimization) or by allowing bioavailable iron and zinc below  
10 the current reference values, but to a limited extent (flexible optimization). Using a comparative risk  
11 assessment model, we estimated the resulting impact on cardiometabolic and colorectal cancer  
12 mortality/morbidity, and changes to iron-deficiency anemia.

13 Results: Under non-flexible optimization, reference values for bioavailable iron and zinc were the most  
14 binding of the 35 nutrient constraints and modeled diets displayed considerable redistributions within  
15 grains and meat. With flexible optimization, modeled diets were healthier as they contained less red meat  
16 and more whole-grain products, but would increase iron-deficiency anemia to 5.0% (95% CI: 3.9%, 6.4%).  
17 Globally, in terms of Disability Adjusted Life Years (DALYs), as the loss due to anemia would represent <30%  
18 of the gain otherwise made on chronic diseases, adding flexibility in the iron and zinc reference values  
19 would result in a further 18% decrease in the disease burden from 84,768 (95% Uncertainty Intervals (UI):  
20 81,066, 88,470) to 99,689 (95,787, 103,591) DALYs averted.

21 Conclusions: Currently estimated requirements for bioavailable iron and zinc proved to be critical factors  
22 when modelling healthy eating patterns. Considering lower reference values enables the identification of  
23 diets that are apparently healthier overall.

24 **Key words:** diet optimization, healthy diet, dietary requirements, dietary patterns, iron and zinc  
25 bioavailability

26

## 27 **Introduction**

28 Nutritional adequacy depends on both the intake of nutrients and their bioavailability, the latter defined  
29 as the proportion of the ingested nutrient that is made available for use in normal functions (1). The  
30 absorption of non-heme iron and zinc, in particular, can vary as a function of many physiological and  
31 dietary factors. Phytate is known to inhibit both the absorption of non-heme iron and zinc (2–4), so that  
32 individuals consuming phytate-rich diets, high in plant products, have a greater dietary requirement for  
33 iron and zinc (3,5). The intake of many nutrients and their status vary largely as a function of the type of  
34 dietary pattern, and Western diets that are more reliant on animal sources, tend towards a better  
35 nutritional status regarding iodine, vitamin B12, calcium, iron and zinc (5).

36 However, current western diets are making a major contribution to the burden of disease (6). Healthier  
37 dietary patterns have been identified using different approaches, including historical diets such as the  
38 Mediterranean diet (7), modeled Healthy Eating Patterns underlying Food-Based Dietary Guidelines  
39 (FBDG)(7–9) or prospective scenarios for human and planetary health (10,11). All these diets contain less  
40 red and processed meats and more whole grains, pulses, nuts, fruit and vegetables. They would therefore  
41 tend to reduce bioavailable iron and zinc by reducing both the intake of zinc and heme iron and the  
42 absorption of zinc and non-heme iron because of higher phytate. Almost no interventional trials have  
43 studied iron or zinc status, and our knowledge is based on modelling (12).

44 Studies modeling healthier diets generally use constant absorption coefficients for iron and zinc (8,10,13)  
45 and seldom take account of variations in their bioavailability induced by dietary changes to modeled diets  
46 (14). Furthermore, uncertainties remain regarding the physiological requirements for iron and zinc  
47 because of a lack of accurate endpoints or intermediate markers and the considerable variability seen  
48 regarding iron requirements, particularly among menstruating females. For instance, the population  
49 reference intake for menstruating females (i.e. the amount of iron that covers the requirements of 95% of  
50 females) is ~50% higher than the that needed to cover the requirements of 80% of females (10).

51 Furthermore, the prevalence of people with insufficient iron intake compared to the estimated  
52 requirement is much higher than the actual prevalence of iron-deficiency anemia, and the clinical impact  
53 of insufficient zinc intake has been little characterized in adults. The reference values used for iron and  
54 zinc might therefore be over-protective and thus excessively constraining when defining or assessing  
55 healthy dietary patterns.

56 During this study, we estimated the amounts of bioavailable iron and zinc in the diets of a reference sample  
57 of an adult population in France, which has similar background intakes and reference values for iron and  
58 zinc as other western countries (15) and then we used multi-criteria optimization to model healthy eating  
59 patterns in order to test the hypothesis that iron and zinc, rather than other nutrients, are important  
60 determinants of optimized healthy eating patterns. We then determined whether, and to what extent,  
61 meeting iron and zinc reference values limited our ability to identify healthier diets.

## 62 **Methods**

### 63 *Input data used for diet modeling*

64 We used food consumption data for males (n=561, 18-64 years old) and pre-menopausal females (n=564,  
65 18-54 years old) classified as non-under-reporters in the French INCA3 national study conducted in 2014-  
66 2015. The survey design and methods have been described in full elsewhere (16,17). The socio-  
67 demographic characteristics and lifestyles of the study population are presented in **Table 1**. Briefly, food  
68 and beverage intake were assessed using three unplanned non-consecutive 24h-dietary recalls collected  
69 by trained interviewers assisted by dietary software. Portion sizes were estimated using validated  
70 photographs (16). Nutrient intake was calculated using the 2016 nutritional composition database from  
71 the French *Centre d'Information sur la Qualité des Aliments; CIQUAL* (18). Food items (n=1533) were  
72 categorized into 45 food groups (10)(Supplemental Table 1). In each food group, the nutrient composition  
73 (for 41 nutrients) was calculated as a composite composition by gender, being the average nutrient  
74 composition of the group food items weighted by their average gender-specific population intake. Using  
75 three 24h-recall provides low precision for the individual estimates of intakes for nutrients that are little  
76 evenly distributed within individual diets (e.g. vitamin A and vitamin B12) but provides a good precision  
77 for estimating the average and inter-individual variability of intakes in a population for most nutrients,  
78 including iron and zinc. Furthermore, remaining error related to the intra-individual variability of intake  
79 for iron and zinc was addressed by extraction when assessing usual intake, as presented below.

### 80 *Iron and zinc bioavailability*

81 We first of all considered heme iron (mainly present in red meat) and non-heme iron (present in other  
82 animal-based and plant-based foods)(19). The following equation was used for the absorption of heme  
83 iron (20):

$$84 \text{ Log Absorption (\%)} = 1.9897 - 0.3092 \times \log (\text{SF})$$

85 where SF is serum ferritin, which was set at 15 µg/L (15). A serum ferritin value of 15 µg/L corresponds to  
 86 an absence of iron reserve and a higher intestinal absorption, without any further functional impact (21).  
 87 This value, as compared to 30 µg/L, leads to a better estimate of iron absorption at marginal levels of iron  
 88 intake. It also provides the lowest estimate of iron requirement, which is the least favourable situation for  
 89 our hypothesis that current estimates of iron requirement limit the identification of healthier diets.

90 For non-heme iron, we used the following equation (22):

$$91 \quad \text{Ln Absorption (\%)} = 6.294 - 0.709 \ln(\text{SF}) + 0.119 \ln(\text{C}) + 0.006 \ln(\text{MFP} + 0.1) \\ 92 \quad - 0.055 \ln(\text{T} + 0.1) - 0.247 \ln(\text{P}) - 0.137 \ln(\text{Ca}) - 0.083 \ln(\text{NH})$$

93 where SF is serum ferritin which was also set at 15 µg/L, C is vitamin C (mg), MFP is meat, fish, and poultry  
 94 (g), T is tea (number of cups), P is phytate (mg), Ca is calcium (mg), and NH is non-heme iron (mg).

95 For zinc absorption, we used the following equation (23):

$$96 \quad \text{TAZ} = 0.5 \times \left\{ 0.033 \times \left( 1 + \frac{\text{TDP}}{0.68} \right) + 0.091 + \text{TDZ} - \sqrt{\left( 0.033 \times \left( 1 + \frac{\text{TDP}}{0.68} \right) + 0.091 + \text{TDZ} \right)^2 - 4 \times 0.091 \times \text{TDZ}} \right\}$$

97 where TAZ is bioavailable zinc (mmol), TDZ is dietary zinc (mmol) and TDP is dietary phytate (mmol).

### 98 *Multi-criteria optimization of the diet*

99 A multi-objective, non-linear, constrained optimization program was developed using the optmodel  
 100 procedure under SAS software (SAS Institute®, Inc., Cary, NC, USA, version 9.4). The decision variables  
 101 were the average daily consumptions of the 45 food groups. We considered male and female populations,  
 102 the latter being divided into two subpopulations as a function of their iron requirement levels (Fe- or Fe+  
 103 females). Indeed, ~80% of pre-menopausal females have "low-to-medium" iron requirements (Fe-) that  
 104 are covered by 1.72 mg/d bioavailable iron, and 20% have "high" iron requirements (Fe+) that are covered  
 105 by 2.52 mg/d (10).



106 The optimization procedure consisted in maximizing the health quality of the modeled diet while  
 107 simultaneously minimizing its deviation from the current diet. We therefore drew upon the multi-criteria  
 108 diet optimization method developed in a previous study by the French Agency for Food, Environmental  
 109 and Occupational Health & Safety (ANSES) on Healthy Eating Pattern modelling for French FBDG (10),  
 110 which considered two sub-functions in the objective function. On the one hand, the *Health* sub-function  
 111 set as its objective compliance with dietary recommendations derived from epidemiological knowledge  
 112 on the associations between the consumption of certain food groups and the risk of chronic diseases (24–  
 113 27). The *Health* sub-function was defined as consumptions to be reduced (red meat including offal,  
 114 processed meat and sweetened beverages), as well as those to be increased (whole grain products, fruit  
 115 and vegetables) in accordance with current French recommendations (24). The *Health* objective sub-  
 116 function was thus expressed and maximized as follows:

$$117 \quad \text{Max Health} = \sum_{i=1}^3 \left[ \frac{\text{Opt}(i)}{\text{P95}(i)} \right] - \sum_{j=1}^3 \left[ \frac{\text{Opt}(j)}{\text{Max}(j)} \right]$$

118 Where  $i$  is the number of food groups to increase (whole grain products, fruit and vegetables),  $j$  is the  
 119 number of food groups to decrease (red meat, processed meat and sweetened beverages),  $\text{Opt}(i)$  and  
 120  $\text{Opt}(j)$  are the optimized consumptions of food groups  $i$  and  $j$ , respectively (in g/d),  $\text{P95}(i)$  is the current  
 121 95<sup>th</sup> percentile of consumption of food group  $i$  (in g/d) and  $\text{Max}(j)$  is the upper limit of consumption of the  
 122 food group as defined by ANSES (in g/d).

123 On the other hand, the *Diet Departure* sub-function was used to minimize the difference between the  
 124 optimized and observed food quantities in order to account for the dietary habits of the population. This  
 125 *Diet Departure* sub-function was defined as the sum of the squares of the differences for each group  
 126 between observed and optimized consumptions standardized by their standard deviations in the observed  
 127 diets. We chose such a quadratic formulation (with the squares of differences) in order to favor numerous

128 small changes across a large number of food groups, rather than a few major changes (28). The *Diet*  
 129 *Departure* sub-function was thus expressed and minimized as follows:

$$130 \quad \text{Min Diet Departure} = \sum_{k=1}^n \left[ \frac{\text{Obs}(k) - \text{Opt}(k)}{\text{SD}(k)} \right]^2$$

131 Where  $k$  is the total number of food groups,  $\text{Obs}(k)$  and  $\text{Opt}(k)$  are the observed and optimized  
 132 consumptions of food group  $k$  (in g/d), respectively, and  $\text{SD}(k)$  is the observed standard deviation of the  
 133 consumption of food group  $k$ .

134 Because some food groups were considered to be more easily interchangeable, they were grouped  
 135 together in the *Diet Departure* sub-function so as to avoid penalizing these substitutions. These non-  
 136 penalized substitutions involved those between different kinds of fruit (fresh/dried/processed), breads  
 137 (refined/whole grain), other starches (refined/whole grain), vegetable fats (low/high in  $\alpha$ -linolenic acid),  
 138 meat (poultry/red meat, excluding offal), sweetened beverages (beverages with added sugar/fruit juices),  
 139 fish (fat/lean), fresh dairy products (natural/sweetened), and soups/bouillons.

#### 140 *Nutritional constraints*

141 A large set of nutritional constraints was applied to ensure that all nutrients requirements were covered,  
 142 as well as a few dietary constraints relative to certain specific food groups under Food-Based Dietary  
 143 Guidelines (FBDG). Nutrient constraints differed for some nutrients depending on the sub-population  
 144 considered (males, Fe- females, Fe+ females) and were based on the recently revised ANSES Reference  
 145 Values (15) (**Table 2**). One exception was vitamin D, for which we did not set any lower constraint, because  
 146 the reference value is known to be much too high to permit a solution from diet optimization, as the  
 147 observed dietary intake is only ~20% of the reference value and diet is not the sole source of body vitamin  
 148 D (10). Dietary constraints were the upper bounds for food groups that had to be reduced according to  
 149 the *Health* objective sub-function (i.e., their upper limits of consumption): 71 g/d for red meat (i.e. ~500

150 g/week (24)), 25 g/d for processed meat, and 2,63 g/d (i.e. the average portion size) for sweetened  
151 beverages (juices, nectars and soft drinks) (10).

#### 152 *Acceptability constraints*

153 Acceptability constraints were used to keep the modeled consumptions per food group within the range  
154 observed in each sub-population (males, Fe- females, Fe+ females; Supplemental Table 2). Acceptability  
155 constraints included lower and higher values, corresponding to the 5th or 95th percentiles of consumption  
156 for all food groups, except those whose upper limit was set as a dietary constraint (red meat, processed  
157 meat and sweetened beverages – see above). In the acceptability constraints, in the same way as for the  
158 *Diet Departure* sub-function, the most substitutable food groups (see above) were grouped together to  
159 define their lower and upper bounds as the 5<sup>th</sup> or 95<sup>th</sup> percentiles of their total consumption.

#### 160 *Standardization of constraints to compare their relative influences*

161 We estimated the dual values associated with each constraint; i.e. estimates of the potential gain in  
162 objective function that would result from relaxing by one unit the limiting bound of the considered  
163 constraint. All constraints were standardized on the value of their limiting bounds (29), so that the  
164 standardized dual values (representing the effect of a 100% relaxation of the limiting bound) could be  
165 compared numerically with each other, and the limiting (i.e., active) constraints for nutrient and food  
166 group intakes classified from the most to the least limiting.

#### 167 *Optimization models without or with flexibility on the nutrient constraints for zinc and iron*

168 We finally used a standard optimization model (Non-Flexible, NFlex) and an alternative optimization model  
169 allowing flexibility on bioavailable iron and zinc (Flexible, Flex), the latter having been identified as the  
170 most binding nutrient constraints in the standard model. This alternative optimization model was  
171 developed with goal programming rather than strict constraints on these nutrient intakes in order to study

172 how the estimated requirements for bioavailable iron and zinc would drive and impact the composition of  
173 the modeled diets. Flexibility regarding zinc and iron intakes was thus introduced by replacing their  
174 nutrient constraints with a new goal variable added to the objective function, in order to minimize  
175 violation of the relaxed nutrient constraints while concomitantly maximizing the *Health* and minimizing  
176 the *Diet Departure* sub-functions. For safety reasons, new lower threshold values for bioavailable zinc and  
177 iron were also introduced as constraints and set as deficiency threshold corresponding to the minimum  
178 intake that would limit the probability of a nutritional deficiency, as previously described (30). The  
179 bioavailable zinc deficiency threshold was set at 1.6mg in males and 1.3mg in females (30). The  
180 bioavailable iron deficiency threshold was recalibrated to match the prevalence of iron-deficiency anemia  
181 in the French population. The distribution of bioavailable iron was log-transformed, and the usual  
182 bioavailable iron distribution was derived by extracting the intra-individual variation using the Nusser  
183 method (31). We then used the probabilistic approach (32) with Monte-Carlo simulation to estimate the  
184 number of individuals with bioavailable iron levels below the requirement, based on the modeled  
185 distribution of usual bioavailable iron and a risk curve obtained from the cumulative distribution of the  
186 requirement as modelled during an earlier work (33) and by ANSES (34). The risk curve was then  
187 recalibrated by translation to obtain prevalence estimates that matched the actual prevalence of iron-  
188 deficiency anemia in the French population (i.e. 0.2% in males and ~4% in females)(35). The deficiency  
189 threshold was set at the 97.5<sup>th</sup> percentile of this recalibrated risk curve, and the values obtained for males  
190 and females are indicated in Table 2.

191 As a complementary analysis, we also ran the two optimization models (without or with flexibility on  
192 bioavailable iron and zinc) while suppressing the *Diet Departure* term in the objective function (NFlex+ and  
193 Flex+, respectively), in order to test whether the effect of flexibility (i.e., between-model differences)  
194 would remain similar when allowing any diet change without penalization.

195 *Characterizing the expected health impact of modeled diets*

196 The EpiDiet model was used to evaluate the health benefits of the modeled diets within each optimization  
197 model (NFlex and Flex), assessing expected changes in death rates, chronic disease risks and disease  
198 burden as the number of years of life lost that would be avoided if French adults would replace their  
199 observed diet with the considered modeled diet (36,37). EpiDiet is a simulation-based nutritional and  
200 epidemiological model previously developed by our group (37) that implements the comparative risk  
201 assessment framework. Like many other such risk assessment models (38,39), it quantifies the positive or  
202 negative changes in risk related to long-term health that would result from changes to the average diet  
203 for an individual, groups or population. In this study, we considered the observed diet in the French  
204 population as the baseline situation and the modeled diets obtained with the NFlex and Flex optimization  
205 models as counterfactual situations. We considered the food and nutrient intakes of males and females,  
206 grouping together Fe- and Fe+ females according to their 80:20 proportions in the population (see above).  
207 Uncertainty Intervals on health estimates, corresponding to the precision of the parameters of the EpiDiet  
208 model, were computed using Monte Carlo simulations. Details of the EpiDiet model and its application are  
209 presented in Supplemental Method 1.

210 We also evaluated changes in the prevalence of iron-deficiency anemia that might be attributable to  
211 changes in bioavailable iron intake in the modeled diets, using the probabilistic approach. Bioavailable iron  
212 distribution was modeled by translating the modeled distribution of usual absorbed iron (see above)  
213 according to the difference between mean intakes for each sex and modeled diet, and used the sex-specific  
214 recalibrated risk curve for iron-deficiency anemia, as described above. Confidence Intervals were build  
215 taking into account sampling error and a binomial distribution.

216 Finally, we estimated the burden of disease as Disability Adjusted Life Years (DALYs) averted or added and  
217 corresponding to changes in the risks of cerebrovascular diseases, ischemic heart diseases, diabetes and  
218 colorectal cancer on the one hand, and changes in estimates of the prevalence of iron-deficiency anemia  
219 on the other hand, for the diets modeled using each optimization model (see Supplemental Method 1).

## 220 **Results**

### 221 *Standard non-flexible (NFlex) optimization model*

222 Compared to the observed diets, the modeled diets obtained using the first, non-flexible (NFlex)  
223 optimization model were characterized by healthier dietary patterns (**Figure 1**) due to some gains in the  
224 *Health* criteria at the cost of some deterioration in the *Diet Departure* criteria (**Table 3**). These healthier  
225 dietary patterns involved a large substitution of refined grain products (with variations of -56% to -95%  
226 between the different sub-populations) with whole grain products, with a total grain product consumption  
227 that remained generally unchanged, alongside an increase in fruit and vegetable consumption (+45% to  
228 +71%), a reduction in processed meats (-17% to -100%) and in soft drinks among males (Supplemental  
229 Table 3). Total red meat consumption remained almost unchanged in males (-10%) but increased markedly  
230 among females (+67%) with a particular increase in offal consumption by Fe+ females. By contrast, poultry  
231 increased in males and Fe+ females (+250% and +247%, respectively, but -33% in Fe- females), so that total  
232 meat consumption was finally almost similar in males (+11%) and Fe- females (+1%) but markedly  
233 increased in Fe+ females (+98%).

234 Whatever the population, the most limiting constraints with the greatest impact on the composition of  
235 modeled diets were bioavailable iron and zinc constraints, which displayed higher dual values than those  
236 for all other constraints affecting nutrients or food groups (Table 3). In the modeled versus the observed  
237 diets, covering nutrient reference values led to increases in bioavailable zinc and iron that were marked  
238 among Fe- females (+42% for iron and +6% for zinc) and even greater in Fe+ females (+108% for iron and  
239 +21% for zinc) (**Figure 2** and Supplemental Table 4). Reaching zinc reference values was more constraining  
240 in males while meeting iron reference value was more constraining in females and particularly in Fe+  
241 females where it required the most important dietary changes (as can be seen from their higher *Diet*  
242 *Departure* value). In addition, the constraints on zinc and iron worked together by involving similar dietary

243 changes, even if the most limiting constraint in each gender (namely, zinc in males and iron in females)  
244 was so predominant that it masked the influence of the other. In males, the influence of the iron  
245 requirement could be revealed when relaxing the zinc requirement, and *vice versa* in females (results not  
246 shown).

#### 247 *Alternative flexible (Flex) optimization model*

248 Under the alternative optimization model (Flex), flexibility was applied simultaneously to the constraints  
249 on bioavailable iron and zinc because of their inter-dependency. When compared to both the observed  
250 and NFlex-modeled diets, Flex-modeled diets contained less meat, and particularly less red meat, and  
251 more grain products, and notably more whole grain products (Figure 1). As compared to NFlex, the Flex  
252 modeling option did result in a reduction in red meat (-87% to -91% vs observed, i.e., a massive and similar  
253 reduction whatever the population) (Supplemental Table 3), and a further increase in whole grain products  
254 (+97% in males, -3% in Fe- females, +153% in Fe+ females, vs NFlex). Unlike with the NFlex-modeled diets,  
255 total meat in the Flex-modeled diets was globally similar to that of the observed diet, as poultry was also  
256 increased less in males and Fe+ females, and total red meat was reduced more in females.

257 Compared to the NFlex option, the Flex option accordingly resulted in better *Health* criteria together with  
258 lower *Diet Departure* criteria (Table 3), since fewer dietary changes were required to cover the lower zinc  
259 and iron constraints that were by construct between the nutrient reference values and the deficiency  
260 thresholds. In the Flex-modeled diets, bioavailable zinc and iron were respectively 20% and 30% lower  
261 than their reference values in males, 14% and 37% lower in Fe- females and 14% and 57% lower in Fe+  
262 females (Table 3, Figure 2 and Supplemental Tables 3 and 5).

263 In the Flex optimization model, i.e. when relaxing the constraints on bioavailable iron and zinc, we found  
264 that six nutritional constraints were limiting, namely (and in decreasing order of importance) sodium,  
265 iodine, saturated fatty acids,  $\alpha$ -linolenic acid, fiber and vitamin A (Table 3). Sodium was the most limiting

266 constraint in both sexes, followed by  $\alpha$ -linolenic acid and saturated fatty acids in males and iodine and  
267 saturated fatty acids in females.

#### 268 *Estimate of changes to the disease burden resulting from modeled diets*

269 We estimated that in French adults, the mortality risk from ischemic heart diseases, cerebrovascular  
270 diseases, diabetes and colorectal cancer would be reduced by 22% in males and 15% in females with the  
271 NFlex-modeled diets, and by 26% in males and 23% in females with the Flex-modeled diets (**Table 4** and  
272 Supplemental Table 6). We also estimated that the burden of these diseases would be reduced by 24% in  
273 males and 15% in females by the NFlex-modeled diets and by 28% in males and 25% in females by the Flex-  
274 modeled diets (Supplemental Table 7). When compared to the NFlex optimization, the Flex optimization  
275 thus resulted in a further decrease in the burden of these diseases of 19% in males (+13,654 DALYs averted)  
276 and 70% in females (+7,131 DALYs averted) (Table 4). By contrast, being more flexible with iron and zinc  
277 reference values would also tend to increase the prevalence of iron-deficiency anemia (from 2.1% (95%  
278 CI: 1.4%, 3.9%) currently to 5.0% (3.9%, 6.4%) in adults, from 0.21% (0.04%, 0.98%) currently to 3.0% (1.8%,  
279 4.6%) in males, and from 3.9% (2.6%, 5.9%) currently to 7.0% (5.1%, 9.4%) in females), whereas the figures  
280 would be virtually null without flexibility (0.11% (0.02%, 0.49%) in adults, 0.17% (0%, 0.65%) in males and  
281 0.05% (0%, 0.66%) in females). However, the DALYs resulting from this increase in iron-deficiency anemia  
282 with flexibility (Flex vs NFlex) would be small compared to the DALYs otherwise averted by the decrease  
283 in chronic disease (2,705 vs 13,654, *i.e.* 20% in males and 3,157 vs 7,131, *i.e.* 44% in females) (Table 4).  
284 Globally, when taking account of all these chronic diseases and anemia and on average over the whole  
285 population, the Flex optimization resulted in a further 18% reduction in the burden of disease compared  
286 to the NFlex optimization (+14,921 DALYs averted).

287 The expected reduction in mortality and disease burden with Flex-modeled diets versus NFlex-modeled  
288 diets was mostly ascribed to the reduction in red meat consumption (Supplemental Tables 6 and 7). The  
289 increase in whole grain products in Flex- versus NFlex-modeled diets did not therefore result in any



290 additional risk reduction under the comparative risk assessment model. The changes in mortality risk  
291 resulting from the changes to red meat consumption were a 3% increase in females under the NFlex option  
292 but a 5% decrease in both males and females under the Flex option, while the changes to mortality risks  
293 resulting from increases in whole grain products were a similar 5% reduction in both males and females  
294 with both options (see Supplemental Table 6). Changes to the risk of morbidity related to cerebrovascular  
295 diseases, ischemic heart diseases, diabetes and colorectal cancer due specifically to red meat involved a  
296 3% increase in females under the NFlex option but a 5-6% decrease in both males and females under the  
297 Flex option, while the changes to these morbidity risks specifically due to an increase in whole grain  
298 consumption were a similar 4-5% decrease in both males and females with both options (see Supplemental  
299 Table 7). Soft drinks were another food group whose variations between the observed and modeled diets  
300 significantly affected the risks of mortality and morbidity, but soft drinks varied less between the NFlex  
301 and Flex options than red meat and whole grain products, and the changes in mortality and morbidity risks  
302 due specifically to a reduction in soft drink consumption were a similar 6-8% decrease with both options  
303 (see Supplemental Tables 6 and 7).

#### 304 *Additional models to test the impact of Diet Departure criteria*

305 We also ran additional models with optimization without the *Diet Departure* criteria (i.e., with optimization  
306 on the *Health* criteria only), without or with flexibility on bioavailable zinc and iron (NFlex+ and Flex+  
307 models, respectively). They all led to healthier dietary patterns than their standard counterparts that  
308 included the *Diet Departure* criteria, by further notable increases in the consumption of fruit and  
309 vegetables and whole grain products (Supplemental Figure 1 and Supplemental Tables 3 and 5). The  
310 differences between Flex+ and NFlex+ were similar to those previously observed between Flex and NFlex  
311 with regard to diet contents in red meat (only reduced under Flex+ and not under NFlex+) and whole grains  
312 (further increased in Flex+ compared to NFlex+), and also with regard to the amounts of bioavailable iron  
313 and zinc that were similarly reduced in the event of flexibility, whether the *Diet Departure* criteria were

314 integrated or not (Supplemental Figure 2). Lastly, the dual values analysis showed that like the NFlex and  
315 Flex models, the most limiting constraint for healthier diets were bioavailable iron and zinc in the NFlex+  
316 model, and sodium, iodine, vitamin A, energy intake, docosahexaenoic acid (DHA) and eicosapentaenoic  
317 acid (EPA) in the Flex+ model (Supplemental Table 8).

## 318 **Discussion**

319 Our study has revealed a conflict between meeting current estimates for iron and zinc requirements that  
320 take account of their bioavailability, and implementing a healthy diet. We have indeed shown that in males  
321 and females, securing iron and zinc provisions precludes a reduction in red meat consumption and limits  
322 any increase in whole grains. By contrast, both of these goals can be achieved by allowing some flexibility  
323 regarding current reference values for bioavailable iron and zinc which leads to contrasted effects on  
324 health (more anemia but less chronic disease) but a better overall balance (18% more DALYs averted with  
325 flexibility than without).

326 Without flexibility, we have shown by dual value analysis that bioavailable iron and zinc were always the  
327 most limiting nutrients when modeling healthier dietary patterns, in both males and females and whether  
328 or not account was taken of dietary cultural inertia (standard NFlex and additional NFlex+ models). This  
329 conflict between meeting the estimated requirements for bioavailable iron and zinc and adopting healthier  
330 dietary patterns therefore appears to concern all populations and prevailing dietary contexts. We have  
331 also shown that this limitation, and the effect of it being removed by flexibility, was further accentuated  
332 when considering females with high iron requirements. In this case, the very high target value for  
333 bioavailable iron fully precluded any reduction in red meat and also largely limited the increase in whole  
334 grains (because of their phytate content that limits iron bioavailability). Although the nutrients with the  
335 greatest influence were zinc in males and iron in females, in all cases zinc and iron were the two most  
336 influential nutrients and worked together by driving similar dietary changes. This could be explained by  
337 the fact that the dietary contributors of iron intake are mostly the same as those of zinc, and iron and zinc  
338 absorption are both largely dependent on phytate (2,3).

339 Animal products, and particularly meat and red meat, are known to be important contributors of iron and  
340 zinc intakes, and iron requirements are known to be high for the top quintile of females of childbearing

341 age, whereas the phytate content in plants is well known to largely inhibit non-heme iron and zinc  
342 absorption (40,41). Yet there are few data in the literature which characterize the importance of this  
343 expected conflict when dealing with the transition toward diets with a higher plant-based content. In  
344 particular, there have been almost no published studies on diet modeling and optimization on health  
345 criteria that account for iron or zinc bioavailability. In a diet optimization study on environmental criteria,  
346 designed to decrease diet-induced environmental pressures that also require a reduction in red meat  
347 consumption, Barre et al. showed that including bioavailability factors tended to limit the reduction in red  
348 and processed meats (14). The model used by these authors integrated 402 food items in the same French  
349 context, whereas in the present model we focused on 45 food groups that prevented the selection of  
350 individual food items that were atypical within their group. The smaller decrease in processed meat when  
351 accounting for bioavailability indicated by Barre et al. (14) was indeed ascribed to a dramatic increase in  
352 the consumption of blood sausage (a processed meat specialty made from pork blood), which was  
353 sufficient to cover the iron reference value (88% of heme iron was sourced by this increase in blood  
354 sausage consumption according to Barre et al., while blood sausage accounted for only 1.5% of its food  
355 group (processed meat) consumption in our study). Ferrari et al. (42) also found that in females, the  
356 constraint related to iron requirement was incompatible with a constraint limiting red meat consumption,  
357 but these authors considered iron intake and not bioavailable iron (42) in females with low iron intakes.  
358 Unlike iron, the importance of zinc when considering healthy dietary patterns has been little emphasized.  
359 This can again be ascribed to the paucity of data considering zinc absorption in diet modeling, and also by  
360 the fact that it remains difficult to define zinc requirements using health-based criteria, as it remains  
361 difficult to assess zinc status. Although the important effect of phytate on zinc absorption is well  
362 documented (43), and sources of zinc are animal-based, and evidence for altered zinc status in vegetarians  
363 is unclear (4). No adequate biomarkers for zinc status are available to derive requirement estimates.

364 Furthermore, zinc requirements have been estimated using a factorial approach to considering  
365 physiological requirements by estimated total daily losses and zinc absorption coefficients (44).

366 The strength of our work was therefore that it evidenced and characterized the importance of the conflict  
367 between iron and zinc on the one hand, and red meat and whole grain consumption on the other. This  
368 conflict stems from the importance of red meat as a contributor to iron and zinc, and the importance of  
369 whole grains in decreasing iron and zinc absorption because of phytate. This work has also highlighted the  
370 importance of uncertainties regarding iron and zinc absorption and phytate contents in foods. In particular,  
371 major modeling efforts have been made to predict iron and zinc bioavailability in diets, but uncertainties  
372 remain (12,14,45).

373 Because iron and zinc are so important to defining healthy eating patterns that can be used to build Food-  
374 Based Dietary Guidelines (FBDG), a precise assessment of iron and zinc requirements and their  
375 recommended dietary allowances is a primary concern. Iron and zinc reference values are based on  
376 physiological requirements assessed from estimates of mandatory losses. For zinc, again, an adequate  
377 marker of status is lacking, and it is difficult to ascertain its relevance to health. There are considerable  
378 variations in iron requirements among females, and this has led to a very high recommended dietary  
379 allowance in order to cover 95% of them whereas most (80%) have much lower requirements. According  
380 to these requirements, iron insufficiency does not match actual iron deficiency as assessed by iron-  
381 deficiency anemia. For example, among French females, the prevalence of iron-deficiency anemia has  
382 been estimated at ~4%, while 20% of females have iron intakes below their requirements and most have  
383 intakes below the population reference intake (10). As demonstrated by Hallberg et al., non-heme iron  
384 absorption is higher in populations that are vulnerable to iron deficiency (46). The risk of iron-deficiency  
385 anemia could therefore be taken as a safeguard which would lead to a much lower reference target value,  
386 indeed as low as the deficiency threshold we used in the model with flexibility (Flex). The provision of iron  
387 at higher levels than this threshold may also have health benefits in preventing iron deficiency without

388 anemia. However, the adverse health effects of iron deficiency have been poorly characterized in literature  
389 studies, due to small sample sizes, confounding by other dietary and lifestyle factors, and by alterations in  
390 iron metabolism in response to infection. Furthermore, thresholds of iron deficiency at which these  
391 adverse effects might develop have not been well characterized and their prevalence in western countries  
392 is unknown (47). Clearly, further research is needed to characterize the relationship between iron intake  
393 and iron deficiency without anemia in adults in western countries, and evaluate its importance for health.  
394 During the present study, we found that waiving the importance of iron and zinc in the Flex model brought  
395 bioavailable iron levels down to the deficiency threshold we used in females, which would translate into  
396 an increase in the prevalence of iron-deficiency anemia among females from ~4% at present to 7% under  
397 the modeled diets. This contrasted with the virtual absence of iron-deficiency anemia (0.05%) in the diets  
398 modeled without flexibility (NFlex) that imposed a reference value for bioavailable iron in Fe+ females that  
399 was triple the deficiency threshold. To further assess the conflict that we have evidenced, this modeled  
400 increase in iron-deficiency anemia was weighed against the expected long-term health benefits that would  
401 result from adopting a healthier diet, which could help to inform about the importance of the iron  
402 reference value. Using the single metric of DALYs averted, we were able to show that the long-term health  
403 benefit of diets identified as being flexible with iron and zinc outweighed the adverse effects resulting  
404 from the increase in iron-deficiency anemia.

405 Our work has implications for healthy eating modeling and thus dietary guidelines. Iron and zinc absorption  
406 have been little studied in this regard. Dietary guidelines usually advocate healthy eating patterns, similar  
407 to the diets identified during the present study (including lower red meat and higher whole grain  
408 consumption) but with uncertainties regarding the actual benchmark levels for meat and red meat (7–9).  
409 Likewise, prospective diets for human and planetary health have defined plant-based diets as the  
410 reference, but the impact on iron status of such diets has not been fully characterized (10–12). Markedly  
411 reducing red meat and increasing whole grains imply lowering levels of bioavailable iron and zinc, and the

412 ensuing risk of an increase in iron-deficiency anemia. This risk may be deemed acceptable if outweighed  
413 by the clearly beneficial effects of healthier dietary patterns on chronic diseases with very high prevalence.  
414 This risk may also be acceptable if it can be mitigated. Indeed, in developed countries, iron-deficiency  
415 anemia can be detected and treated on an individual basis, and could also be prevented by food  
416 fortification at the population level (48).

#### 417 *Strengths and limitations*

418 Our study had certain strengths and limitations. One strength was the use of data and equations to  
419 monitor bioavailable iron and zinc in the modeled diets, but these bioavailability estimates involved some  
420 uncertainties (49,50). A second strength was the use of advanced optimization models with multi-criteria  
421 optimization by nonlinear programming, in order to identify the food groups and nutrient-related factors  
422 that hinder or favor healthier dietary patterns. However, in terms of limitations, diet modeling and  
423 optimization can exacerbate uncertainties and are reliant on a complex definition of constraints and  
424 objectives, which often involves an implicit weighting of numerous criteria (10). For instance, regarding  
425 the constraint on bioavailable iron, although we used the most accurate estimates available, some  
426 uncertainty remained in the equation used to calculate its absorption and in the estimate of the deficiency  
427 threshold we used in the case of flexibility. The number of food groups also greatly influenced the model  
428 by smoothing the nutritional contents of the groups and thus masking any specificity of certain  
429 contributors within each group, at a more detailed level. However, the food groups in the modeled diet  
430 remained interpretable because they continued to reflect the true food consumption at present within  
431 these groups. Lastly we used recent, representative data for food consumption, with a sample size  
432 ( $n=1,125$ ) that may appear to be low. A higher sample size would have been useful for better characterizing  
433 the variability of the dietary patterns in the population, but since the study mainly relies on modelled shifts  
434 in average intakes from observed diets using optimization models, the sample size is large enough to

435 provide a good precision for these population estimates and to run nutritional/health impact analysis  
436 based on the modeled diets.

#### 437 *Conclusion*

438 Using diet modeling and considering bioavailability, we have evidenced that iron and zinc are the most  
439 critical nutritional factors with respect to healthy eating patterns. Lower iron and zinc intakes from a lower  
440 consumption of meat (especially red meat) and a higher phytate intake from eating more plant-based  
441 products (especially whole grains) result in low bioavailable iron and zinc in modeled diets that tend to  
442 limit the overall health benefits of the healthiest dietary patterns. Our results highlight the predominance  
443 of iron and zinc reference values in diet modeling for Food-Based Dietary Guidelines.

444

#### 445 **Acknowledgements**

446 A.D., H.F., E.K-G. and F.M. designed research; A.D. and H.F. conducted research; AD conducted data  
447 analysis and statistical analyses; H.F., M.S., E. K-G., J.W., J-F.H. and F.M. provided tools and methodological  
448 support; A.D., H.F., E. K-G., and F.M. interpreted the results; A.D. drafted and A.D. and F.M. wrote the  
449 manuscript and all authors provided critical comments on the manuscript. A.D. and F.M. have primary  
450 responsibility for the final content. All authors have read and approved the final manuscript.

451 MS's PhD fellowship is currently being funded in part by a research contract with Terres Univia, the French  
452 Interbranch organization for plant oils and proteins. FM is the scientific leader of this contract.



## References

1. Fairweather-Tait S. Bioavailability of dietary minerals. *Biochemical Society transactions* 1996;24:775–80.
2. Bel-Serrat S, Stammers A-L, Warthon-Medina M, Moran VH, Iglesia-Altaba I, Hermoso M, Moreno LA, Lowe NM. Factors that affect zinc bioavailability and losses in adult and elderly populations. *Nutrition Reviews* 2014;72:334–52.
3. Hallberg L, Brune M, Rossander L. Iron absorption in man: ascorbic acid and dose-dependent inhibition by phytate. *The American Journal of Clinical Nutrition* 1989;49:140–4.
4. Gibson RS, Raboy V, King JC. Implications of phytate in plant-based foods for iron and zinc bioavailability, setting dietary requirements, and formulating programs and policies. *Nutr Rev* 2018;76:793–804.
5. Phillips SM, Fulgoni VL, Heaney RP, Nicklas TA, Slavin JL, Weaver CM. Commonly consumed protein foods contribute to nutrient intake, diet quality, and nutrient adequacy. *The American Journal of Clinical Nutrition* 2015;101:1346S-1352S.
6. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, Abbasi-Kangevari M, Abbastabar H, Abd-Allah F, Abdelalim A, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet* 2020;396:1204–22.
7. Trichopoulou A, Martínez-González MA, Tong TY, Forouhi NG, Khandelwal S, Prabhakaran D, Mozaffarian D, de Lorgeril M. Definitions and potential health benefits of the Mediterranean diet: views from experts around the world. *BMC Medicine* 2014;12:112.
8. Dietary Guidelines Advisory Committee. Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services [Internet]. Washington, DC: U.S. Department of Agriculture, Agricultural Research Service; 2020. Available from: [https://www.dietaryguidelines.gov/sites/default/files/2020-07/ScientificReport\\_of\\_the\\_2020DietaryGuidelinesAdvisoryCommittee\\_first-print.pdf](https://www.dietaryguidelines.gov/sites/default/files/2020-07/ScientificReport_of_the_2020DietaryGuidelinesAdvisoryCommittee_first-print.pdf)
9. A modeling system to inform the revision of the Australian guide to healthy eating [Internet]. Australian Government. Department of Health and Ageing. National Health and Medical Research Council (NHMRC); 2011 Dec p. 621. Report No.: N55c. Available from: [https://www.eatforhealth.gov.au/sites/default/files/files/public\\_consultation/n55a\\_dietary\\_guidelines\\_food\\_modelling\\_111216.pdf](https://www.eatforhealth.gov.au/sites/default/files/files/public_consultation/n55a_dietary_guidelines_food_modelling_111216.pdf)
10. Mariotti F, Havard S, Morise A, Nadaud P, Sirot V, Wetzler S, Margaritis I. Perspective: Modeling Healthy Eating Patterns for Food-Based Dietary Guidelines-Scientific Concepts, Methodological Processes, Limitations, and Lessons. *Advances in Nutrition* 2021;12:590–9.
11. van de Kamp ME, van Dooren C, Hollander A, Geurts M, Brink EJ, van Rossum C, Biesbroek S, de Valk E, Toxopeus IB, Temme EHM. Healthy diets with reduced environmental impact? - The greenhouse

gas emissions of various diets adhering to the Dutch food based dietary guidelines. *Food Res Int* 2018;104:14–24.

12. Jennings A, Tang J, Gillings R, Perfecto A, Dutton J, Speakman J, Fraser WD, Nicoletti C, Berendsen AAM, de Groot LCPGM, et al. Changing from a Western to a Mediterranean-style diet does not affect iron or selenium status: results of the New Dietary Strategies Addressing the Specific Needs of the Elderly Population for Healthy Aging in Europe (NU-AGE) 1-year randomized clinical trial in elderly Europeans. *Am J Clin Nutr* 2020;111:98–109.
13. Collings R, Harvey LJ, Hooper L, Hurst R, Brown TJ, Ansett J, King M, Fairweather-Tait SJ. The absorption of iron from whole diets: a systematic review. *Am J Clin Nutr* 2013;98:65–81.
14. Barré T, Perignon M, Gazan R, Vieux F, Micard V, Amiot M-J, Darmon N. Integrating nutrient bioavailability and co-production links when identifying sustainable diets: How low should we reduce meat consumption? de Souza RJ, editor. *PLoS ONE* [Internet] 2018 [cited 2021 Jun 22];13. Available from: <https://dx.plos.org/10.1371/journal.pone.0191767>
15. The nutritional guideline update for vitamins and minerals [Internet]. Paris, France: The French Agency for Food, Environmental and Occupational Health & Safety (ANSES); 2021 Mar p. 241. Available from: <https://www.anses.fr/fr/system/files/NUT2018SA0238Ra.pdf>
16. The Third Individual and National Survey on Food Consumption (INCA3 Survey) [Internet]. The French Agency for Food, Environmental and Occupational Health & Safety (ANSES); 2017 Jun p. 24. Available from: <https://www.anses.fr/en/system/files/NUT2014SA0234Ra.pdf>
17. Dubuisson C, Dufour A, Carrillo S, Drouillet-Pinard P, Havard S, Volatier J-L. The Third French Individual and National Food Consumption (INCA3) Survey 2014–2015: Method, design and participation rate in the framework of a European harmonization process. *Public Health Nutrition* Cambridge University Press; 2019;22:584–600.
18. The ANSES-CIQUAL food composition table [Internet]. [cited 2021 Jun 22]. Available from: <https://ciqual.anses.fr/#>
19. Moretti D. Plant-Based Diets and Iron Status. *Vegetarian and Plant-Based Diets in Health and Disease Prevention*. Academic Press. 2017. p. 715–27.
20. Hallberg L, Hulthén L. Prediction of dietary iron absorption: an algorithm for calculating absorption and bioavailability of dietary iron. *The American Journal of Clinical Nutrition* 2000;71:1147–60.
21. Walters GO, Miller FM, Worwood M. Serum ferritin concentration and iron stores in normal subjects. *J Clin Pathol* 1973;26:770–2.
22. Armah SM, Carriquiry A, Sullivan D, Cook JD, Reddy MB. A Complete Diet-Based Algorithm for Predicting Nonheme Iron Absorption in Adults. *The Journal of Nutrition* 2013;143:1136–40.
23. Scientific Opinion on Dietary Reference Values for zinc [Internet]. Parma, Italy: European Food Safety Authority (EFSA); 2014 p. 76. Available from: <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2014.3844>

24. Study of the relationship between food group consumption and risk of chronic non-communicable diseases [Internet]. Paris, France: The French Agency for Food, Environmental and Occupational Health & Safety (ANSES); 2016 Nov p. 186. Available from: <https://www.anses.fr/en/system/files/NUT2012SA0103Ra-3.pdf>
25. Harguess JM, Crespo NC, Hong MY. Strategies to reduce meat consumption: A systematic literature review of experimental studies. *Appetite* 2020;144.
26. Cocking C, Walton J, Kehoe L, Cashman K, Flynn A. The role of meat in the European diet: current state of knowledge on dietary recommendations, intakes and contribution to energy and nutrient intakes and status. *Nutrition Reviews* 2020;33:181–9.
27. Recommendations concerning diet, physical activity and sedentary behavior for adults. Paris, France: French Public Health Agency; 2019 Aug p. 62.
28. Kramer GFH, Martinez EV, Espinoza-Orias ND, Cooper KA, Tyszler M, Blonk H. Comparing the Performance of Bread and Breakfast Cereals, Dairy, and Meat in Nutritionally Balanced and Sustainable Diets. *Front Nutr* 2018;5:9.
29. Mausser H, Grodzevich O, Romanko O, Ding Y, Gregov S, Halevy I, Kavazovic Z, Seeman T, Shioda R, Youbiss F. Normalization and Other Topics in MultiObjective Optimization. *Fields-MITACS Industrial Problem Solving Workshop and the Algorithmics Inc 2006*;pp.59-101.
30. Salomé M, Kesse-Guyot E, Fouillet H, Touvier M, Herberg S, Huneau J-F, Mariotti F. Development and evaluation of a new dietary index assessing nutrient security by aggregating probabilistic estimates of the risk of nutrient deficiency in two French adult populations. *Br J Nutr* 2020;1–12.
31. Hoffmann K, Boeing H, Dufour A, Volatier J, Telman J, Virtanen M, Becker W, De Henauw S. Estimating the distribution of usual dietary intake by short-term measurements. *European Journal of Clinical Nutrition*. 2002;56, Suppl 2, S53–62.
32. National Research Council (US) Subcommittee on Criteria for Dietary Evaluation. *Nutrient Adequacy: Assessment Using Food Consumption Surveys* [Internet]. Washington (DC): National Academies Press (US); 1986 [cited 2021 Jun 22]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK217533/>
33. de Gavelle E, Huneau J-F, Mariotti F. Patterns of Protein Food Intake Are Associated with Nutrient Adequacy in the General French Adult Population. *Nutrients* 2018;10:226.
34. Updating of the PNNS guidelines: Revision of the food-based dietary guidelines [Internet]. Paris, France: The French Agency for Food, Environmental and Occupational Health & Safety (ANSES); 2016 Dec p. 190. Available from: <https://www.anses.fr/fr/system/files/NUT2012SA0103Ra-1.pdf>
35. Environment, Biomonitoring, Physical Activity and Nutrition Health Study (Esteban 2014-2016). Nutrition Component. Chapter Bioassays: vitamins and minerals [Internet]. Saint-Maurice, France: French Public Health Agency; 2019 Dec p. 61. Available from: <https://www.santepubliquefrance.fr/determinants-de-sante/nutrition-et-activite-physique/documents/rapport-synthese/etude-de-sante-sur-l-environnement-la->

biosurveillance-l-activite-physique-et-la-nutrition-esteban-2014-2016-.-volet-nutrition.-  
chapitre-dosages

36. Schwingshackl L, Knüppel S, Michels N, Schwedhelm C, Hoffmann G, Iqbal K, De Henauw S, Boeing H, Devleeschauwer B. Intake of 12 food groups and disability-adjusted life years from coronary heart disease, stroke, type 2 diabetes, and colorectal cancer in 16 European countries. *Eur J Epidemiol* 2019;34:765–75.
37. Kesse-Guyot E, Chaltiel D, Wang J, Pointereau P, Langevin B, Allès B, Rebouillat P, Lairon D, Vidal R, Mariotti F, et al. Sustainability analysis of French dietary guidelines using multiple criteria. *Nature Sustainability* Nature Publishing Group; 2020;3:377–85.
38. Scarborough P, Harrington RA, Mizdrak A, Zhou LM, Doherty A. The Preventable Risk Integrated ModEl and Its Use to Estimate the Health Impact of Public Health Policy Scenarios. *Scientifica* 2014;2014:1–21.
39. Murray CJL, Lopez AD. Measuring the Global Burden of Disease. *N Engl J Med* 2013;369:448–57.
40. Van Mierlo K, Rohmer S, Gerdessen JC. A model for composing meat replacers: Reducing the environmental impact of our food consumption pattern while retaining its nutritional value. *Journal of Cleaner Production* 2017;165:930–50.
41. Schlemmer U, Frølich W, Prieto R, Grases F. Phytate in foods and significance for humans: Food sources, intake, processing, bioavailability, protective role and analysis. *Mol Nutr Food Res* 2009;53 Suppl 2: S330-75.
42. Ferrari M, Benvenuti L, Rossi L, De Santis A, Sette S, Martone D, Piccinelli R, Le Donne C, Leclercq C, Turrini A. Could Dietary Goals and Climate Change Mitigation Be Achieved Through Optimized Diet? The Experience of Modeling the National Food Consumption Data in Italy. *Frontiers in Nutrition* 2020;7.
43. Miller LV, Krebs NF, Hambidge KM. A Mathematical Model of Zinc Absorption in Humans As a Function of Dietary Zinc and Phytate. *The Journal of Nutrition* 2007;137:135–41.
44. Dietary Reference Values for nutrients Summary report [Internet]. The European Food Safety Authority (EFSA); 2017 Dec p. 98. Available from: <https://efsa.onlinelibrary.wiley.com/doi/abs/10.2903/sp.efsa.2017.e15121>
45. Miller LV, Krebs NF, Hambidge KM. Mathematical model of zinc absorption: effects of dietary calcium, protein and iron on zinc absorption. *British Journal of Nutrition* Cambridge University Press; 2013;109:695–700.
46. Hallberg L, Hultén L, Gramatkovski E. Iron absorption from the whole diet in men: how effective is the regulation of iron absorption? *Am J Clin Nutr* 1997;66:347–56.
47. Iron and Health [Internet]. London, United Kingdom: Scientific Advisory Committee on Nutrition; 2010 p. 361. Available from: [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/339309/SACN\\_Iron\\_and\\_Health\\_Report.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/339309/SACN_Iron_and_Health_Report.pdf)

48. Das JK, Salam RA, Mahmood SB, Moin A, Kumar R, Mukhtar K, Lassi ZS, Bhutta ZA. Food fortification with multiple micronutrients: impact on health outcomes in general population. *Cochrane Database Syst Rev* 2019;12.
49. Hurrell R, Egli I. Iron bioavailability and dietary reference values. *The American Journal of Clinical Nutrition* 2010;91:1461S-1467S.
50. Hunt JR. Algorithms for iron and zinc bioavailability: are they accurate? *Int J Vitam Nutr Res* 2010;80:257–62.

**TABLE 1** Lifestyle and sociodemographic characteristics of the sample of adults ( $n = 1,125$ ) extracted from the French national INCA3 study, 2014-2015.

	Males ( $n = 564$ )	Females ( $n = 561$ )
<b>Age, %</b>		
< 25y	9%	8%
25-35y	16%	25%
35-50y	38%	52%
50-65y	37%	15%
<b>Level of education, %</b>		
< High-school diploma	34%	23%
High-school diploma	21%	21%
Post-secondary graduation	44%	56%
<b>Body Mass Index, %</b>		
< 18.5 kg·m <sup>-2</sup>	2%	4%
18.5-24.99 kg·m <sup>-2</sup>	49%	59%
25-29.99 kg·m <sup>-2</sup>	38%	24%
> 30 kg·m <sup>-2</sup>	11%	12%
<b>Alcohol consumption, %</b>		
Non-drinker	30%	54%
Moderate drinker <sup>1</sup>	70%	46%
Heavy drinker	-	-

<sup>1</sup> <20g/d for females and <30 g/d for males)

**TABLE 2** Nutritional constraints used in the optimization models

Nutrient	Unit	Lower bounds <sup>1</sup>		Upper bounds <sup>2</sup>	
		Males (18-64 y)	Females (18-54 y)	Males (18-64 y)	Females (18-54 y)
Energy intake <sup>3</sup>	kcal·d <sup>-1</sup>	2,470	1,995	2,730	2,205
Retinol	µg·d <sup>-1</sup>	-	-	3,000	3,000
Vitamin A	µg·d <sup>-1</sup>	750	650	-	-
Thiamin	µg·(kcal·d) <sup>-1</sup>	0.418	0.418	-	-
Riboflavin	mg·d <sup>-1</sup>	1.6	1.6	-	-
Niacin	mg NE·(kcal·d) <sup>-1</sup>	0.0067	0.0067	-	-
Pantothenic acid	mg·d <sup>-1</sup>	3.77	3.22	-	-
Vitamin B6	mg·d <sup>-1</sup>	1.7	1.6	25	25
Folate	µg·d <sup>-1</sup>	330	330	-	-
Vitamin B12	µg·d <sup>-1</sup>	4	4	-	-
Vitamin C	mg·d <sup>-1</sup>	110	110	-	-
<i>Vitamin D</i>	µg·d <sup>-1</sup>	-	-	100	100
Vitamin E	mg·d <sup>-1</sup>	5.28	4.37	-	-
Vitamin K1	µg·d <sup>-1</sup>	39.47	34.48	-	-
Calcium	mg·d <sup>-1</sup>	950	950	2,500	2,500
Copper	mg·d <sup>-1</sup>	1.07	0.89	5	5
Bioavailable iron - NFlex model <sup>4</sup>	mg·d <sup>-1</sup>	1.72	1.72 or 2.52 <sup>5</sup>	-	-
Bioavailable iron - Flex model <sup>4</sup>	mg·d <sup>-1</sup>	0.83	1.08	-	-
Iodine	µg·d <sup>-1</sup>	150	150	600	600
Magnesium	mg·d <sup>-1</sup>	254	195	-	-
Manganese	mg·d <sup>-1</sup>	1.99	1.52	-	-
Phosphorus	mg·d <sup>-1</sup>	550	550	-	-
Potassium	mg·d <sup>-1</sup>	3,500	3,500	-	-
Selenium	µg·d <sup>-1</sup>	70	70	300	300
Sodium	mg·d <sup>-1</sup>	1,500	1,500	2,300	2,300
Bioavailable Zinc - NFlex model <sup>4</sup>	mg·d <sup>-1</sup>	3.63	3.23	25	25
Bioavailable Zinc - Flex model <sup>4</sup>	mg·d <sup>-1</sup>	1.6	1.3	25	25
Water	g·d <sup>-1</sup>	2,500	2,000	-	-
Saturated fatty acids	%EI·d <sup>-1</sup>	-	-	12%	12%
Lauric, myristic and palmitic acids	%EI·d <sup>-1</sup>	-	-	8%	8%
Linoleic acid	%EI·d <sup>-1</sup>	4%	4%	-	-
α-linolenic acid	%EI·d <sup>-1</sup>	1%	1%	-	-
Linoleic acid : α-linolenic acid	-	-	-	5	5
EPA+DHA <sup>3</sup>	g·d <sup>-1</sup>	0.5	0.5	-	-
Sugar excluding lactose	g·d <sup>-1</sup>	-	-	100	100
Protein	g·(kg_bw·d) <sup>-1</sup>	0.83	0.83	2.3	2.3
Fiber	g·d <sup>-1</sup>	30	30	-	-

<sup>1</sup> Lower bounds are the Population Reference Intake or lowest value of the macronutrient reference intake range.

<sup>2</sup> Upper bounds are the Tolerable Upper Intake Level or highest value of the macronutrients reference intake range.

<sup>3</sup> Deficiency thresholds. DHA, docosahexaenoic acid; EI, energy intake; EPA, eicosapentaenoic acid. 1 kcal = 0.0042 MJ. <sup>4</sup>NFlex, standard multicriteria optimization model; Flex, goal programming option allowing flexibility regarding

nutrient constraints for zinc and iron. <sup>5</sup>for females with low-to-medium (Fe- females) / high (Fe+ females) iron requirements.



**TABLE 3** Values of the objective sub-functions used during optimization in males, females with low-to-medium iron requirements (Fe-), and females with high iron requirements (Fe+), using the standard multicriteria optimization model (NFlex) or the goal programming option allowing flexibility regarding nutrient constraints for zinc and iron (Flex)

	Males			Females Fe-			Females Fe+		
	Observed diet	Modeled diets		Observed diet	Modeled diets		Observed diet	Modeled diets	
		NFlex	Flex		NFlex	Flex		NFlex	Flex
<b>Objective sub-functions <sup>1</sup></b>									
Health	-3.18	0.17	1.04	-1.78	-0.44	0.80	-1.78	-1.53	0.81
Diet Departure	0.00	5.32	3.43	0.00	4.63	3.12	0.00	65.18	3.13
Goal		0.00	0.50		0.00	0.51		0.00	0.71
<b>Deviations from requirements <sup>2</sup></b>									
Bioavailable iron		0.00	0.30		0.00	0.37		0.00	0.57
Bioavailable zinc		0.00	0.20		0.00	0.14		0.00	0.14
<b>Dual values of nutrient constraints <sup>3</sup></b>									
Bioavailable zinc		<b>34</b>	0		0	0		0	0
Bioavailable iron		4	0		<b>23</b>	0		<b>645</b>	0
Sodium		-10	<b>-8</b>		-12	<b>-8</b>		-57	<b>-8</b>
Iodine		0	2		13	7		0	7
Saturated fatty acids		-3	-3		-2	-5		0	-5
Alpha-linolenic acid		4	4		5	4		9	4
Fiber		9	1		7	4		13	4
Vitamin A		2	3		1	4		0	4

<sup>1</sup>Multi-criteria optimization consisted in maximizing the Health criteria while minimizing the Diet Departure and Goal criteria, with the Goal criteria being the sum of the goal variables regarding bioavailable zinc and iron intakes. <sup>2</sup>Relative deviations from reference values (e.g. bioavailable iron = 0.30 means that the value is 30% below requirement), whose sum is equal to the Goal criteria. <sup>3</sup>Standardized dual values representing the potential effect of a 100% relaxation of the limiting bound of the constraint considered, to classify the nutritional constraints from the most to the least limiting (i.e., active). Limiting constraints have a positive (negative) value if the lower (upper) bound is binding. Only nutrients with a limiting

*constraint (i.e. with a non-null dual value) are presented here. For each scenario, the most limiting constraint (i.e., with the highest absolute value) is in bold.*

**TABLE 4** Expected changes to mortality and morbidity in French adults resulting from the adoption of modeled diets as compared to observed diets

	Adults (over 18 y)		Males (18-64 y)		Females <sup>1</sup> (18-54 y)	
	Modeled diets		Modeled diets		Modeled diets	
	NFlex	Flex	NFlex	Flex	NFlex	Flex
<b>Decrease in mortality risk, % (95%UI) <sup>2,3</sup></b>						
Ischemic Heart Diseases	20 (18, 22)	19 (18, 21)	20 (18, 22)	19 (17, 21)	24 (21, 27)	23 (19, 26)
Cerebrovascular Diseases	16 (13, 18)	23 (21, 26)	17 (14, 20)	24 (21, 27)	11 (8, 13)	21 (18, 24)
Diabetes	35 (34, 37)	46 (44, 48)	37 (35, 39)	47 (45, 49)	21 (18, 23)	39 (37, 41)
Colorectal Cancer	23 (21, 25)	31 (29, 34)	26 (23, 28)	33 (31, 36)	12 (10, 14)	24 (22, 26)
<b>Total</b>	<b>21</b> (19, 23)	<b>25</b> (24, 27)	<b>22</b> (20, 24)	<b>26</b> (24, 28)	<b>15</b> (13, 16)	<b>23</b> (21, 25)
<b>DALYs averted (95% UI) <sup>2,3,4</sup></b>						
Ischemic Heart Diseases	28,130 (25,581, 30,678)	27,156 (24,648, 29,664)	25,468 (22,942, 27,994)	24,618 (22,133, 27,104)	2,661 (2,324, 2,999)	2,538 (2,200, 2,875)
Cerebrovascular Diseases	14,359 (12,370, 16,348)	21,870 (19,794, 23,945)	11,541 (9,657, 13,426)	16,185 (14,244, 18,127)	2,817 (2,182, 3,453)	5,684 (4,950, 6,418)
Diabetes	22,023 (21,180, 22,865)	29,150 (28,237, 30,064)	19,681 (18,882, 20,479)	24,678 (23,795, 25,562)	2,342 (2,073, 2,611)	4,472 (4,239, 4,705)
Colorectal Cancer	18,708 (17,202, 20,215)	25,827 (24,267, 27,388)	16,379 (14,901, 17,857)	21,241 (19,718, 22,763)	2,329 (2,034, 2,625)	4,587 (4,243, 4,930)
<b>Sub-total</b>	<b>83,220</b> (79,555, 86,884)	<b>104,003</b> (100,279, 107,727)	<b>73,069</b> (69,498, 76,640)	<b>86,723</b> (83,111, 90,334)	<b>10,150</b> (9,327, 10,973)	<b>17,281</b> (16,372, 18,189)
<b>Δ vs NFlex</b>		<b>20,784</b> (15,559, 26,009)		<b>13,654</b> (8,574, 18,733)		<b>7,131</b> (5,905, 8,356)
<b>Iron deficiency anemia</b>	<b>1,548</b> (1,087, 2,138)	<b>-4,313</b> (-5,500, -3,169)	<b>30</b> (27, 129)	<b>-2,675</b> (-3,556, -1,771)	<b>1,518</b> (1,060, 2,009)	<b>-1,638</b> (-1,944, -1,398)
<b>Δ vs NFlex</b>		<b>-5,862</b> (-7,141, -4,584)		<b>-2,705</b> (-3,599, -1,811)		<b>-3,157</b> (-3,705, -2,610)
<b>Total</b>	<b>84,768</b> (81,066, 88,470)	<b>99,689</b> (95,787, 103,591)	<b>73,100</b> (69,528, 76,671)	<b>84,048</b> (80,327, 87,768)	<b>11,668</b> (10,718, 12,618)	<b>15,641</b> (14,693, 16,590)
<b>Δ vs NFlex</b>		<b>14,921</b> (9,542, 20,300)		<b>10,948</b> (5,791, 16,105)		<b>3,973</b> (2,631, 5,315)

<sup>1</sup>Food and nutrient intakes of Fe- and Fe+ females, used to estimate changes to risk as compared to the observed situation in females using comparative risk assessment, were averaged according to their 80:20 ratio in the population. <sup>2</sup>Estimated changes to the risk of mortality in France comparing diets modeled using different optimization models with the current observed diet in the French adult population. <sup>3</sup>95% Uncertainty Intervals (UI) of the estimated impacts were computed from modeled errors in model parameters estimates using Monte Carlo simulations. <sup>4</sup>DALYs, Disability-adjusted life years averted, comparing diets modeled with different optimization models with the currently observed diet in the French adult population. NFlex, standard multicriteria optimization model; Flex, goal programming option allowing flexibility regarding nutrient constraints for zinc and iron. Uncertainty intervals for averted DALYs are shown in brackets.

## Legends for Figures

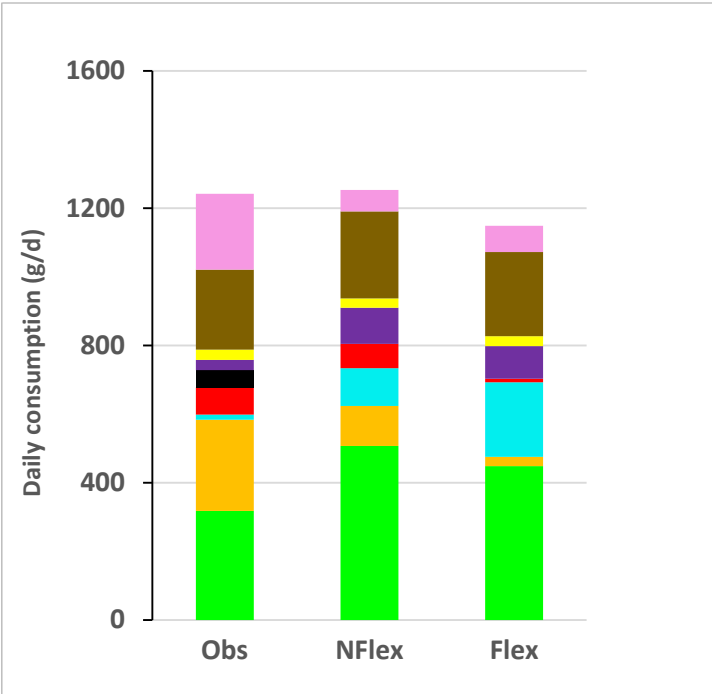
**FIGURE 1** Daily food category consumption in the observed diets (Obs) and modeled diets in males (panel A), females with “low-to-medium” iron requirements (Fe-) (panel B), and females with high iron requirements (Fe+) (panel C), using either the standard multicriteria optimization model (NFlex) or the goal programming option allowing flexibility regarding the nutrient constraints for zinc and iron (Flex)

For clarity, the 45 modeled food groups are not represented here but grouped into broader categories that are included in the Health sub-function (such as red meat, processed meat, soft drinks, grain products, fruit and vegetables) or represent other protein sources (poultry, fish and dairy products), and other food groups have been grouped as “others” (20 groups) and “other drinks” (3 groups). Details are shown in Supplemental Tables 1 and 5.

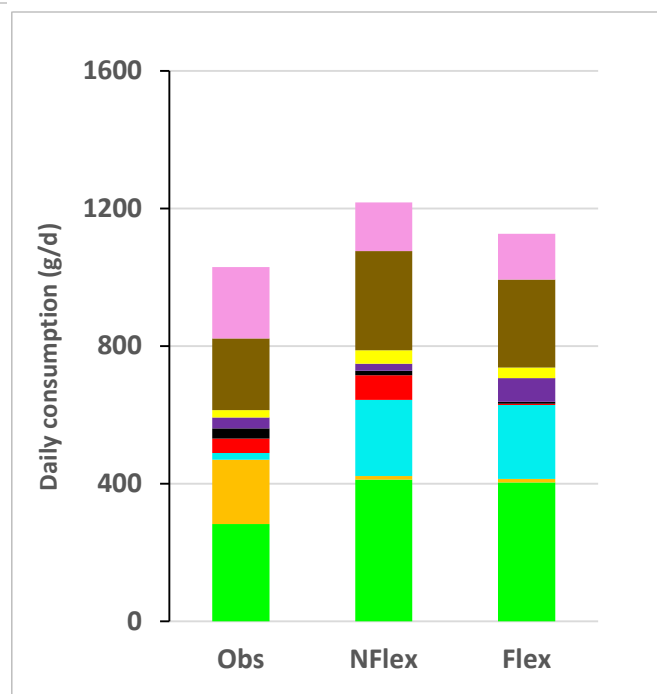
**FIGURE 2** Amount of absorbed iron (upper panel A) and absorbed zinc (lower panel B) under the observed diets (Obs) and modeled diets in males, females with “low-to-medium” iron requirements (Fe-), and females with high iron requirements (Fe+) using either the standard multicriteria optimization model (NFlex) or the goal programming option allowing flexibility regarding nutrient constraints for zinc and iron (Flex)

The solid lines indicate the current reference values for the nutrient and population considered, which are used as the lower bound of the constraint in the NFlex model, and the broken lines indicate the deficiency threshold for the nutrient and population considered that is used as the lower bound of the constraint in the Flex model.

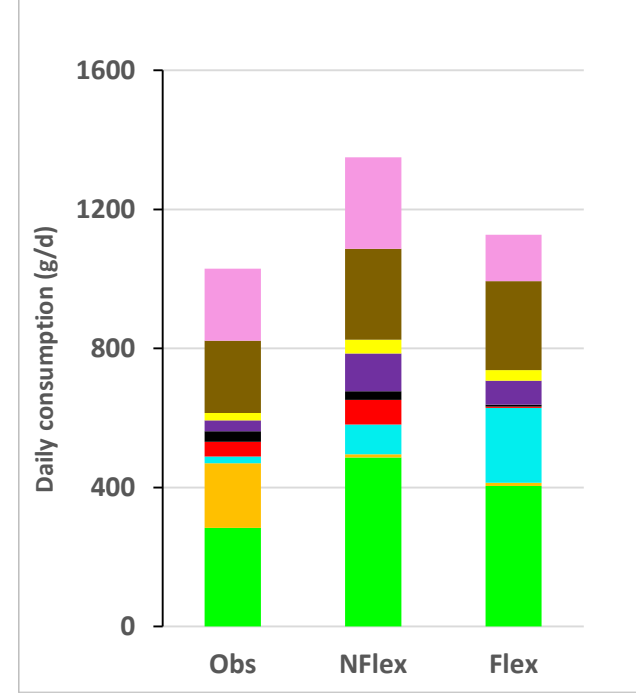
### A. Males



### B. Females Fe-

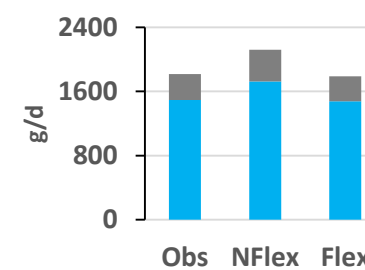
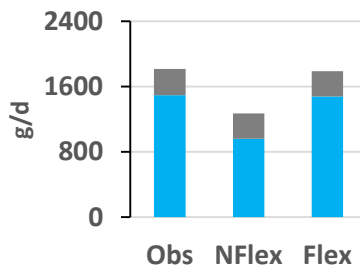
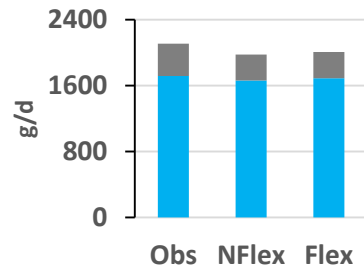


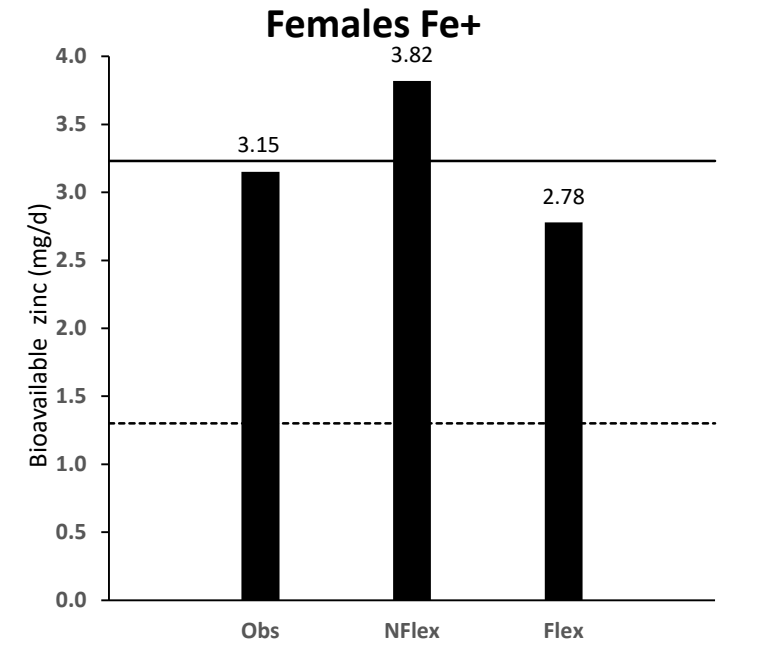
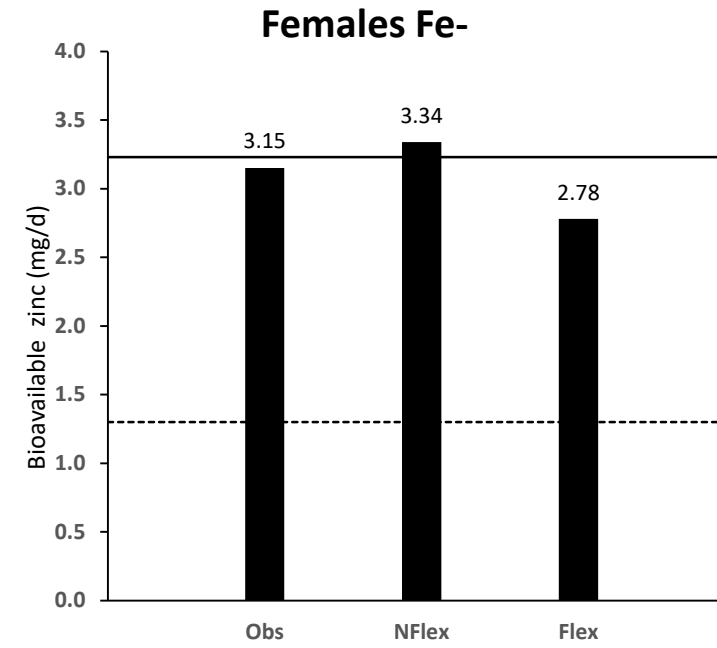
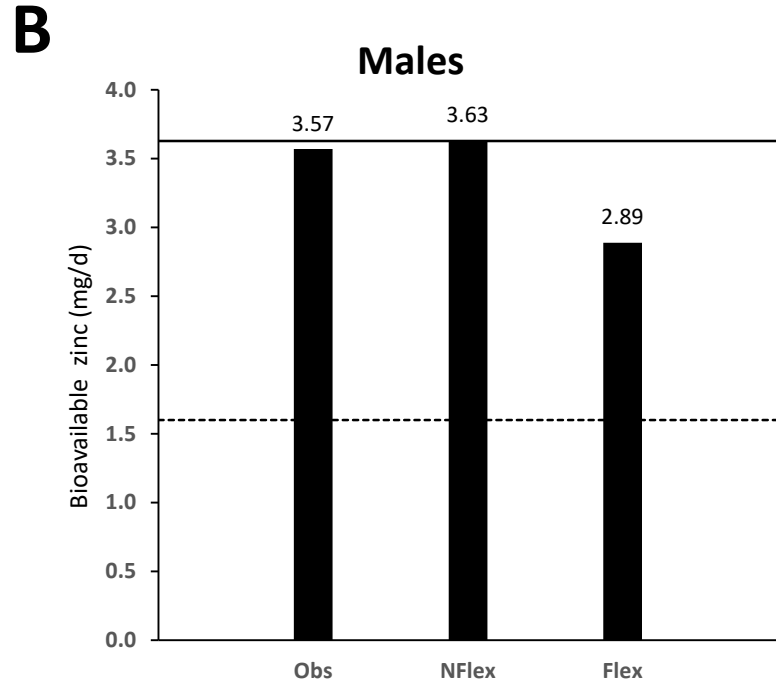
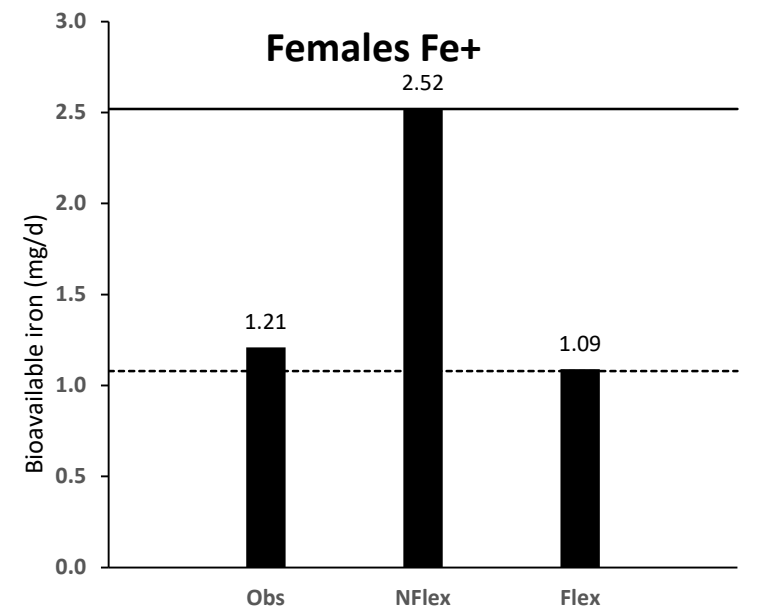
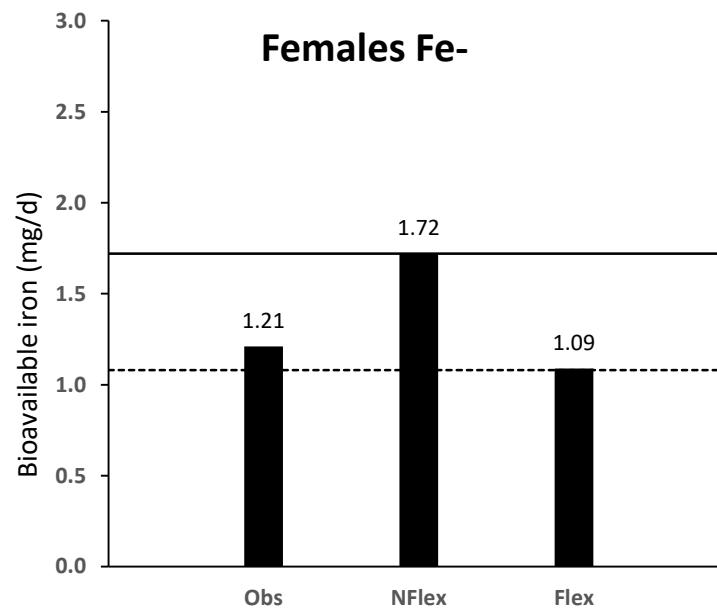
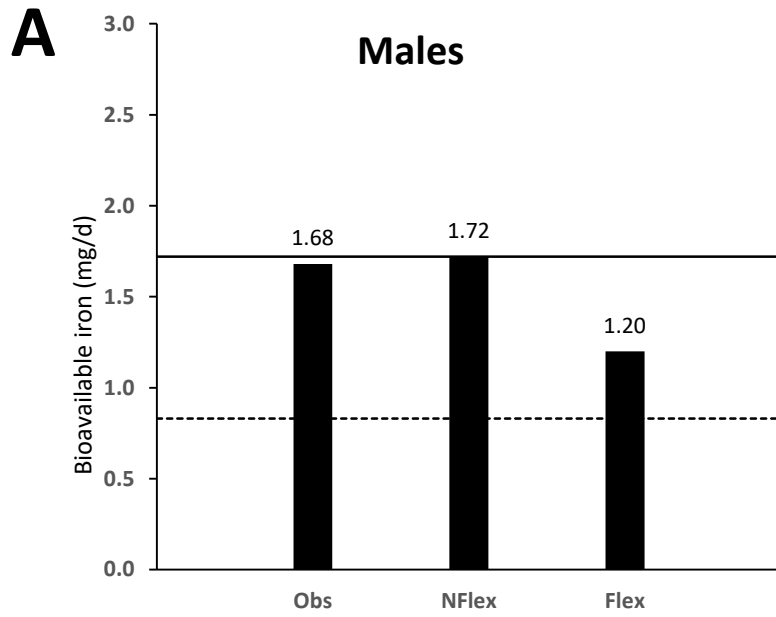
### C. Females Fe+



- Soft Drinks
- Dairy Products
- Fish
- Poultry
- Processed Meat
- Red Meat
- Whole Grain Products
- Refined Grain Products
- Fruit and Vegetables

- Others
- Other Drinks





————— current reference value

- - - - - deficiency threshold

**Modeled healthy eating patterns are largely constrained by currently estimated requirements for bioavailable iron and zinc – a diet optimization study in French Adults.**

Dussiot *et al.*

Online Supplementary Material

## Online Supplementary Material

**SUPPLEMENTAL TABLE 1** Summary of foods groups formed for food categorization

Food category (Number of food items per category)	Food group (Number of food items per group)	Proportion of food group within the category	Main types of foods (Proportion of foods within the group)
Fruit and vegetables (244)	Vegetables (149)	61%	Raw vegetables (~ 40%) Cooked vegetables (~ 30%)
	Fresh fruit (50)	20%	Raw fruit (100%)
	Dried fruits (9)	4%	Dried fruits (70%) Chestnuts (30%)
	Processed fruits: compotes and cooked fruit (13)	5%	Compote (40%) Fruit in syrup (40%)
	Nuts, seeds and oleaginous fruits (23)	9%	Oleaginous fruits (~ 50%) Seeds (~ 40%)
Starches (171)	Bread and refined bakery products (36)	21%	Breads (~ 50%) Rusks (~ 20%)
	Whole meal and semi-refined bread and bakery products (15)	9%	Breads (~ 50%) Rusks (~ 30%)
	Other refined starches (13)	8%	Rice (~ 30%) Pasta (~ 20%)
	Other complete and semi- complete starches (11)	6%	Wheat (50%) Quinoa (20%)
	Starch-based products, sweet/fat processed (61)	36%	Breakfast cereals (~ 50%) Cookies (~ 20%)
	Salt/fat processed starch products (15)	9%	Savory cookies (~ 50%) Chips: 4 foods (~ 20%)
	Potatoes and other tubers (20)	12%	Potatoes (~ 50%) Other tubers (~ 20%)
Legumes (16)	Legumes (16)	100%	Dried beans (~ 50%) Lentils (15%)



## Online Supplementary Material

Food category (Number of food items per category)	Food group (Number of food items per group)	Proportion within the category	Main types of foods (Proportion of food within the group)
Meats, Processed meats, Fish products, Eggs (315)	Poultry (24)	8%	Chicken (~ 30%) Duck (~ 20%)
	Beef and veal (40)	13%	Beef (~ 65%) Veal (~ 35%)
	Pork and other meats (39)	12%	Pork (~ 40%) Lamb (~ 30%)
	Offal (19)	6%	Beef and veal (~ 50%)
	Processed meats (71)	23%	Sausages, "andouilles" (~ 35%) "Rillettes", "pâtés", "terrines", "foie gras" (~ 35%)
	Oily fish (32)	10%	Salmon (~ 30%) Mackerel (~ 20%)
	Other fish (55)	17%	Tuna (~ 15%) Trout (~ 10%)
	Mollusks and crustaceans (21)	7%	Mollusks excluding cephalopods (40%) Crustaceans (~ 30%)
	Eggs and egg-based dishes (14)	4%	Whole eggs (~ 65%) Egg yolks (~ 20%)
Milk and dairy products (192)	Milk (15)	8%	Semi-skimmed cow's milk (40%) Whole cow's milk (25%)
	Fresh natural dairy products (18)	9%	Yoghurts, fermented milks and dairy specialties (~ 55%) Cottage cheeses, "Faisselles", "Petit Suisse" (~ 45%)
	Fresh sweetened dairy products (39)	20%	Yoghurts, fermented milks and dairy specialties (~ 65%) Cottage cheeses, "Faisselles", "Petit Suisse" (~ 25%)
	Sweet milky desserts (22)	11%	Cream desserts (~ 60%) Other sweet desserts (~ 25%)
	Cheese (98)	51%	-

## Online Supplementary Material

Food category (Number of food items per category)	Food group (Number of food items per group)	Proportion within the category	Main types of foods (Proportion of food within the group)
Added fats and oils (98)	Animal fats and assimilated fats (4)	4%	Lard, bacon, duck or goose fat
	Butter and low-fat butter (11)	11%	Butter (55%) Low-fat butter (45%)
	Vegetable fats rich in alpha-linoleic acid (4)	4%	Vegetable oils (100%): rapeseed, flax, walnut, soybean
	Vegetable fats rich in alpha-linoleic acid (24)	24%	Vegetable oils (peanut, sunflower, palm, frying) (33%) Vegetable fats (margarine type) (67%)
	Sauces and fresh creams (55)	56%	Hot sauces (80%) Cold sauces (ketchup, mustard, mayo, miso)
Sweet products or Sweet and fatty products (198)	Sweet products or sweet and fatty products (198)	100%	Pastries (~ 15%) Cookies (~ 10%)
Drinking water (44)	Drinking water (44)	100%	-
Alcohol-free soft drinks (74)	Sweetened soda-type drinks (45)	61%	-
	Fruit juices (29)	39%	-
Hot drinks (22)	Hot drinks (22)	100%	Coffee and related products (~ 60%) Tea and herbal teas (~ 30%)
Salt (6)	Salt (6)	100%	-
Condiments (13)	Condiments (13)	100%	Olives or similar (~ 50%) Vinegar products (~ 20%)
Aromatic herbs, Spices except salt (38)	Aromatic herbs, spices except salt (38)	100%	Aromatic herbs (~ 65%) Spices (35%)

## Online Supplementary Material

Food category (Number of food items per category)	Food group (Number of food items per group)	Proportion within the category	Main types of foods (Proportion of food within the group)
Soups and Bouillons (38)	Soups (30)	79%	Vegetable soups (with or without cheese) (85%) Soups with OPV (15%)
	Bouillons (8)	21%	Broths with meat (75%) Vegetable broths only (25%)
Substitutes of animal products (9)	Substitutes for animal products (9)	100%	Soy products (~ 90%) Almond drink (~ 10%)
Other foods (14)	Other foods (14)	100%	Fish eggs (~ 40%) Vinegars (25%)
Alcoholic drinks (41)	Alcoholic drinks (41)	100%	-

## Online Supplementary Material

**SUPPLEMENTAL TABLE 2** Summary of constraints and criteria for each food group retained in the optimization model for males and females

Food group	Optimization objective	Males				Females			
		Observed consumption (g/d)	Constraints			Observed consumption (g/d)	Constraints		
			Lower limit (g/d)	Upper limit (g/d)	Upper joint limit (g/d)		Lower limit (g/d)	Upper limit (g/d)	Upper joint limit (g/d)
Vegetables		176	20	400	-	160	18	387	-
Fresh fruit		128	0	-	-	107	0	-	-
Dried fruits	Maximization	1	0	-	453	1	0	-	359
Processed fruit: compotes and cooked fruit		13	0	-	-	15	0	-	-
Nuts, seeds and oleaginous fruit		3	0	20	-	2	0	14	-
Bread and refined bakery products		168	27	-	-	115	10	-	-
Complete and semi-complete bread and bakery products	Maximization	11	0	-	-	15	0	-	-
Other refined starches		98	0	-	-	72	0	-	-
Other complete and semi-complete starches	Maximization	4	0	-	-	4	0	-	-
Starch-based products, sweet/fat processed		22	0	97	-	19	0	82	-
Salt/fat processed starch products		4	0	21	-	2	0	14	-
Potatoes and other tubers		79	0	264	-	49	0	196	-
Legumes		13	0	86	-	6	0	43	-
Poultry		30	0	108	-	31	0	109	-
Beef and veal		48	0	-	-	28	0	-	-
Pork and other meats	Minimization	27	0	-	71	13	0	-	71
Offal		4	0	-	-	1	0	-	-
Processed meats	Minimization	50	0	25	-	30	0	25	-
Oily fish		8	0	54	-	6	0	41	-
Other fish		22	0	110	-	15	0	80	-

## Online Supplementary Material

Food group	Optimization objective	Males				Females			
		Observed consumption (g/d)	Constraints			Observed consumption (g/d)	Constraints		
			Lower limit (g/d)	Upper limit (g/d)	Upper Joint limit (g/d)		Lower limit (g/d)	Upper limit (g/d)	Upper joint limit (g/d)
Mollusks and crustaceans		5	0	28	-	4	0	26	-
Eggs and egg-based dishes		14	0	61	-	14	0	70	-
Milk		84	0	343	-	75	0	322	-
Fresh natural dairy products		31	0	138	-	33	0	143	-
Fresh sweetened dairy products		50	0	179	-	48	0	168	-
Sweet milky desserts		19	0	93	-	16	0	73	-
Cheeses		49	0	131	-	36	0	94	-
Animal fats and assimilated fats		1	1	1	-	0	0	0	-
Butter and light butter		10	0	33	-	10	0	30	-
Vegetable fats rich in alpha-linoleic acid		0	0	-	32	0	0	-	30
Vegetable fats rich in alpha-linoleic acid		12	0	-		10	0	-	
Sauces and fresh creams		35	0	118	-	32	0	100	-
Sweet products or sweet and fatty products		103	9	251	-	83	9	215	-
Drinking water		1,007	182	-	-	929	75	-	-
Sweetened soda-type drinks	Minimization	141	0	-	263	140	0	-	263
Fruit juices		80	0	-		67	0	-	
Hot drinks		494	0	494	-	507	0	507	-
Salt		1	0	4	-	1	0	4	-
Condiments		4	0	29	-	3	0	21	-
Aromatic herbs, Spices except salt		2	0	7	-	2	0	6	-
Soups		71	0	434	-	75	0	381	-
Bouillons		5	0	21	-	4	0	25	-

## Online Supplementary Material

Food group	Optimization objective	Males				Females			
		Observed consumption (g/d)	Constraints			Observed consumption (g/d)	Constraints		
			Lower limit (g/d)	Upper limit (g/d)	Upper joint limit (g/d)		Lower limit (g/d)	Upper limit (g/d)	Upper joint limit (g/d)
Substitutes for animal products		3	0	29	-	5	0	29	-
Other foods		4	4	4	-	2	2	2	-
Alcoholic drinks		216	0	216	-	59	0	59	-
Bread and bakery products		178	-	354	-	130	-	316	-
Other starches		102	-	276	-	76	-	188	-
Liquids		2,098	1,061	3,777	-	1,857	738	3,087	-

## Online Supplementary Material

**SUPPLEMENTAL TABLE 3** Changes to food category consumption under observed and modeled diets in males, females with low to medium iron requirements (Fe-), and females with high iron requirements (Fe+)

	Modeled diets											
	Males				Females Fe-				Females Fe+			
	NFlex	Flex	NFlex+	Flex+	NFlex	Flex	NFlex+	Flex+	NFlex	Flex	NFlex+	Flex+
<b>Differences from observed diets, %</b>												
Δ Fruit & Vegetables	59%	41%	168%	168%	45%	43%	163%	163%	71%	43%	163%	163%
Δ Refined Grain Products	-56%	-90%	-90%	-90%	-95%	-95%	-95%	-95%	-95%	-95%	-95%	-95%
Δ Whole Grain Products	633%	1,347%	2,027%	2,707%	1,051%	1,015%	1,731%	1,959%	341%	1,015%	870%	1,954%
Δ Red Meat	-10%	-87%	-59%	-100%	67%	-91%	-48%	-100%	67%	-91%	67%	-100%
Δ Processed meat	-100%	-100%	-100%	-100%	-57%	-83%	-100%	-100%	-17%	-83%	-100%	-100%
Δ Poultry	250%	217%	260%	260%	-33%	120%	247%	247%	247%	120%	247%	247%
Δ Fish	-10%	-3%	30%	-43%	82%	45%	82%	-16%	82%	45%	82%	-16%
Δ Dairy Products	9%	5%	230%	9%	38%	23%	126%	19%	26%	23%	-33%	76%
Δ Soft Drinks	-72%	-65%	-100%	-100%	-32%	-36%	-100%	-100%	27%	-36%	-100%	-100%
Δ Other Drinks	-3%	-2%	113%	-27%	-36%	-1%	-61%	22%	15%	-1%	81%	-53%
Δ Others	-19%	-18%	-45%	-12%	-3%	-4%	-50%	-55%	23%	-3%	20%	-56%
<b>Differences from observed diets, g/d</b>												
Δ Fruit & Vegetables	189	131	535	535	129	121	463	463	203	121	463	463
Δ Refined Grain Products	-149	-239	-239	-239	-176	-176	-176	-176	-176	-176	-176	-176
Δ Whole Grain Products	95	202	304	406	203	196	334	378	66	196	168	377
Δ Red Meat	-8	-69	-47	-79	29	-38	-20	-42	29	-38	29	-42
Δ Processed meat	-50	-50	-50	-50	-17	-25	-30	-30	-5	-25	-30	-30
Δ Poultry	75	65	78	78	-10	38	78	78	78	38	78	78
Δ Fish	-3	-1	9	-13	18	10	18	-3	18	10	18	-3
Δ Dairy Products	21	12	535	22	80	47	262	39	54	48	-69	158
Δ Soft Drinks	-159	-144	-221	-221	-67	-75	-208	-208	55	-75	-208	-208
Δ Other Drinks	-56	-28	1,933	-464	-534	-17	-906	328	229	-17	1,207	-789
Δ Others	-75	-72	-177	-45	-11	-12	-161	-178	73	-11	65	-181

Observed diet: Obs, Diet modeled with the non-flexible optimization model: NFlex, Diet modeled with the flexible optimization model: Flex, Diet modeled with the non-flexible optimization model without the Diet Departure criteria: NFlex+, Diet modeled with the flexible optimization model without the Diet Departure criteria: Flex+. The 45 food groups are not represented here but only those food categories included in the Health sub-function (red meat, processed meat, soft drinks, cereal products, fruit and vegetables) as well as other protein sources (poultry, fish and dairy products). "Others" are 20 food groups combined together for clarity. "Other drinks" are three food groups. Full details are provided in Supplemental Tables 1 and 4. Data are means for each population.

## Online Supplementary Material

**SUPPLEMENTAL TABLE 4** Daily energy and nutrient intakes under the observed diets (Obs) and modeled diets in males, females with low to medium iron requirements (Fe-), and females with high iron requirements (Fe+), using either the standard multicriteria optimization model (NFlex) or the goal programming optimization allowing flexibility regarding nutrient constraints for zinc and iron (Flex)

Nutrient	Unit	Males			Females Fe-			Females Fe+		
		Observed diet	Modeled diets		Observed diet	Modeled diets		Observed diet	Modeled diets	
			NFlex	Flex		NFlex	Flex		NFlex	Flex
Energy intake	kcal·d <sup>-1</sup>	<b>2,731</b>	2,531	<b>2,470</b>	2,024	<b>2,205</b>	2,130	2,024	<b>2,205</b>	2,128
Retinol	µg·d <sup>-1</sup>	573	468	496	395	375	375	395	1,067	375
Vitamin A	µg·d <sup>-1</sup>	805	<b>750</b>	<b>750</b>	<b>608</b>	<b>650</b>	<b>650</b>	<b>608</b>	1,435	<b>650</b>
Vitamin B1	µg·(kcal·d) <sup>-1</sup>	0.54	0.48	0.51	0.56	0.55	0.56	0.56	0.65	0.56
Vitamin B2	mg·d <sup>-1</sup>	2.2	2.3	2.1	1.7	1.8	1.9	1.7	2.3	1.9
Vitamin B3	mg·(kcal·d) <sup>-1</sup>	0.020	0.020	0.020	0.020	0.010	0.020	0.020	0.020	0.020
Vitamin B5	mg·d <sup>-1</sup>	6.9	7.4	6.9	5.3	6.1	6.3	5.3	8.2	6.3
Vitamin B6	mg·d <sup>-1</sup>	2.1	2.3	2.0	<b>1.5</b>	2.0	1.8	<b>1.5</b>	2.8	1.8
Vitamin B9	µg·d <sup>-1</sup>	347	380	381	<b>280</b>	371	359	<b>280</b>	488	359
Vitamin B12	µg·d <sup>-1</sup>	6.3	8.3	6.0	4.3	7.3	5.1	4.3	14	5.1
Vitamin C	mg·d <sup>-1</sup>	<b>98</b>	<b>110</b>	<b>110</b>	<b>84</b>	114	<b>110</b>	<b>84</b>	158	<b>110</b>
Vitamin D	µg·d <sup>-1</sup>	3.5	3.5	3.5	2.9	3.8	3.5	2.9	4.3	3.5
Vitamin E	mg·d <sup>-1</sup>	13	15	15	11	14	13	11	15	13
Vitamin K1	µg·d <sup>-1</sup>	118	164	150	111	156	151	111	215	151
Calcium	mg·d <sup>-1</sup>	1,065	1,104	1,028	<b>892</b>	<b>950</b>	991	<b>892</b>	<b>950</b>	991
Copper	mg·d <sup>-1</sup>	2.1	2.2	2.2	1.6	1.9	2.0	1.6	3.3	2.0
Iron	mg·d <sup>-1</sup>	13	14	13	10	13	12	10	17	12
Bioavailable Iron	mg·d <sup>-1</sup>	<b>1.68</b>	<b>1.72</b>	<b>1.20</b>	<b>1.21</b>	1.72	<b>1.09</b>	<b>1.21</b>	<b>2.52</b>	<b>1.09</b>
Bioavailable Iron (ratio)	%	13%	12%	9%	12%	13%	9%	12%	15%	9%
Iodine	µg·d <sup>-1</sup>	175	160	<b>150</b>	<b>145</b>	<b>150</b>	<b>150</b>	<b>145</b>	176	<b>150</b>
Magnesium	mg·d <sup>-1</sup>	409	463	465	330	382	435	330	406	435

Obs, observed diet; NFlex, diet modeled using the standard non-flexible optimization model for bioavailable zinc and iron; Flex, diet modeled using the flexible optimization model for bioavailable zinc and iron. In the observed diets, out of bounds intakes are in bold. In the modeled diets, intakes being at the bound (i.e.,



## Online Supplementary Material

corresponding to active and binding constraints) are in white on a black background and those allowed to go below the standard bounds (cases of iron and zinc in Flex) are framed on a grey background.

## Online Supplementary Material

**SUPPLEMENTAL TABLE 4 CONT.** Daily energy and nutrient intakes under the observed diets (Obs) and modeled diets in males, females with “low-to-medium” iron requirements (Fe-), and females with high iron requirements (Fe+), using either the standard multicriteria optimization model (NFlex) or the goal programming option allowing flexibility regarding nutrient constraints for zinc and iron (Flex)

Nutrient	Unit	Males			Females Fe-			Females Fe+		
		Observed diet	Modeled diets		Observed diet	Modeled diets		Observed diet	Modeled diets	
			NFlex	Flex		NFlex	Flex		NFlex	Flex
Manganese	mg·d <sup>-1</sup>	3.6	3.9	4.4	3.1	4.0	4.3	3.1	3.4	4.3
Phosphorus	mg·d <sup>-1</sup>	1,483	1,600	1,462	1,128	1,422	1,341	1,128	1,571	1,339
Potassium	mg·d <sup>-1</sup>	3,736	4,413	3,983	<b>2,906</b>	3,611	3,788	<b>2,906</b>	4,762	3,787
Selenium	μg·d <sup>-1</sup>	146	139	127	120	113	120	120	161	120
Sodium	mg·d <sup>-1</sup>	<b>3,938</b>	<b>2,300</b>	<b>2,300</b>	<b>3,100</b>	<b>2,300</b>	<b>2,300</b>	<b>3,100</b>	<b>2,300</b>	<b>2,300</b>
Zinc	mg·d <sup>-1</sup>	12	13	9.6	8.8	12	8.8	8.8	13	8.8
Bioavailable zinc	mg·d <sup>-1</sup>	<b>3.57</b>	3.63	<b>2.89</b>	<b>3.15</b>	3.34	<b>2.78</b>	<b>3.15</b>	3.82	<b>2.78</b>
Bioavailable zinc (ratio)	%	30%	27%	30%	36%	28%	32%	36%	29%	32%
Water	g·d <sup>-1</sup>	2,780	2,699	2,643	2,422	2,016	2,458	2,422	2,995	2,459
Saturated fatty acids	%EI·d <sup>-1</sup>	<b>14%</b>	<b>12%</b>	<b>12%</b>	<b>15%</b>	<b>12%</b>	<b>12%</b>	<b>15%</b>	10%	<b>12%</b>
Lauric + myristic + palmitic acids	%EI·d <sup>-1</sup>	8%	8%	8%	9%	8%	8%	9%	7%	8%
Linoleic acid	%EI·d <sup>-1</sup>	<b>3%</b>	<b>4%</b>	<b>4%</b>	<b>3%</b>	<b>4%</b>	<b>4%</b>	<b>3%</b>	5%	<b>4%</b>
α-linolenic acid	%EI·d <sup>-1</sup>	<b>0%</b>	<b>1%</b>	<b>1%</b>	<b>0%</b>	<b>1%</b>	<b>1%</b>	<b>0%</b>	<b>1%</b>	<b>1%</b>
Linoleic acid: α-linolenic acid	-	<b>8</b>	4	4	<b>7</b>	4	4	<b>7</b>	5	4
EPA+DHA	g·d <sup>-1</sup>	<b>0.33</b>	<b>0.50</b>	0.51	<b>0.22</b>	<b>0.50</b>	<b>0.50</b>	<b>0.22</b>	<b>0.50</b>	<b>0.50</b>
Sugar without lactose	g·d <sup>-1</sup>	<b>102</b>	<b>100</b>	<b>100</b>	80	<b>100</b>	<b>100</b>	80	<b>100</b>	<b>100</b>
Protein	g·(kg <sub>bw</sub> ·d) <sup>-1</sup>	105	113	92	77	90	82	77	114	81
Fiber	g·d <sup>-1</sup>	<b>23</b>	<b>30</b>	<b>30</b>	<b>19</b>	<b>30</b>	<b>30</b>	<b>19</b>	<b>30</b>	<b>30</b>
Phytate	mg·d <sup>-1</sup>	730	829	1,020	595	977	985	595	639	985
Salt	g·d <sup>-1</sup>	9.8	5.7	5.7	7.8	5.9	5.7	7.8	5.8	5.7
Lipids	g·d <sup>-1</sup>	98	97	94	78	85	81	78	83	81

## Online Supplementary Material

Nutrient	Unit	Males			Females Fe-			Females Fe+		
		Observed diet	Modeled diets		Observed diet	Modeled diets		Observed diet	Modeled diets	
			NFlex	Flex		NFlex	Flex		NFlex	Flex
<i>MUFA</i>	<i>g·d<sup>-1</sup></i>	34	36	35	27	32	29	27	33	29
<i>PUFA</i>	<i>g·d<sup>-1</sup></i>	13	16	17	10	15	14	10	16	14
<i>Alcohol</i>	<i>g·d<sup>-1</sup></i>	23	17	22	4.9	4.9	4.9	4.9	4.8	4.9
<i>Cholesterol</i>	<i>mg·d<sup>-1</sup></i>	394	422	357	300	357	308	300	644	308

Obs, observed diet; NFlex, diet modeled using the standard non-flexible optimization model for bioavailable zinc and iron; Flex, diet modeled using the flexible optimization model for bioavailable zinc and iron. In the observed diets, out of bounds intakes are in bold. In the modeled diets, intakes being at the bound (i.e., corresponding to active and binding constraints) are in white on a black background and those allowed to go below the standard bounds (case of iron and zinc in Flex) are framed on a grey background. DHA, docosahexaenoic acid; EI, energy intake; EPA, eicosapentaenoic acid. MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids. 1 kcal = 0.0042 MJ.

## Online Supplementary Material

**SUPPLEMENTAL TABLE 5** Absolute amounts of food category consumption under observed and modeled diets in males, females with low to medium iron requirements (Fe-), and females with high iron requirements (Fe+)

	Males					Females Fe-					Females Fe+				
	Observed diet	Modeled diets				Observed diet	Modeled diets				Observed diet	Modeled diets			
		NFlex	Flex	NFlex+	Flex+		NFlex	Flex	NFlex+	Flex+		NFlex	Flex	NFlex+	Flex+
<b>Diet composition, g/d</b>															
Fruit & Vegetables	318	507	449	853	853	283	412	404	746	746	283	486	404	746	746
Refined Grain Products	266	117	27	27	27	186	10	10	10	10	186	10	10	10	10
Whole Grain Products	15	110	217	319	421	19	222	215	353	397	19	85	215	187	396
Red meat	79	71	10	32	0	42	71	4	22	0	42	71	4	71	0
Processed meat	50	0	0	0	0	30	13	5	0	0	30	25	5	0	0
Poultry	30	105	95	108	108	31	21	69	109	109	31	109	69	109	109
Fish	30	27	29	39	17	21	39	31	39	18	21	39	31	39	18
Dairy products	233	254	245	768	255	208	288	255	470	247	208	262	256	139	366
Soft drinks	221	62	77	0	0	208	141	133	0	0	208	263	133	0	0
Other Drinks	1,717	1,661	1,689	3,650	1,253	1,495	961	1,478	589	1,823	1,495	1,724	1,478	2,702	706
Others	391	316	319	214	346	323	312	311	162	145	323	396	312	388	142

Observed diet: Obs, Diet modeled with the non-flexible optimization model: NFlex, Diet modeled with the flexible optimization model: Flex, Diet modeled with the non-flexible optimization model without the Diet Departure criteria: NFlex+, Diet modeled with the flexible optimization model without the Diet Departure criteria: Flex+. The 45 food groups are not represented here but only those food categories included in the Health sub-function (red meat, processed meat, soft drinks, cereal products, fruit and vegetables) as well as other protein sources (poultry, fish and dairy products). "Others" are 20 food groups combined together for clarity. "Other drinks" are three food groups. Data are means for each population.

## Online Supplementary Material

**SUPPLEMENTAL TABLE 6** Overall decrease in mortality risks between modeled and observed diets in adult males and females as a function of disease and dietary factors

		Adults												
Modeled diets	Diseases	Food category											Overall	
		Fruit	Vegetables	Nuts	Whole Grain Products	Red meat	Processed meat	Soft Drinks	Refined Grain Products	Eggs	Dairy Products	Fish		Legumes
<b>NFlex</b>	Ischemic Heart Diseases	0.9%	1.6%	0.2%	5.8%			11%			0.1%	0.0%	1.9%	20%
	Cerebrovascular Diseases	0.4%	0.2%			-0.5%	9.6%	5.7%			0.4%	0.3%		16%
	Diabetes	0.6%	0.6%		2.5%	-0.2%	21%	13%	4.4%	-1.1%	0.4%			35%
	Colorectal Cancer	0.8%	1.7%		8.7%	-0.6%	13%				1.8%			23%
	Total	0.7%	1.2%	0.1%	5.0%	-0.3%	7.1%	7.2%	0.3%	-0.1%	0.6%	0.1%	0.8%	<b>21%</b>
<b>Flex</b>	Ischemic Heart Diseases	0.9%	1.4%	0.3%	5.8%			11%			0.1%	0.3%	0.8%	19%
	Cerebrovascular Diseases	0.5%	0.2%			7.6%	10%	5.7%			0.3%	0.5%		23%
	Diabetes	0.6%	0.5%		2.4%	13%	22%	13%	6.5%	-0.9%	0.4%			46%
	Colorectal Cancer	0.7%	1.3%		8.8%	10%	13%				1.5%			31%
	Total	0.7%	1.0%	0.1%	5.0%	5.3%	7.5%	7.2%	0.5%	-0.1%	0.5%	0.3%	0.4%	<b>25%</b>

Estimated number of averted deaths in France expressed as a change to the overall death rate. Observed data are from the Individual and National Study on Food Consumption Survey 3,  $n = 1,125$ . Diet modeled with the non-flexible optimization model: NFlex, Diet modeled with the flexible optimization model: Flex. Percentage of mortality risk averted = (No. of deaths averted estimated under the modeled diet - No. of deaths averted observed under the observed diet) / No. of deaths averted observed under the observed diet. In this table, each dietary factor is considered to be independent and uncorrelated.

## Online Supplementary Material

Males														
Modeled diets	Diseases	Food category												Overall
		Fruits	Vegetables	Nuts	Whole Grain Products	Red meat	Processed meat	Soft Drinks	Refined Grain Products	Eggs	Dairy Products	Fish	Legumes	
<b>NFlex</b>	Ischemic Heart Diseases	0.9%	1.6%	0.2%	5.8%			11%			0.1%	-0.1%	1.9%	20%
	Cerebrovascular Diseases	0.4%	0.2%			0.2%	11%	5.4%			0.4%	-0.1%		17%
	Diabetes	0.6%	0.6%		2.5%	0.3%	23%	12%	4.3%	-1,0%	0.4%			37%
	Colorectal Cancer	0.8%	1.7%		8.7%	0.4%	15%				1.7%			26%
	Total	0.8%	1.2%	0.1%	5.0%	0.2%	7.6%	7.3%	0.4%	-0.1%	0.6%	-0.1%	0.9%	<b>22%</b>
<b>Flex</b>	Ischemic Heart Diseases	0.9%	1.4%	0.3%	5.9%			11%			0.1%	0.3%	0.8%	19%
	Cerebrovascular Diseases	0.4%	0.2%			8.1%	11%	5.4%			0.3%	0.3%		24%
	Diabetes	0.6%	0.5%		2.5%	14%	23%	12%	6.6%	-0.9%	0.4%			47%
	Colorectal Cancer	0.8%	1.4%		8.9%	11%	15%				1.5%			33%
	Total	0.7%	1.1%	0.1%	5.1%	5.4%	7.6%	7.3%	0.5%	-0.1%	0.5%	0.2%	0.4%	<b>26%</b>

Females														
Modeled diets	Diseases	Food category												Overall
		Fruit	Vegetables	Nuts	Whole Grain Products	Red meat	Processed meat	Soft Drinks	Refined Grain Products	Eggs	Dairy Products	Fish	Legumes	
<b>NFlex</b>	Ischemic Heart Diseases	0.5%	1.5%	0.0%	5.4%			14%			0.2%	1.9%	1.8%	24%
	Cerebrovascular Diseases	0.5%	0.4%			-2.9%	3.9%	6.9%			0.5%	2.1%		11%
	Diabetes	0.5%	0.6%		2.0%	-5.2%	6.9%	15%	4.8%	-1.9%	0.5%			21%
	Colorectal Cancer	0.4%	1.3%		8.6%	-4.6%	5.0%				2.2%			12%
	Total	0.5%	1,0%	0.0%	4.5%	-3.0%	3.6%	6.4%	0.3%	-0.1%	1.1%	1.2%	0.4%	<b>15%</b>
<b>Flex</b>	Ischemic Heart Diseases	0.9%	1.2%	0.6%	5.4%			14%			0.2%	1.2%	0.5%	23%
	Cerebrovascular Diseases	0.8%	0.3%			5.6%	7.8%	6.9%			0.3%	1.3%		21%
	Diabetes	0.8%	0.5%		2,0%	9.7%	14%	15%	4.8%	-1.1%	0.4%			39%
	Colorectal Cancer	0.7%	0.9%		8.6%	5.9%	8.4%				1.5%			24%
	Total	0.8%	0.7%	0.1%	4.5%	4.7%	6.7%	6.4%	0.3%	-0.1%	0.8%	0.7%	0.1%	<b>23%</b>

Food and nutrient intakes of Fe- and Fe+ females, used to estimate changes to risk as compared to the observed situation in females using comparative risk assessment, averaged according to the 80:20 ratio in the population.

## Online Supplementary Material

**SUPPLEMENTAL TABLE 7** Overall changes to averted Disability Adjusted Life Years (DALYs) in adult males and females as a function of diseases and dietary factors

		Adults												
Modeled diets	Diseases	Food category											Overall	
		Fruit	Vegetables	Nuts	Whole Grain Products	Red meat	Processed meat	Soft Drinks	Refined Grain Products	Eggs	Dairy Products	Fish		Legumes
<b>NFlex</b>	Ischemic Heart Diseases	1,285 (0.9%)	2,204 (1.6%)	260 (0.2%)	7,994 (5.8%)			15,676 (11%)			177 (0.1%)	68 (0.0%)	2,592 (1.9%)	28,130 (20%)
	Cerebrovascular Diseases	485 (0.5%)	229 (0.2%)			-679 (-0.7%)	8,589 (9.1%)	5,625 (5.9%)		374 (0.4%)	473 (0.5%)		14,359 (15%)	
	Diabetes	408 (0.6%)	417 (0.6%)		1,518 (2.4%)	-450 (-0.7%)	12,791 (20%)	8,468 (13%)	2,845 (4.4%)	-762 (-1.2%)	263 (0.4%)			22,023 (34%)
	Colorectal Cancer	631 (0.8%)	1,361 (1.6%)		7,215 (8.7%)	-616 (-0.7%)	10,342 (13%)				1,488 (1.8%)			18,708 (23%)
	<b>Total</b>	2,809 (0.7%)	4,212 (1.1%)	260 (0.1%)	16,727 (4.4%)	-1,745 (-0.5%)	31,722 (8.4%)	29,768 (7.8%)	2,845 (0.7%)	-762 (-0.2%)	2,303 (0.6%)	541 (0.1%)	2,592 (0.7%)	<b>83,220</b> <b>(22%)</b>
<b>Flex</b>	Ischemic Heart Diseases	1,249 (0.9%)	1,889 (1.4%)	415 (0.3%)	8,028 (5.8%)			15,676 (11%)		161 (0.1%)	476 (0.3%)	1,125 (0.8%)	27,156 (20%)	
	Cerebrovascular Diseases	568 (0.7%)	207 (0.6%)			6,962 (7.4%)	9,666 (10%)	5,625 (5.9%)		316 (0.3%)	539 (0.6%)		21,870 (23%)	
	Diabetes	429 (0.8%)	355 (0.6%)		1,491 (2.3%)	8,277 (13%)	13,681 (21%)	8,468 (13%)	4,070 (6.3%)	-624 (-1.0%)	229 (0.4%)		29,150 (45%)	
	Colorectal Cancer	641 (0.8%)	1,072 (1.3%)		7,288 (8.8%)	8,170 (9.9%)	11,003 (13%)				1,277 (1.5%)			25,827 (31%)
	<b>Total</b>	2,887 (0.8%)	3,524 (0.9%)	415 (0.1%)	16,808 (4.4%)	23,409 (6.2%)	34,350 (9.1%)	29,768 (7.8%)	4,070 (1.1%)	-624 (-0.2%)	1,982 (0.5%)	1,014 (0.3%)	1,125 (0.3%)	<b>104,003</b> <b>(27%)</b>

DALYs averted, comparing the modeled diet with the current observed diet in the French adult population. Observed data are from the Individual and National Study on Food Consumption Survey 3, n = 1,125. Diet modeled with the non-flexible optimization model: NFlex, Diet modeled with the flexible optimization model: Flex. Percentage of variation vs observed diet are shown in parentheses. DALYs averted = (DALYs estimated in the modeled diet - DALYs observed in the observed diet).

## Online Supplementary Material

		Males												
		Food category												
Modeled diets	Diseases	Fruit	Vegetables	Nuts	Whole Grain Products	Red meat	Processed meat	Soft Drinks	Refined Grain Products	Eggs	Dairy Products	Fish	Legumes	Overall
<b>NFlex</b>	Ischemic Heart Diseases	1,225 (1.0%)	2,026 (1.6%)	262 (0.2%)	7,374 (5.8%)			14,091 (11%)			150 (0.1%)	-149 (-0.1%)	2,388 (1.9%)	25,468 (20%)
	Cerebrovascular Diseases	343 (0.5%)	126 (0.2%)			107 (0.2%)	7,558 (11%)	3,812 (5.6%)			240 (0.4%)	-82 (-0.1%)		11,541 (17%)
	Diabetes	353 (0.7%)	339 (0.6%)		1,277 (2.4%)	152 (0.3%)	11,997 (23%)	6,762 (13%)	2,287 (4.3%)	542 (-1;0%)	200 (0.4%)			19,681 (37%)
	Colorectal Cancer	550 (0.9%)	1,115 (1.8%)		5,557 (8.7%)	257 (0.4%)	9,359 (15%)				1,060 (1.7%)			16,379 (26%)
	Total	2,471 (0.8%)	3,606 (1.2%)	262 (0.1%)	14,208 (4.6%)	517 (0.2%)	28,914 (9.3%)	24,665 (7.9%)	2,287 (0.7%)	-542 (-0.2%)	1,650 (0.5%)	-231 (-0.1%)	2,388 (0.8%)	<b>73,069</b> <b>(24%)</b>
<b>Flex</b>	Ischemic Heart Diseases	1,147 (0.9%)	1,752 (1.4%)	342 (0.3%)	7,409 (5.9%)			14,091 (11%)			141 (0.1%)	345 (0.3%)	1,063 (0.8%)	24,618 (20%)
	Cerebrovascular Diseases	336 (0.5%)	121 (0.2%)			5,469 (8.1%)	7,558 (11%)	3,812 (5.6%)			223 (0.3%)	179 (0.3%)		16,185 (24%)
	Diabetes	331 (0.6%)	295 (0.6%)		1,253 (2.4%)	7,161 (14%)	11,997 (23%)	6,762 (13%)	3,513 (6.7%)	-499 (-0.9%)	186 (0.4%)			24,678 (47%)
	Colorectal Cancer	498 (0.8%)	889 (1.4%)		5,630 (8.9%)	7,039 (11%)	9,359 (15%)				982 (1.5%)			21,241 (33%)
	Total	2,312 (0.7%)	3,057 (1.0%)	342 (0.1%)	14,293 (4.6%)	19,669 (6.3%)	28,914 (9.3%)	24,665 (7.9%)	3513 (1.1%)	-499 (-0.2%)	1,532 (0.5%)	523 (0.2%)	1,063 (0.3%)	<b>86,723</b> <b>(28%)</b>



## Online Supplementary Material

		Females												
		Food category												
Modeled diets	Diseases	Fruit	Vegetables	Nuts	Whole Grain Products	Red meat	Processed meat	Soft Drinks	Refined Grain Products	Eggs	Dairy Products	Fish	Legumes	Overall
<b>NFlex</b>	Ischemic Heart Diseases	59 (0.5%)	178 (1.6%)	-3 (0.0%)	620 (5.5%)			1,585 (14%)			28 (0.2%)	217 (1.9%)	204 (1.8%)	2,661 (24%)
	Cerebrovascular Diseases	142 (0.5%)	103 (0.4%)			-786 (-2.9%)	1,031 (3.8%)	1,812 (6.7%)			135 (0.5%)	555 (2.1%)		2,817 (11%)
	Diabetes	55 (0.5%)	78 (0.7%)		241 (2.1%)	-602 (-5.2%)	794 (6.8%)	1,706 (15%)	558 (4.8%)	-220 (-1.9%)	62 (0.5%)			2,342 (20%)
	Colorectal Cancer	81 (0.4%)	247 (1.3%)		1,658 (8.6%)	-874 (-4.6%)	983 (5.1%)				428 (2.2%)			2,329 (12%)
	Total	337 (0.5%)	606 (0.9%)	-3 (0.0%)	2,519 (3.6%)	-2,262 (-3.3%)	2,808 (4.1%)	5,103 (7.4%)	558 (0.8%)	-220 (-0.3%)	653 (0.9%)	771 (1.1%)	204 (0.3%)	<b>10,150</b> <b>(15%)</b>
<b>Flex</b>	Ischemic Heart Diseases	102 (0.9%)	137 (1.2%)	73 (0.6%)	619 (5.5%)			1,585 (14%)			20 (0.2%)	131 (1.2%)	62 (0.5%)	2,538 (22%)
	Cerebrovascular Diseases	232 (0.9%)	86 (0.3%)			1,493 (5.5%)	2,109 (7.8%)	1,812 (6.7%)			93 (0.3%)	360 (1.3%)		5,684 (21%)
	Diabetes	97 (0.8%)	61 (0.5%)		238 (2.0%)	1,116 (9.6%)	1,683 (15%)	1,706 (15%)	557 (4.8%)	-125 (-1.1%)	43 (0.4%)			4,472 (39%)
	Colorectal Cancer	143 (0.7%)	183 (1.0%)		1,658 (8.6%)	1,130 (5.9%)	1,644 (8.6%)				294 (1.5%)			4,587 (24%)
	Total	574 (0.8%)	467 (0.7%)	73 (0.1%)	2,515 (3.6%)	3,740 (5.4%)	5,436 (7.9%)	5,103 (7.4%)	557 (0.8%)	-125 (-0.2%)	450 (0.7%)	491 (0.7%)	62 (0.1%)	<b>17,281</b> <b>(25%)</b>

Food and nutrient intakes of Fe- and Fe+ females, used to estimate changes to risk as compared to the observed situation in females using comparative risk assessment, averaged according to the 80:20 ratio in the population.

## Online Supplementary Material

**SUPPLEMENTAL TABLE 8** Values of the objective sub-functions used during optimization in males, females with low to medium iron requirements (Fe-) and females with high iron requirements (Fe+), using the standard multicriteria optimization model (NFlex) or the goal programming option allowing flexibility regarding nutrient constraints for zinc and iron (Flex), or two complementary optimization models (without or with flexibility on bioavailable iron and zinc) when suppressing the *Diet Departure* term in the objective function (NFlex+ and Flex+, respectively)

	Males					Females Fe-					Females Fe+				
	Observed diet	Modeled diets				Observed diet	Modeled diets				Observed diet	Modeled diets			
		NFlex	Flex	NFlex+	Flex+		NFlex	Flex	NFlex+	Flex+		NFlex	Flex	NFlex+	Flex+
<b>Objectives sub-function<sup>1</sup></b>															
Health	-3.18	0.17	1.04	2.16	2.80	-1.78	-0.44	0.80	2.52	2.93	-1.78	-1.53	0.81	1.44	2.93
Diet Departure	0.00	5.32	3.43	48.12	32.65	0.00	4.63	3.12	46.59	38.28	0.00	65.18	3.13	128.39	36.77
Goal		0.00	0.50	0.00	0.22		0.00	0.51	0.00	0.23		0.00	0.71	0.00	0.49
<b>Deviations from requirements<sup>2</sup></b>															
Bioavailable iron		0.00	0.30	0.00	0.02		0.00	0.37	0.00	0.15		0.00	0.57	0.00	0.43
Bioavailable zinc		0.00	0.20	0.00	0.20		0.00	0.14	0.00	0.08		0.00	0.14	0.00	0.06
<b>Dual values of nutrient constraints<sup>3</sup></b>															
Bioavailable zinc		<b>34</b>	0	<b>3</b>	0		0	0	<b>2</b>	0		0	0	0	0
Bioavailable iron		4	0	2	0		<b>23</b>	0	2	0		<b>645</b>	0	7	0
Sodium		-10	<b>-8</b>	-1	<b>-1</b>		-12	<b>-8</b>	-1	<b>-1</b>		-57	<b>-8</b>	<b>-1</b>	<b>-1</b>
Iodine		0	2	0	0		13	7	0	0		0	7	0	0
Vitamin A		2	3	0	0		1	4	0	0		0	4	0	0
Energy intake		0	3	0	0		-5	0	-1	0		-9	0	-1	0
EPA+DHA		0	0	0	0		1	0	0	0		2	0	0	0

<sup>1</sup>Multi-criteria optimization consisted in maximizing the Health criteria while minimizing the Diet Departure and Goal criteria, with the Goal criteria being the sum of the goal variables on bioavailable zinc and iron intakes. <sup>2</sup>Relative deviations from reference values (e.g. bioavailable iron = 0.30 means that the value is 30% below the requirement), whose sum is equal to the Goal criteria. <sup>3</sup>Standardized dual values representing the potential effect of a 100% relaxation of the limiting bound of the considered constraint, in order to classify the nutritional constraints from the most to the least active. Active constraints have a positive (negative) value if the lower (upper) bound is binding. Only nutrients with an active constraint (i.e. with a non-null dual value) are presented here. For each scenario, the most limiting constraint (i.e., with the highest absolute value) is in bold.

## Online Supplementary Material

After relaxing the constraints on bioavailable iron and zinc (Flex optimization model), better values were obtained for the *Health and Diet Departure* criteria and five nutritional constraints were identified as still exerting a significant influence (sodium, vitamin A, alpha-linolenic acid, iodine, saturated fatty acids). Among these active constraints, sodium was the most binding in all sub-populations, as its upper limit opposed the introduction of more whole grain breads that are very high in sodium.

## Online Supplementary Material

### SUPPLEMENTAL METHOD 1 The EpiDiet model

#### *General Principle*

EpiDiet (Evaluate the Potential Impact of a Diet) is a simulation-based nutritional and epidemiological model. Like many other simulation-based risk assessment models (1–3), EpiDiet combines modeling, stochastic and optimization techniques to describe and analyze connections between diet, nutrition and the prevention of diet-related diseases, and can be used to quantify the positive or negative changes in risk related to long-term health that would result from changes in the average diet for an individual, groups or population.

The conceptual basis and methodological foundation of the EpiDiet model are laid out in the *Comparative Risk Assessment* framework (4), which has been proven effective and is used extensively by various groups and organizations such as The EAT-Lancet Commission on Food, Planet and Health (3), the World Health Organization (4), and the Global Burden of Diseases (GBD) (5).

Our analyses proceeded in three steps. In each component of our analyses, the data were stratified by age-band and sex in order to better take account of disparities in diet, diseases and relative risks between individuals. We selected diseases and risk factors for which hazards from mutually controlled risks were available and implemented methods that enabled account to be taken of the joint effects of changes to multiple risk factors.

First, we estimated the impact of dietary changes on the risks of morbidity and mortality from a set of chronic non-communicable diseases, using the standard computable Potential Impact Fraction (PIF) formula for a dietary factor:

$$PIF = \frac{\int_{x \in X_b} RR(x)P(x)dx - \int_{x \in X_c} RR(x)P'(x)dx}{\int_{x \in X_b} RR(x)P(x)dx}$$

Where  $RR(x)$  is the relative risk of the disease at the dietary intake-level  $x$ ,  $P(x)$  denotes the number of individuals in the population whose dietary intake is at level  $x$  in the baseline scenario,  $P'(x)$  denotes the number of individuals in the population whose dietary intake is at level  $x$  in the counterfactual scenario,  $X_b$  and  $X_c$  are, respectively, the sets of all possible values for  $x$  in the baseline and counterfactual scenarios.

To access the joint effects of changes to multiple dietary factors, we used a formula derived from the concept of PAF (Population Attributable Fraction) widely used in the GBD (Global Burden Diseases) study, as follows:

$$PIF_{joint} = 1 - \prod_{f=1}^M (1 - PIF_f)$$

Where  $f$  denotes each individual dietary factor, and  $M$  is a collection encompassing all the factors considered in the study. We assumed that dietary factors were independent and uncorrelated and the corresponding relative risks were mutually adjusted for potential confounding.

Finally, sensitivity analyses were performed to enable the prioritization of risk factors according to their contribution to global risk reduction or benefit gain. For each risk factor, we reported several metrics

## Online Supplementary Material

including that part of risk reduction that would be attributable to the factor and the part that would be avoidable if the factor had been removed.

### *Diet-Disease Relationships and Covariate Data*

In this study, we set up the EpiDiet model using the values reported in a series of validated international meta-analyses published by a European team (6–10). We selected 12 diet-related factors (including the consumption of fruit, vegetables, nuts or seeds, whole grains, unprocessed red meats, processed meats, sugar-sweetened beverages, fish, dairy products, eggs, refined grains and legumes) and four diet-related diseases (including coronary heart disease, stroke, type 2 diabetes and colorectal cancer). The association between the diets and health endpoints was synthesized from epidemiological evidence, observational studies and randomized controlled trials, where bias from confounding was reduced and from which multivariable adjustments, factors with major overlapping effects or insufficient evidence for casual relationships were excluded, and the effect-size of food-disease associations was expressed in terms of relative risk for case-specific mortality. Finally, diet-disease relationships were described using a set of continuous non-linear dose–response functions. Each function was modelled by a restricted cubic spline (11), allowing the expression of a change in the risk of a disease for a unit increase in a dietary risk factor. Other covariates used were age, sex, and energy intake. The data were stratified by 5-year age bands and sex. Food intakes were supposed to be isocaloric and controlled over the total energy intake using the residual method (12).

### *Scenario Design*

The baseline scenarios were derived from current food consumption observed during the most recent French survey: the third Individual and National Study on Food Consumption Survey (INCA3) (13). Based on consumption, we broke down the foods into ingredients from the recipes and gathered them into food and beverage groups using the CIQUAL (French Data Centre on Food Quality) food composition database (14). Energy intake estimates were derived from the same database. Under-reporting and over-reporting participants were identified by comparing their reported energy intake to the basal metabolic rate estimated using the Henry equation (15) and excluded according to the cut-off points proposed by Black (16) with physical activity levels of 1.4, 1.6 and 1.8 for little active (sedentary), moderately active and active lifestyles, respectively (17). The dietary pattern of the baseline scenario corresponded to the daily average intake of each food and beverage group per capita in the sub-population.

The counterfactual scenarios were calculated from theoretical optimized diets (NFlex and Flex), as described in the Methods section of the manuscript. The optimized diets were obtained using a nonlinear optimization algorithm (NLP, with multistart to avoid local minima) under the OPTMODEL procedure (SAS 9.4, SAS Institute Inc., Cary, NC, USA.). The optimization problem was to find diets that maximized a health criterion based on dietary recommendations and at the same time deviated as little as possible from the observed diet while meeting all nutrient reference values, either strictly (non-flexible optimization, NFlex) or allowing some tolerance regarding the recommended intakes of bioavailable iron and zinc (flexible optimization, Flex).

### *Population Demographics and Cause-Specific Mortality*

We used the French population observed in 2014 as the reference population, and generalized the scenarios formed above from INCA3 to the whole French population, using a standardized weighting

## Online Supplementary Material

method based on recalibration that accounts for sex, age, educational attainment, geographic location and type of eating in order to correct imbalances between the samples in the survey and the target population (18).

Data on population demographics and national disease-specific deaths were supplied by the National Institute of Statistics and Economic Studies (19) and the Epidemiological Centre on Medical Causes of Death (20), respectively.

Diseases were defined according to the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, including coronary heart disease (I20-I25), stroke (I60-I69), type 2 diabetes (E11,E14), and colorectal cancer (C18-20).

### *Estimate of Preventable DALYs Attributable to Dietary Factors*

Disability Adjusted Life Years (DALYs) were estimated. The DALY is a normalized disease burden metric. It measures the number of years lost due to living with disease or dying before a predetermined life expectancy, and includes two components: the premature mortality component and the morbidity component. The premature mortality component (YLL-Years of Life Lost) is defined as the number of potential years of life lost due to premature death. YLLs are computed by multiplying the number of premature deaths at each age by a standard life expectancy at that age. In this study, the number of premature deaths was computed using the EpiDiet model and the standard expectation of life was extracted from the lifetables supplied by the GBD Group ([ghdx.healthdata.org/gbd-results-tool](http://ghdx.healthdata.org/gbd-results-tool)). The morbidity component is defined as the equivalent years of healthy life because of states of poor health or disability (YLDs). YLDs are estimated as the incidence of cases of different disease sequelae multiplied by the duration and disability weighting of each sequela. Our estimates of YLDs were calculated by multiplying the total YLLs by a conversion rate specific to age, sex and disease, which was calculated from the estimates provided by the GBD Group 2017 study via the GBD Results Tool (<http://ghdx.healthdata.org/gbd-results-tool>). The use of a conversion rate made it possible to bypass the procedures for estimating disease duration as they are usually complex, requiring dynamic modelling and conservative assumptions (21,22).

Furthermore, uncertainty analysis on measurement error was performed to evaluate the influence that variability of the diet-disease relative risk estimates due to sampling error has on the health impact of dietary changes. First, we estimated the probabilistic distributions of the actual relative risk using data reported in published meta-analyses, and then drew 100,000 stochastic simulations using Monte Carlo simulation. Each simulation was propagated to the health outcomes. The corresponding uncertainty intervals (UI) are based on the 2.5th and 97.5th percentiles of the outputs.

### *Estimate of DALYs Attributable to Iron Deficiency Anemia*

The risk of iron-deficiency anemia was first estimated for each scenario, and the DALYs attributable to this risk, including mild and moderate anemia, were then calculated from the estimated prevalence of iron-deficiency anemia using the standard expectation of life and the DALY disability weighting obtained from World Health Organization Health Statistics and Information Systems ([www.who.int/healthinfo](http://www.who.int/healthinfo)). The estimated prevalence of anemia in counterfactual scenarios was deduced from the estimated prevalence of anemia in the French population (0.2% for men aged 18-64 years, 2.8% for females aged 18-39 years, and 5.5% for females aged 40-54 years) (23) and the bioavailable iron levels in the different scenarios,

## **Online Supplementary Material**

using a Monte Carlo simulation on 100,000 individuals, as described in the Methods section of the manuscript.

## Online Supplementary Material

**SUPPLEMENTAL FIGURE 1** Daily food category consumption in the observed diets (Obs) and modeled diets in males (panel A), females with “low-to-medium” iron requirements (Fe-)(panel B), and females with high iron requirements (Fe+) (panel C), using either the standard multicriteria optimization model (NFlex) or the goal programming option allowing flexibility regarding nutrient constraints for zinc and iron (Flex) and two complementary optimization models (without or with flexibility on bioavailable iron and zinc) when suppressing the *Diet Departure* term in the objective function (NFlex+ and Flex+, respectively)

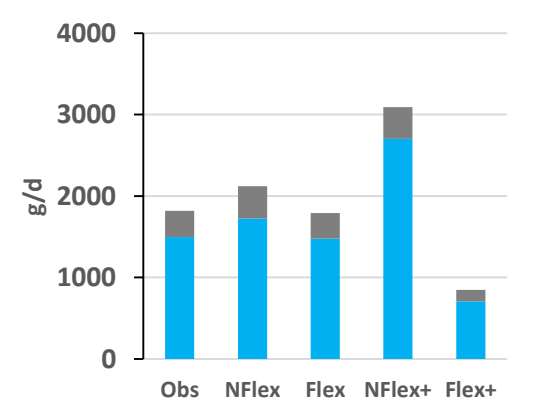
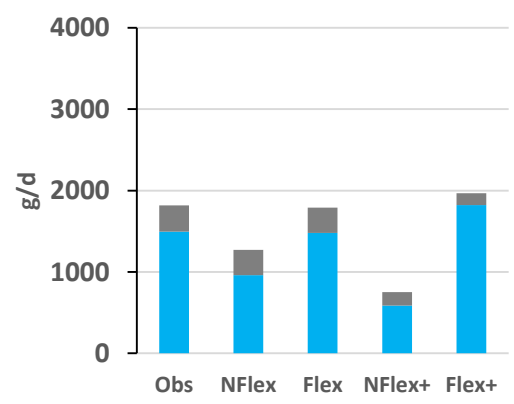
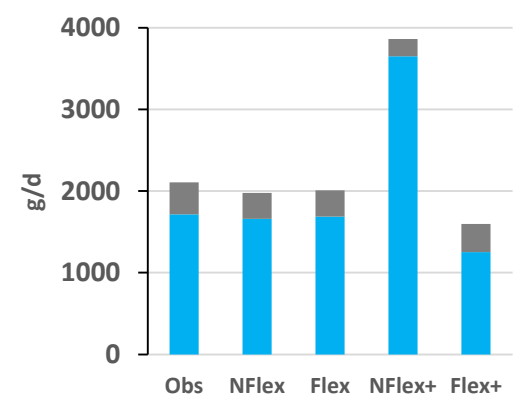
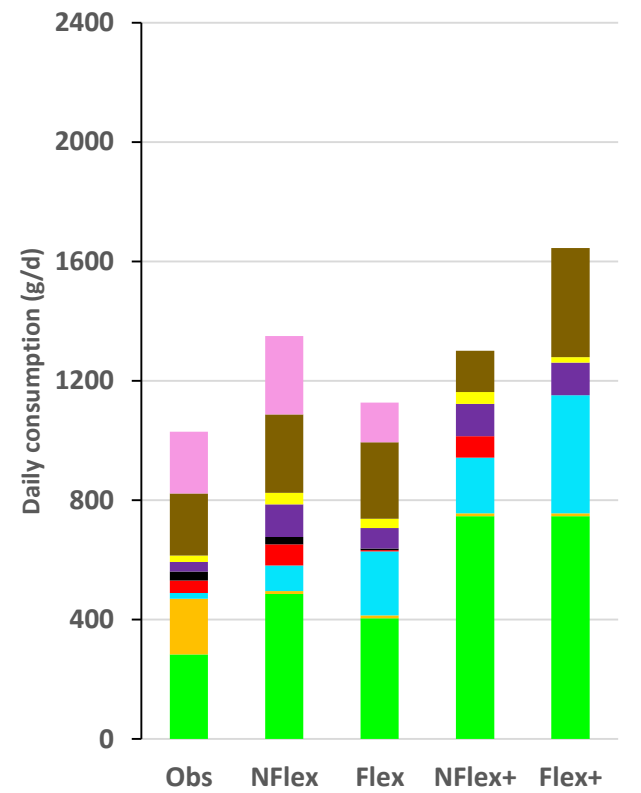
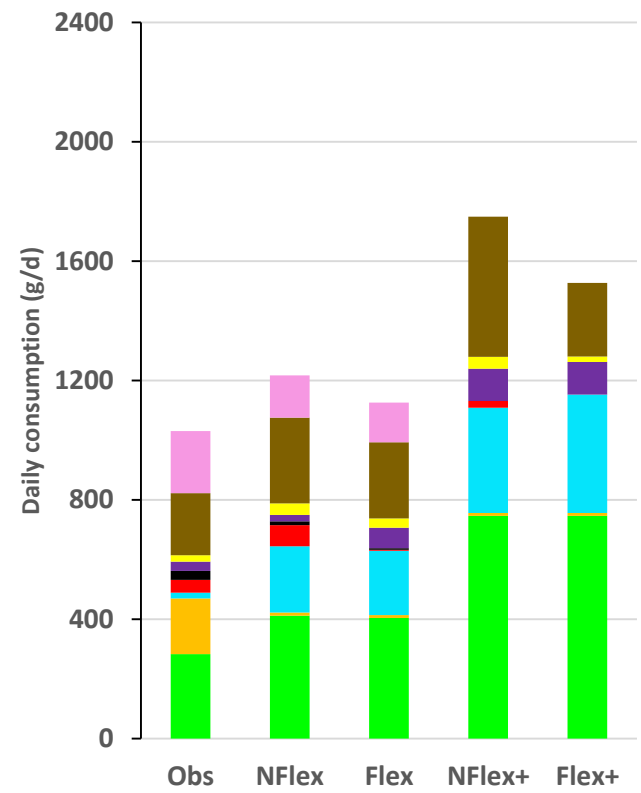
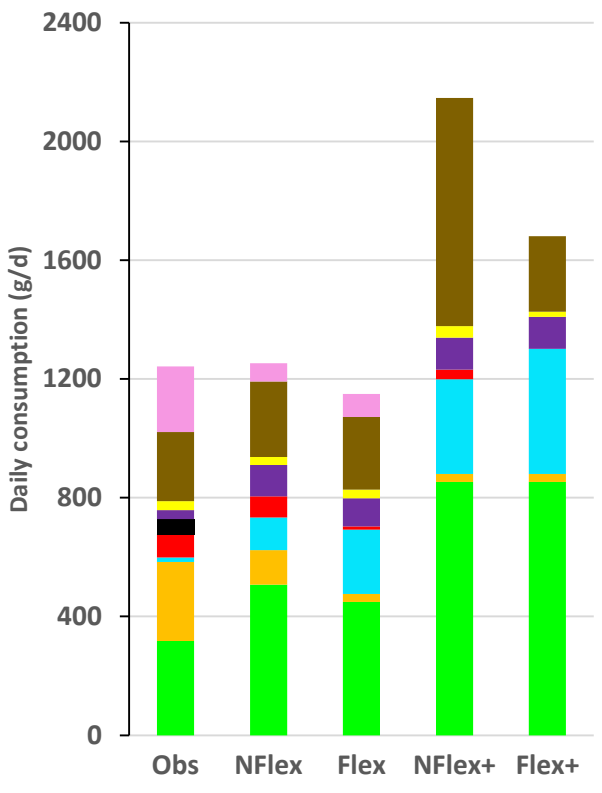


### A. Males

### B. Females Fe-

### C. Females Fe+

- Soft Drinks
- Dairy Products
- Fish
- Poultry
- Processed Meat
- Red Meat
- Whole Grain Products
- Refined Grain Products
- Fruit and Vegetables

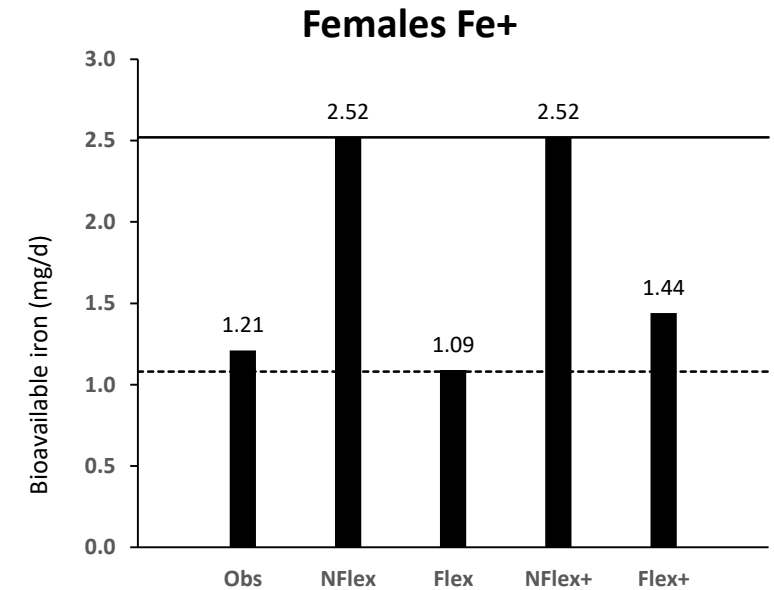
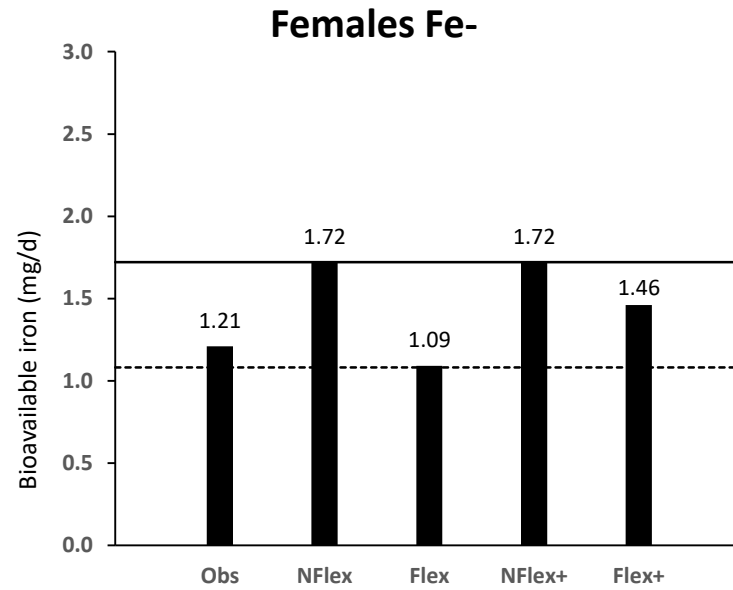
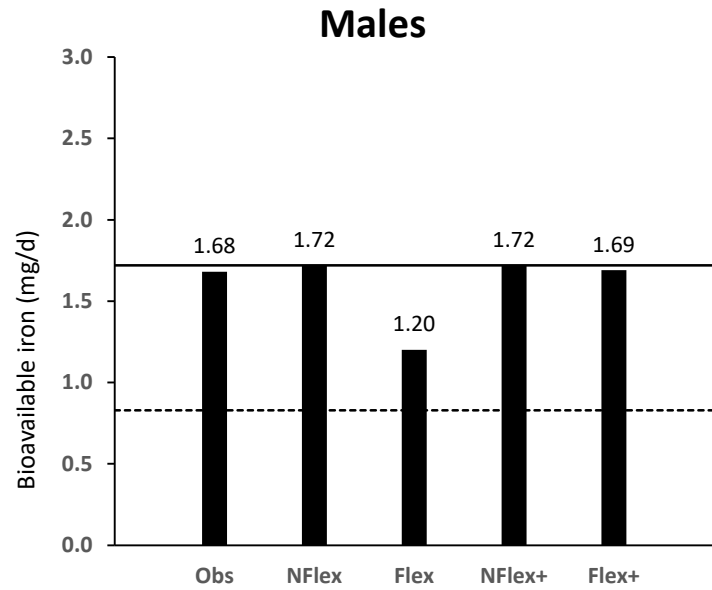
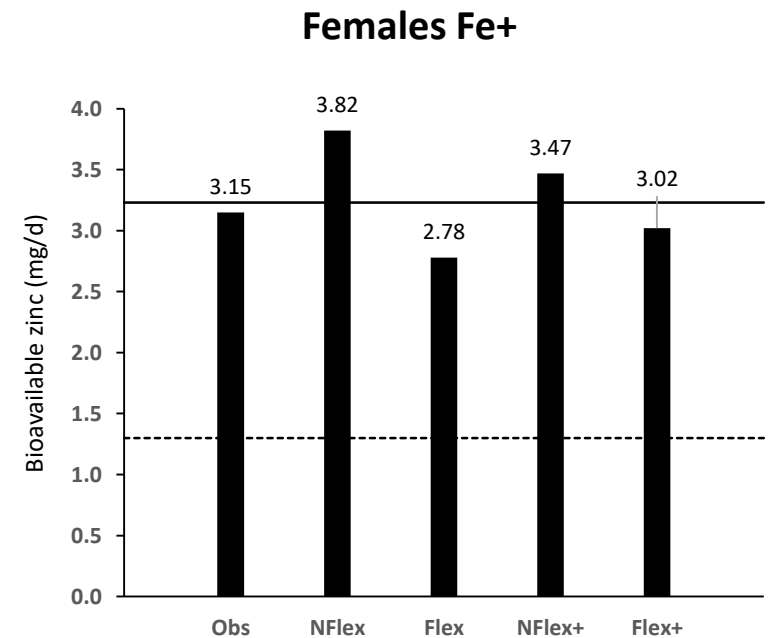
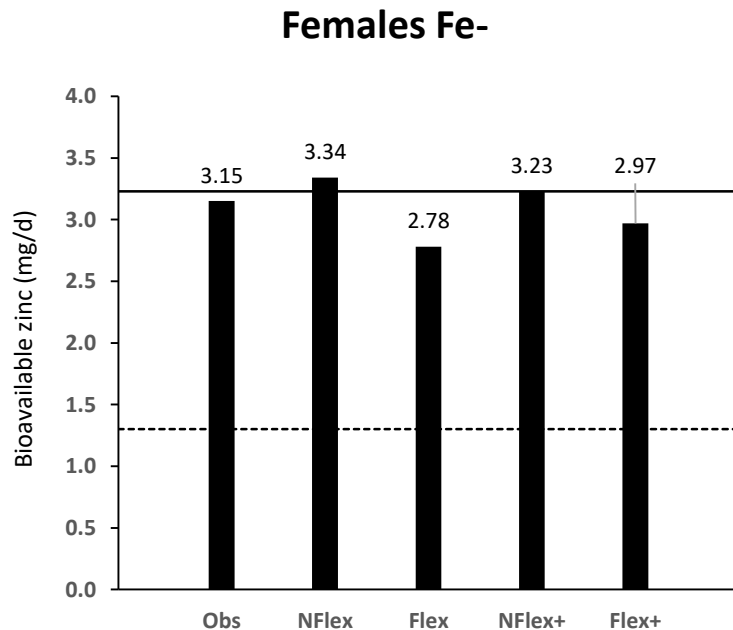
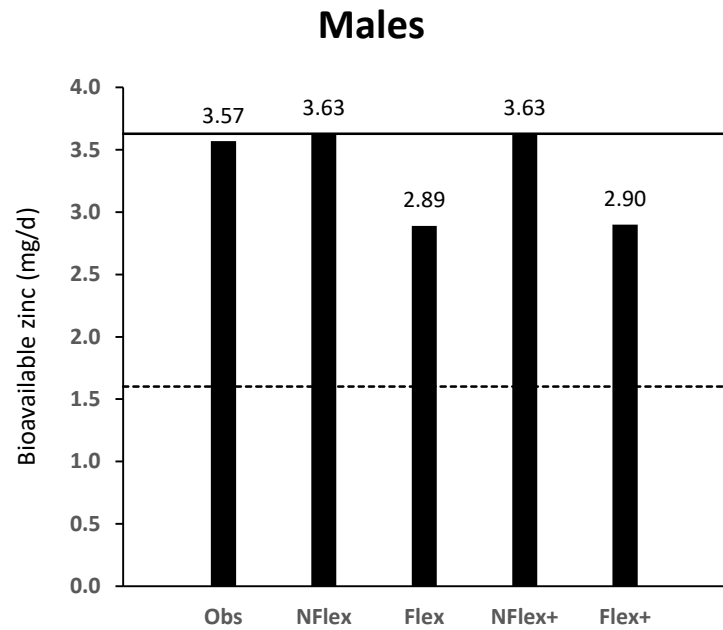


- Others
- Other Drinks

## Online Supplementary Material

**SUPPLEMENTAL FIGURE 2** Amounts of absorbed iron (upper panel A) and absorbed zinc (lower panel B) under the observed diets (Obs) and modeled diets in males, females with “low-to-medium” iron requirements (Fe-), and females with high iron requirements (Fe+) using either the standard multicriteria optimization model (NFlex) or the goal programming option allowing flexibility regarding nutrient constraints for zinc and iron (Flex) and two complementary optimization models (without or with flexibility on bioavailable iron and zinc) when suppressing the *Diet Departure* term in the objective function (NFlex+ and Flex+, respectively)

The solid lines indicate the current reference values for the nutrient and population considered, which is used as the lower bound of the constraint in the NFlex and NFlex+ models, and broken lines indicate the deficiency threshold for the nutrient and population considered which is used as the lower bound of the constraint in the Flex and Flex+ models.

**A****B**

———— current reference value

----- deficiency threshold

## Online Supplementary Material

### References

1. Scarborough P, Harrington RA, Mizdrak A, Zhou LM, Doherty A. The Preventable Risk Integrated Model and Its Use to Estimate the Health Impact of Public Health Policy Scenarios. *Scientifica* 2014;2014:1–21.
2. Grieger JA, Johnson BJ, Wycherley TP, Golley RK. Evaluation of Simulation Models that Estimate the Effect of Dietary Strategies on Nutritional Intake: A Systematic Review. *J Nutr* 2017;147:908–31.
3. Willett W, Rockström J, Loken B, Springmann M, Lang T, Vermeulen S, Garnett T, Tilman D, DeClerck F, Wood A, et al. Food in the Anthropocene: the EAT–Lancet Commission on healthy diets from sustainable food systems. *The Lancet Elsevier*; 2019;393:447–92.
4. Murray CJL, Lopez AD. Measuring the Global Burden of Disease. *N Engl J Med* 2013;369:448–57.
5. GBD 2019 Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020;396:1223–49.
6. Bechthold A, Boeing H, Schwedhelm C, Hoffmann G, Knüppel S, Iqbal K, De Henauw S, Michels N, Devleesschauwer B, Schlesinger S, et al. Food groups and risk of coronary heart disease, stroke and heart failure: A systematic review and dose-response meta-analysis of prospective studies. *Crit Rev Food Sci Nutr* 2019;59:1071–90.
7. Schwingshackl L, Boeing H, Stelmach-Mardas M, Gottschald M, Dietrich S, Hoffmann G, Chaimani A. Dietary Supplements and Risk of Cause-Specific Death, Cardiovascular Disease, and Cancer: A Systematic Review and Meta-Analysis of Primary Prevention Trials. *Adv Nutr* 2017;8:27–39.
8. Schwingshackl L, Hoffmann G, Lampousi A-M, Knüppel S, Iqbal K, Schwedhelm C, Bechthold A, Schlesinger S, Boeing H. Food groups and risk of type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies. *Eur J Epidemiol* 2017;32:363–75.
9. Schwingshackl L, Schwedhelm C, Hoffmann G, Knüppel S, Preterre AL, Iqbal K, Bechthold A, Henauw SD, Michels N, Devleesschauwer B, et al. Food groups and risk of colorectal cancer. *International Journal of Cancer* 2018;142:1748–58.
10. Schwingshackl L, Knüppel S, Michels N, Schwedhelm C, Hoffmann G, Iqbal K, De Henauw S, Boeing H, Devleesschauwer B. Intake of 12 food groups and disability-adjusted life years from coronary heart disease, stroke, type 2 diabetes, and colorectal cancer in 16 European countries. *Eur J Epidemiol* 2019;34:765–75.
11. Gauthier J, Wu QV, Gooley TA. Cubic splines to model relationships between continuous variables and outcomes: a guide for clinicians. *Bone Marrow Transplantation* Nature Publishing Group; 2020;55:675–80.
12. Willett WC, Howe GR, Kushi LH. Adjustment for total energy intake in epidemiologic studies. *Am J Clin Nutr* 1997;65:1220S–1228S; discussion 1229S–1231S.
13. The Third Individual and National Survey on Food Consumption (INCA3 Survey) [Internet]. The French Agency for Food, Environmental and Occupational Health & Safety (ANSES); 2017 Jun p. 24. Available from: <https://www.anses.fr/en/system/files/NUT2014SA0234Ra.pdf>

## Online Supplementary Material

14. The ANSES-CIQUAL food composition table [Internet]. [cited 2021 Jun 22]. Available from: <https://ciqual.anses.fr/#>
15. Henry CJK. Basal metabolic rate studies in humans: measurement and development of new equations. *Public Health Nutr* 2005;8:1133–52.
16. Black AE. Critical evaluation of energy intake using the Goldberg cut-off for energy intake:basal metabolic rate. A practical guide to its calculation, use and limitations. *Int J Obes Relat Metab Disord* 2000;24:1119–30.
17. Salomé M, Arrazat L, Wang J, Dufour A, Dubuisson C, Volatier J-L, Huneau J-F, Mariotti F. Contrary to ultra-processed foods, the consumption of unprocessed or minimally processed foods is associated with favorable patterns of protein intake, diet quality and lower cardiometabolic risk in French adults (INCA3). *Eur J Nutr* 2021;
18. Deville J-C, Sarndal C-E. Calibration Estimators in Survey Sampling. *Journal of the American Statistical Association* [American Statistical Association, Taylor & Francis, Ltd.]; 1992;87:376–82.
19. Évolution et structure de la population en 2014 | Insee [Internet] [Internet]. 2019 [cited 2021 Apr 12]. Available from: <https://www.insee.fr/fr/statistiques/2862200>
20. Classification internationale des maladies (CIM) | CépiDc [Internet] [Internet]. 2019 [cited 2021 Apr 12]. Available from: <https://cepidc.inserm.fr/causes-medicales-de-deces/classification-internationale-des-maladies-cim>
21. A generic model for the assessment of disease epidemiology: the computational basis of DisMod II | Population Health Metrics | Full Text [Internet]. [cited 2021 May 18]. Available from: <https://pophealthmetrics.biomedcentral.com/articles/10.1186/1478-7954-1-4>
22. Peterson HM, Flaxman AD. Meta-regression with DisMod-MR: how robust is the model? *The Lancet* 2013;381:S110.
23. Environment, Biomonitoring, Physical Activity and Nutrition Health Study (Esteban 2014-2016). Nutrition Component. Chapter Bioassays: vitamins and minerals [Internet]. Saint-Maurice, France: French Public Health Agency; 2019 Dec p. 61. Available from: <https://www.santepubliquefrance.fr/determinants-de-sante/nutrition-et-activite-physique/documents/rapport-synthese/etude-de-sante-sur-l-environnement-la-biosurveillance-l-activite-physique-et-la-nutrition-esteban-2014-2016-.volet-nutrition.-chapitre-dosages>