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Modelled impacts of substituting meat and dairy with plant-based substitutes on risk of nutrient deficiency and chronic disease mortality: a microsimulation study in French adults.

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4 figures, 0 table.

1 supplementary data (including 4 tables).

Declaration of interests

FM declare the following as potential sources of conflict of interest. FM has received research grants for PhD fellowships under his direction by AgroParisTech and INRAE from Terres Univia and Ecotone Foundation, under the aegis of the Foundation de France. One of these grants was used for MS's PhD fellowship. The other authors declare no potential source of conflict of interest.

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Abstract:

Background: Meat and dairy substitutes are gaining popularity, but their expected overall impact on health remains unclear.

Objectives: We aimed to simulate the complete substitution of meat, milk, and dairy desserts with plant-based substitutes (PBS) to assess the impact on nutrient deficiency risk and chronic disease mortality.

Methods: Using individual baseline dietary data from adults in the latest French national survey (n=2121, INCA3), we simulated isoenergetic diets where all meat, milk, and dairy desserts were replaced by an equivalent amount of PBS. We constructed average PBS profiles of varying nutritional quality (high, average, low) based on the nutrient compositions of 96 PBS and legumes. Intermediate scenarios (meat only or dairy-only substitution) were also analyzed. Deficiency risk was assessed using the SecDiet probabilistic system, and the number of deaths averted was projected using the Preventable Risk Integrated Model (PRIME).

Results: On average, PBS substitution did not increase the overall risk of deficiency (SecDiet score: 0.90 ± 0.11 – 0.91 ± 0.11 vs. 0.91 ± 0.11 in the observed diet). However, replacing meat and dairy products increased the risk of riboflavin and vitamin B12 deficiency. Using meat PBS – with reduced consumption of red and processed meat, increased fiber and improved fatty acid intake – would be the most effective in reducing premature deaths from cardiometabolic diseases and cancer. However, meat PBS led to higher sodium intake, which would slightly offset these benefits. Overall, replacing meat and dairy with PBS would avert between 3721 (95%UI: 2712, 4713) and 6671 (5527, 7778) deaths from chronic diseases annually, depending on the quality of the PBS (nutrient content and energy density).

Conclusion: As modeled, full substitution of animal products with PBS would result in limited increases in deficiency risk, and decreases in chronic disease mortality, with meat replacement providing most of the benefits. Expected effects vary widely depending on the nutritional quality of the substitutes.

Abbreviations: INCA3: Third Individual and National Study on Food Consumption Survey; PANDiet: Probability of Adequate Nutrient Intake; PBS: Plant-based substitutes; PRIME: Preventable Risk Integrated ModEl; SecDiet: Nutrient security of the diet; UPF: Ultra-processed foods.

Keywords: plant-based substitutes; meat; dairy; nutritional adequacy; deficiency risk; risk of chronic disease; mortality; diet modeling; microsimulation; comparative risk assessment.

Introduction

In high-income countries, there is a clear trend toward adopting diets that are more plant based (1, 2). Plant-based food analogs, which ease the transition by offering a simple direct replacement for animal foods, have moved out of the vegetarian market niche (3) and a wide variety of different types of plant-based substitutes (PBS) continue to enter a growing market and become increasingly popular with consumers (2, 4, 5).

The benefits of PBS for environmental pressures have been widely described, particularly for reducing greenhouse gas emissions, land use and water use (6-10). In contrast, the nutritional and health benefits of PBS have been and continue to be much debated (10, 11). In fact, the use of PBS has long been questioned because of the risk of nutrient deficiencies, since the animal products they replace are rich in indispensable nutrients (12). Conversely, the use of plant products and a shift to a more plant-based diet could be expected to reduce the long-term risk of chronic diseases (11, 13).

The nutritional value of PBS is usually inferred from the nutrient content of the products as compared to their animal counterparts, which does not take into account the final impact on the diet and its nutritional characteristics. Very few studies have modeled the effects of introducing PBS into the diets of representative samples of the population (11).

The few simulation studies conducted to date have reported that the use of some PBS to replace some specific animal categories could reduce nutrient adequacy, such as calcium or iodine adequacy when using milk PBS or iron adequacy when using meat PBS (11), in line with observational evidence (14). However, we have little direct information about the final picture when PBS from different categories are used together, although people who reduce their consumption of animal products seem to use both milk/dairy PBS and meat PBS more (15-17).

Furthermore, as noted in the literature, PBS could affect the intake of nutrients that have important implications for long-term health. In particular, extensive use of different types of PBS could markedly increase fiber intake and decrease SFA intake (18). However, because the sodium content of PBS varies widely, it remains unknown whether and to what extent it might moderate the benefits of changes in dietary fiber and SFA (10, 11). The effect of PBS should also depend on their energy density. Therefore, the impact of the use of PBS should be studied by modeling their introduction into the diet and estimating the final impact on health. The latter can be assessed using the Comparative Risk Assessment framework (19), to understand the effect of the nutritional characteristics of the PBS and their animal counterparts on the expected changes in the risk of mortality from chronic diseases.

Finally, there are only few interventional studies of the effects of using PBS (10). Although they are necessary for a direct insight into the effect of PBS, these studies are also short-term and use a limited number of risk factors as intermediate endpoints to study health effects. A drawback of clinical trials is that they rely on one or a limited number of specific treatments with one or a limited set of PBS, which cannot be generalized to the large set of different PBS and the way they are used to replace their animal counterparts. In fact, the literature has reported great heterogeneity in the composition of PBS on the market, both in terms of indispensable nutrients and nutrients that are risk factors for chronic diseases (10, 11). Therefore, there is a need to carry out *in silico*

experimental studies aimed at understanding to what extent this heterogeneity of composition may lead to a high variability in the nutritional and health effects of using PBS.

Methods

Study Population and Consumption Data

The data used in this study came from the French Third Individual and National Study on Food Consumption Survey (INCA3), which is a nationwide and representative cross-sectional survey. This study was performed in mainland France in 2014–2015 and its methods, design, and participant characteristics have been fully described elsewhere (20, 21). Of the 4114 participants in total, our analysis focused on 2121 adults (887 males and 1234 females, aged 18–79 y; median age: 51 y), selected using a two-stage stratified random sampling design to ensure representativeness of the population. The INCA3 survey was carried out in accordance with the Declaration of Helsinki guidelines and was approved by the Advisory Committee on Information Processing in Health Research. Verbal consent was obtained from, witnessed and formally recorded for all subjects. Briefly, dietary data were collected using three non-consecutive validated 24-h dietary recalls over a 3-week period. Professional interviewers were responsible for collecting the dietary records by telephone, and participants were not aware of the days of the call. All participants provided at least two recalls, and 92% provided 3 recalls. Portion sizes were estimated using validated photographic aids. The nutritional composition of foods was obtained from the food composition database of the French Information Centre on Food Quality (22). The study population and consumption data are the same as in our previous work (23).

Scenarios of Substituting Meat, Milk, and Dairy Desserts with Equivalent Plant-Based Substitutes

Foods to be replaced

As previously described (23), we firstly identified foods in the overall diet of INCA3 study participants that could potentially be replaced by PBS, i.e. foods that could be substituted with a plant-based alternative because of the expected use of the alternative, as understood from the type of alternatives in our database. We considered food as finally consumed and not ingredients from disaggregation of foods using recipes, for sake of simplicity. For meat, this includes commonly consumed meat cuts served as the main course (including sausages but excluding, for example, *saucisson* (dry sausage)). Regarding milk, it encompasses various types of milk (cow, goat, whole, semi-skimmed, etc.), excluding powdered milk or condensed milk. For dairy desserts, this includes all prepared yogurts and dairy desserts (e.g., custard). Composite foods (pizzas, etc.) and meat or milk within composite foods were not considered substitutable.

Foods used for substitutions

In this study, we set up a limited number of substitution scenarios by defining a series of average PBS, using a database of PBS originating from the French food composition database CIQUAL version 2020 and the food database of the *NutriNet-Santé* cohort, extracted in 2020), as previously described (23). As with substituted foods, PBS were foods as directly consumed and not ingredients. PBS were assigned to one of the three categories, either meat PBS (n=43), milk PBS (n=16) or dairy dessert PBS (n=24). For example, the meat PBS category comprises “soy and cheese patty” and “plant-based sausage with wheat or seitan”, the milk PBS category comprises “calcium-fortified flavored soy beverages” and “Almond drink, plain, unsweetened, unenriched”, and dairy dessert PBS comprises “flavored soy cream dessert #1” and “Plant-based chocolate mousse” (**Supplementary Table 1**). For each category (meat, milk, and dairy desserts), we created an overall “average” substitute with the mean nutrient composition of all substitutes in that category. To account for the variability in nutrient content among substitutes, we also created for each category a “higher-range average” substitute and a “lower-range average” substitute, according to the ranking of the nutritional quality of the substitutes. This ranking was done based

on the modelled effect of the substitution of each PBS on the changes in PANDiet, a score of the overall nutrient quality of the diet (23). Therefore, the “higher-range average” substitute represents the mean nutrient composition of the 5 ‘best’ substitutes, and “Lower-range average” substitute that of the 5 ‘worst’ PBS, per category. Finally, for the meat category, a “Legumes” average substitute was created using the nutritional compositions of 13 legumes to compare legumes with meat PBS (as the “average” PBS excluding legumes). The list of substitutes used to create each average substitute is presented in Supplementary Table 1.

Models of substitution

Then, we modelled the substitutions following a previously described principle (23). In this in silico study, making substitutions means replacing one line of consumption with another in the 24-h recalls of individuals. For each scenario, we replaced all identified substitutable foods with the specified substitute corresponding to the scenario. First, all consumed meat, milk, and dairy desserts were substituted with an average substitute of their respective category (meat substitute, plant-based beverage, plant-based dessert), being either an overall average substitute, a higher-range average substitute or a lower-range average substitute. These scenarios are identified by the acronym “M&D” (for “Meat & Dairy Products”), followed by “-s” indicating the substitution, and ending with a reference to the average substitute used (“-avg”, “-high”, “-low”, **Figure 1**). We also built two intermediate scenarios of this overall composite scenario, where only meat was replaced (scenarios “M” for “Meat”), with either the average, higher-range average, lower-range average, or legumes substitute, and only milk and dairy desserts were replaced (scenarios “D” for “Dairy Products”) with either the average, higher-range average, or lower-range average substitute of each category. Throughout this paper, the term “dairy products” refers to milk and dairy desserts but excludes cheese.

The substituted foods were replaced with the same amount of substitute, and the difference in energy intake was redistributed to the rest of the diet (excluding beverages). Thus, for an individual, the simulated diets had the same energy intake as the observed diet.

Nutrient Security

We calculated the SecDiet score as previously described (24). This score assesses the likelihood of having nutrient intakes exceeding a predefined "deficiency" threshold and includes 12 nutrients: thiamin, riboflavin, niacin, folate, vitamins A, B12 and C, calcium, (bioavailable) iron, iodine, selenium, and (bioavailable) zinc. For iron and zinc the risk of deficiency takes into account the predicted absorbed amounts. The SecDiet score offers a nutrient-specific approach and provides an overall score that estimates the risk of nutrient deficiency. The score ranges from 0 to 1, with a higher score indicating a lower risk of deficiency.

Assessing plant/animal protein intake and the consumption of ultra-processed food

To assess the effect of the substitutions on the level of plant/animal content in the diet, we estimated the amount of plant and animal protein in the diet, following desegregation of foods of mixed origin, as previously described (25). Because PBS are ultra-processed foods (UPF), we also aimed to assess to what extent the substitution would increase the level of UPF in the diets (reported as the percentage of energy intake derived from UPF), as previously described (25). Briefly, NOVA4 was assigned based on expert consensus on the degree of processing based on the method of preparation, which was known for most of the foods consumed by each individual, or otherwise assigned to the most common method (25).

Comparative risk assessment of premature deaths avoided from chronic diseases

We used the Comparative Risk Assessment framework (26) to assess the long-term consequences of substituting animal products with plant-based alternatives. We estimated the number of premature deaths from chronic diseases (including cardiovascular diseases, diabetes,

and cancer) averted or added by these substitutions using the PRIME model (Preventable Risk Integrated ModEl) developed by Scarborough et al. (27) and updated to include red meat and processed meat consumption (28). This comparative risk assessment model assesses the population-level impact of dietary changes, physical activity, alcohol consumption, or tobacco use on mortality from non-communicable diseases (27). In our scenarios, we considered only factors related to diet (fruit, vegetables, fiber, salt, lipids, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, dietary cholesterol, red meat, and processed meat). As described in detail elsewhere (27), in the PRIME model, consumption of these foods/nutrients is related to mortality from chronic diseases either directly or indirectly. Direct relationships are based on relative risks derived from literature data. Indirect effects are first related to the effects on a risk factor and the subsequent relationship of that risk factor to chronic disease mortality. Thus, the PRIME model integrates the effects of fatty acid intake (total fat, SFAs, MUFAs, PUFAs) and cholesterol intake on plasma cholesterol, and the effect of sodium intake on blood pressure, using meta-analyses of RCT results. All of these dietary factors are finally related to a wide set of non-communicable chronic diseases including CHD, stroke, diabetes and various cancers. Reimplementing this model (29), we assessed deaths from chronic diseases avoided or added by the modeled diets (resulting from the substitutions), as a counterfactual to the observed diet (reference situation). The population distribution by sex and 10-year age groups in 2014, provided by the French National Institute for Statistics and Economic Studies (INSEE) (30), and mortality data in 2014 from the French Center for Epidemiology on Medical Causes of Death (CépiDc) (31) were used to ensure data consistency with the year of data collection in the INCA3 study and to represent at best the baseline scenario (diet and mortality) in the Comparative Risk Analysis paradigm. Uncertainty intervals (UI) were estimated using Monte Carlo simulations, as the 2.5th and 97.5th percentiles of results generated from 10⁵ iterations of the PRIME models, where the estimates of relative risks used to parameterize the model were allowed to vary stochastically

according to the distributions reported in the literature (27, 28). The PRIME algorithm was implemented in R.

Statistical Analyses

In this microsimulation study, the modeled diets are only the results of the substitutions, and each individual is his/her own control. Therefore, the effects of the substitutions can be inferred by comparing the modelled diets with the observed background diets, using individual data, with all other variables held constant, as in a perfectly well-controlled cross-over clinical trial. Thus, the modelled diets (with respect to dietary characteristics and nutrient security) were compared with the observed diet by ANOVA, added with post-hoc tests with Bonferroni correction for multiple comparisons. For the overall SecDiet score and components of deficiency risk, analyses were performed using a nonparametric Kruskal-Wallis test, followed by Dwass-Steel-Critchlow-Fligner post-hoc tests. All 10 simulated diet scenarios and the observed diet were considered together in the same model for both ANOVA and Kruskal-Wallis tests. Analyses were performed for the entire population and stratified by sex, because males and females have different background diets, nutrient reference values and baseline health risks and mortality. All statistical analyses were run using SAS 9.4 software.

Results

Plant protein intake and Ultra-Processed Foods consumption

Substitution of meat and/or dairy products resulted in an increase in the proportion of plant-based protein in the diet, rising from $33 \pm 10\%$ in the observed diet to $38-40 \pm 11\%$ with the dairy substitution, $51-55 \pm 13\%$ with the meat substitution, and $61-63 \pm 13\%$ with both meat and dairy substitution (**Figure 2**). The contribution of UPF to total energy intake also increased, except when meat was replaced by legumes (Figure 2). Notably, lower-quality substitutes led to a more

substantial increase in the percentage of UPF than higher-quality substitutes. For instance, in the case of substitution of both meat and dairy products (M&D scenarios), the percentage of energy from UPF reached $46 \pm 16\%$ (vs. $31 \pm 16\%$ initially) with lower-range average substitutes, compared to $41 \pm 15\%$ with average substitutes and $36 \pm 15\%$ with higher-range substitutes.

Nutrient security

The SecDiet score and the probabilities of having sufficient intakes to avoid deficiencies for each nutrient (hereafter referred to as “deficiency risk”) are presented in **Figure 3** for four substitution scenarios and in **Supplementary Table 2** for all simulated diets. Compared to the observed diet (0.91 ± 0.11), the SecDiet score significantly decreased, indicating a higher deficiency, only for the scenarios "M&D-s-low" (0.87 ± 0.13) and "D-s-low" (0.88 ± 0.12).

In general, the risk of deficiency increased for riboflavin and vitamin B12 and decreased for folate. The risk for iron decreased in the "M&D" and "D" scenarios but increased in the "M" scenarios, while the risk for calcium decreased in the "M" scenarios and increased in the "D" scenarios. The risk for zinc increased slightly in the "M-s-Legumes" scenario (0.98 ± 0.06 vs. 0.99 ± 0.04) and decreased for the "M-s-high" scenario. The risk of iodine deficiency decreased in the "M&D" and "D" scenarios with higher-range substitutes but increased with lower-range substitutes.

Similar trends were observed in both males and females, but the SecDiet score was initially lower in females than in males (0.89 ± 0.11 vs. 0.93 ± 0.10), and some deficiency risks were also higher in females (especially for riboflavin, folate, calcium, iron, and iodine). The positive and negative impact of substitutions were generally higher in females than in males. For instance, in the M&D scenario, the risk of deficiency for riboflavin increased more in females than in males, and the risk of folate deficiency decreased more.

Deaths averted from chronic diseases

Considering the dietary factors included in the PRIME model (**Supplementary Table 3**), most simulated diets showed increases in fiber and polyunsaturated fatty acid intakes, and decreases in saturated fatty acids and dietary cholesterol. In the "M&D" and "M" scenarios, there was a decrease in red meat and processed meat consumption and an increase in salt intake in some scenarios (e.g., 9.6g of salt in the "M&D-s-avg" diet compared to 9.0g in the observed diet for males). The consumption of fruit and vegetables, which could vary as a function of the energy adjustment, did not vary according to the average PBS scenarios, and increased only slightly with scenario using higher-quality PBS (up to +3.5%) and decreased only slightly in the lower-quality PBS scenarios (up to -5.2%).

Figure 4 shows details of premature deaths averted or added by changes in the dietary factors (Figure 4.A) and premature deaths averted by type of chronic diseases (Figure 4.B). Across all "M&D" and "M" scenarios, reductions in red meat and processed meat consumption were estimated to account for ~2900 averted deaths, while increases in fiber intake would account for ~1800 averted deaths (**Supplementary Table 4**). Changes in blood cholesterol levels (resulting from changes in fatty acid intake) would avert ~900 deaths. In contrast, changes in blood pressure, resulting from a higher sodium intake, could account for added premature deaths, ranging from 9 (95%UI: 3;17) added deaths (scenario "M-s-high") to 1132 (471; 1817) deaths (scenario "M-s-low"). Overall, in the "M&D" scenarios, the highest number of premature chronic diseases deaths averted was estimated for the "M&D-s-high" substitute (6671 (5527, 7778) deaths averted, representing 4.8% of chronic disease mortality in the French population), while the lowest impact was estimated for the "M&D-s-low" substitution (3721 (2712, 4713) deaths averted). In the "M" scenarios, the substitution with legumes would be the most beneficial (6450 (5221, 7636) deaths averted), while the "M-s-low" substitute would have the least benefit (3072 (2015, 4104) deaths averted). In the "M&D" and "M" scenarios, the number of deaths averted from cancer and type 2 diabetes was similar across different scenarios (about ~2100 and ~1100 deaths averted,

respectively), while the number of deaths averted from cardiovascular disease varied largely (ranging from 15 to 3448 deaths averted). For the dairy substitution scenarios, the number of deaths averted (~1100 deaths averted) was much lower than for the other scenarios and was mainly explained by an increase in dietary fiber intake. Irrespective of the scenario, the highest percentage of deaths averted was found in the age groups 35-44 years and 45-54 years, and the highest number of deaths averted was found in the age groups >55y (**Supplementary Table 5**).

Discussion

In this study, we simulated the substitution of animal products (meat, milk and dairy desserts) with plant-based substitutes in the diets of French adults. We found that these substitutions would not lead to an increased risk of deficiencies for most nutrients and would lead to a decrease in chronic disease mortality.

In our study, the SecDiet score; which assesses the overall risk of deficiency, did not change in the average total substitution scenario. In terms of individual nutrient risks, this scenario resulted in an increased risk of deficiency for riboflavin and vitamin B12 and a decreased risk of deficiency for folate. The increased risk for riboflavin was due to cumulative effects of similar magnitude from meat and dairy substitution, whereas the increased risk for vitamin B12 and the decreased risk for folate were mainly due to meat substitution. These findings underscore the importance of meat for vitamin B12 intake, and its absence in meat substitutes, while the opposite is true for folate. Vitamin B12 supplementation is strongly recommended for individuals following a vegan diet to prevent overt deficiency, and less commonly for vegetarians to prevent elevated homocysteine concentrations (32, 33). Here our results suggest that meat substitution may slightly increase the risk of overt deficiency (represented by megaloblastic anemia) if the substitutes are not fortified with vitamin B12. In meat-free dietary models, increasing fish and seafood consumptions can provide ample amounts of vitamin B12 (34).

For riboflavin, we found a cumulative effect because meat and dairy products are important contributors to intake (approximately 30% of adult intake in the INCA3 study (21)). Therefore, the amount of riboflavin in PBS may be important when reducing consumption of animal products. Importantly, we observed that the increase in estimated risk of deficiency was much less pronounced with higher quality substitutes than with lower quality substitutes. Nonetheless, the prevalence of overt deficiency (namely ariboflavinosis) is virtually nil in high-income countries, and the characterized adverse effect on health of milder forms of riboflavin deficiency remains uncertain, except in individuals with the MTHFR 677TT genotype (35). Therefore, further studies are needed to better characterize the adverse effects of low riboflavin intake.

The risk of calcium deficiency did not change in the average total substitution scenario, because the decrease in calcium intake following dairy product substitution was offset by higher levels in meat substitutes. This limited decrease in calcium intake may also be explained by the fact that cheese was not included in the substitutions. It is noteworthy that dairy PBS vary widely in calcium content, so that substitution with high quality PBS, which were often fortified with calcium, resulted in a less significant decrease in calcium intake. In total scenarios (i.e., substituting for both meat and dairy products) with high-quality PBS, the substitution finally led to a lower risk of calcium deficiency. For (bioavailable) iron, we found little effect in the total scenario. The risk decreased with the substitution of dairy products, explained by the higher iron content of the substitutes than in dairy products (36, 37) and a decrease in calcium intake, which favored iron bioavailability (calcium being an inhibitor of non-heme iron absorption (38)). On the other hand, the risk of deficiency (as iron-deficiency anemia) was slightly increased by replacing meat with legumes or lower-quality substitutes, but not with other substitutes. This finding may be surprising given the classical importance of meat in iron intake (34) and in contrast to what can be inferred from the composition of meat analogs, (4, 39), but indeed it remains unclear whether a meat-free diet increases the risk of iron-deficiency anemia (40). Our findings are also consistent with the

literature, which reports that high-quality meat substitute can contain important amounts of iron (41-43), although their fortification much improves their potential as a lever for healthy diets with less meat (44).

Another objective of this study was to assess the potential changes in premature mortality from chronic diseases resulting from the substitution of animal products with PBS. In the average total scenario, we found an overall reduction in mortality risk of 5513 deaths per year. Reduced consumption of red and processed meat, increased fiber intake, and a shift in fatty acid intake (lower SFA and higher PUFA intakes) would help avoid premature deaths. On the other hand, meat PBS led to increased salt consumption, which resulted in additional deaths mediated by increased blood pressure (27). Notably, our results show that the number of deaths averted from cancer and diabetes was relatively similar across PBS, whereas the number of deaths averted from by cardiovascular disease varied significantly across meat substitutes. Therefore, our data suggest that the sodium content of meat substitutes partially offset the beneficial effects on cardiovascular mortality. However, sodium content varied among meat PBS, and scenarios with better PBS resulted in almost no additional deaths associated with changes in blood pressure. For example, "Average" and "Average-low" substitutes contained about 500 and 600 mg/100g of sodium, respectively, while "Average-Plus" and "Legume" substitutes contained just over 100 mg/100g of sodium. The World Health Organization (WHO) has set a target of less than 250 mg of sodium per 100 g for meat substitutes (45).

One limitation of our analysis is that we did not consider the addition of salt during the preparation or consumption of meat. The simulations involved replacing meat with PBS without considering the likely change in added salt. Because meat PBS are processed foods, salt is more often pre-incorporated into the recipe, as opposed to meat, which is more often presented in raw or minimally processed form, but we could not evaluate the potential difference in salt addition.

To avoid bias due to changes in energy intake when estimating changes in mortality using comparative risk assessment methods, we modeled isoenergetic substitutions. Because animal products were replaced by an equivalent amount of plant substitutes, we reported the energy difference in the rest of the diet. Although this adjustment was necessary, it had some indirect effects via changes in other dietary factors included in the PRIME model. In particular, because lower-quality PBS are more energy-dense than higher-quality PBS, the decrease in consumption of the rest of the diet was more important when using the former. Alternatively, we could have chosen to replace animal products with an equivalent caloric intake of PBS. However, we chose to replace animal products with the same amount of plant substitutes because these products have the same intended use and similar portion sizes. Energy compensation by the rest of the diet, as implied by isoenergetic scenarios, remains the simplest and most realistic scenario. It should be noted however that energy compensation is certainly not total, and therefore, we may have underestimated the health effects of plant substitutes that are less energy dense and therefore could lead to overall lower energy intakes in the long term (46).

Estimates of changes in mortality (up to 5%) are in the same order of magnitude as the recent work from Springmann, who used a different comparative risk assessment model (47). In contrast, those estimates were low when compared to some other studies using the PRIME model or previous versions, which reported that following dietary guidelines could prevent 14% of deaths in Sweden (48) and the United Kingdom (49), and 36% in Canada (50). However, in these studies, a significant proportion of the avoided deaths was explained by increased consumption of fruit and vegetables, whereas these two factors changed minimally in our substitution scenarios. In fact, the dietary changes considered in these studies were extensive and corresponded to the adoption of dietary patterns very different from those observed, in contrast to the more limited changes that we have simulated here. We also showed that replacing animal products with plant substitutes could increase the energy contribution of UPF (up to 46% of total energy intake), whereas a wealth

of data strongly suggests that UPF increase the risk of many chronic diseases (51, 52) and these relationships are not considered in comparative risk assessment models. However, it has been argued that many of the common criticisms of UPFs do not apply to PBS of meat and dairy (53), and a subgroup analysis of the association between UPF and multimorbidity found no association for PBS (54). Further studies are needed to elucidate all potential beneficial or adverse characteristics of PBS (and their animal counterparts) on health.

In this study, we considered PBS using a market benchmark based on data in 2020, whereas the supply of different PBS is constantly growing and changing. However, we covered a wide range of PBS types of varying quality, and could compare PBS of higher and lower quality. Therefore, although we cannot draw conclusions about current and future changes in the supply of PBS, our findings provide an insight into the importance of variations in the quality of PBS, especially meat PBS. Lastly, while the composition of PBS may vary across countries – for instance regarding micronutrient fortification (11) – their technological production methods and marketing strategies remain largely standardized in high-income markets (55). Therefore, our findings could be generalized to most high-income countries, given the documented convergence of Western dietary patterns (56, 57).

In conclusion, we found that replacing a significant proportion of animal products with PBS would have almost no impact on overall deficiency risk, although with a higher risk for riboflavin and B12. According to the comparative risk assessment model that we used, replacing animal products, especially meat, with plant substitutes would be expected to reduce mortality from chronic diseases, although some of the benefits on cardiovascular disease mortality would be slightly offset by the often high sodium content of meat substitutes. Overall, we confirm the concerns and expectations raised about the heterogeneity of PBS (10) by showing that there was an important impact of differences in the quality of the plant substitutes, with higher quality substitutes contributing most to both limiting the risk of deficiency and reducing mortality. To ensure adequate

nutrient intakes, better designed PBS or fortified versions would be needed. As an alternative, or as a complement, other dietary changes would need to be considered as part of a wider review of the dietary patterns to improve health outcome.

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Data availability

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

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Legends for figures

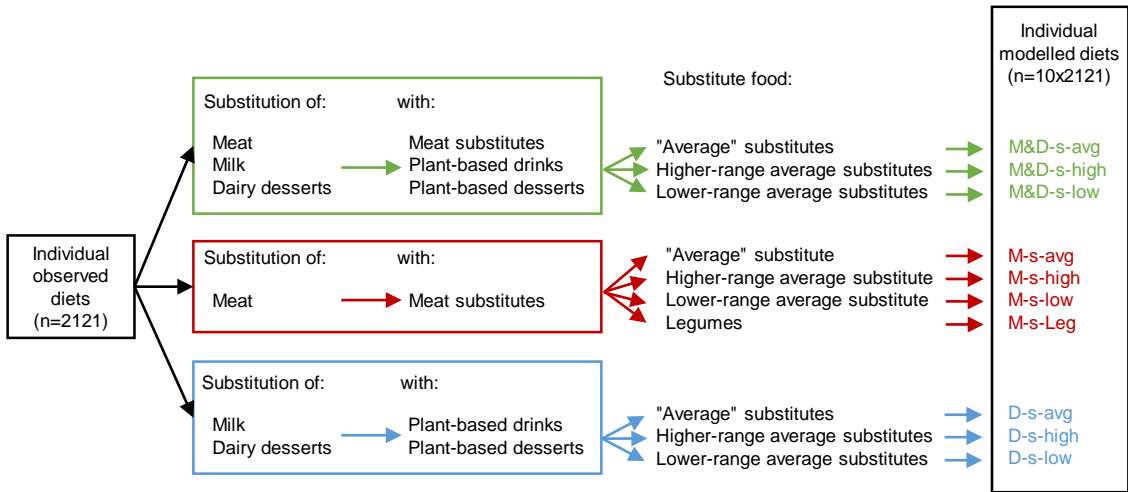
Figure 1: Diets modeled following 10 scenarios of substitution of animal products with plant-based substitutes, according to the categories substituted and the substitute foods considered. Observed diets are from the INCA3 survey (n=2121). Modeled diets are n=10x2121.

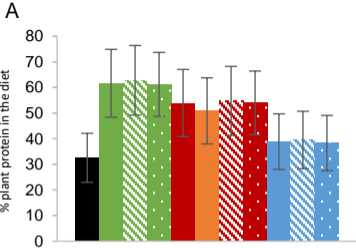
Figure 2: Percentage of plant protein in total protein intake (Panel A) and percentage of energy intake from ultra-processed foods (Panel B) in the modeled diets according to the substitution scenarios. Error bars are SD. The scenario acronyms correspond to the type of substitution: either meat (M) or milk or dairy desserts (D) or both (M&D); followed by a reference to the nutritional quality of the substitute, either the grand average substitute (“-avg”), an average substitute of higher (“-high”) quality, or an average substitute of lower (“-low”) quality. Substitution (of meat only) by legumes is indicated by “-leg”.

Figure 3: SecDiet Scores and their nutrient components as means of individual probabilities of adequacy (reflecting estimated risk of deficiency), in the observed diets and in 4 modeled diets according to substitution scenarios of meat by an average meat substitute (M-s-avg) or by legumes (M-s-Leg); of milk and dairy desserts by an average substitute (D-s-avg); and of meat, milk and dairy desserts by their average substitutes (M&D-s-avg), in the total population (Panel A), in Males (Panel B) and Females (Panel C). +/-, significantly different (higher/lower) than the observed diet, as assessed by Kruskal-Wallis and Dwass-Steel-Critchlow-Fligner tests.

Figure 4: Estimated numbers of averted premature deaths from chronic diseases according to the 10 counterfactual substitution scenarios as compared to the baseline scenario (observed diets) as assessed using the PRIME model. Panel A shows the positive or negative contribution of each risk factor to the total number of averted deaths, shown at the top of each bar (with 95% uncertainty intervals). Blood pressure changes are the modeled results of changes in salt intake, and blood cholesterol changes are the modeled results of changes in lipids, SFA, MUFA, PUFA and dietary

cholesterol intakes. Panel B shows the cause of the averted premature deaths. The scenario acronyms correspond to the type of substitution: either meat (M) or milk or dairy desserts (D) or both (M&D); followed by a reference to the nutritional quality of the substitute, either the grand average substitute ("-avg"), an average substitute of higher ("-high") quality, or an average substitute of lower ("-low") quality. Substitution (of meat only) by legumes is indicated by "-leg".



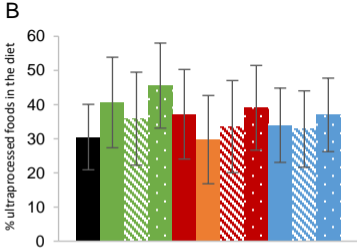


■ Observed diets

■ M&D-s-avg

▨ M&D-s-high

■ M&D-s-low



■ M-s-avg

■ M-s-leg

▨ M-s-high

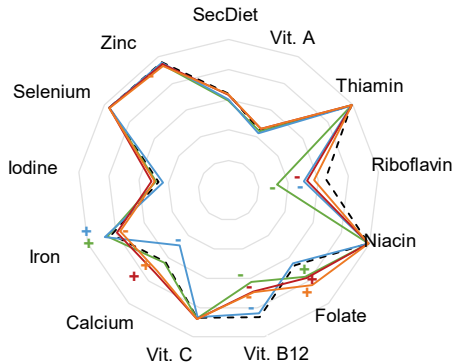
■ M-s-low

■ D-s-avg

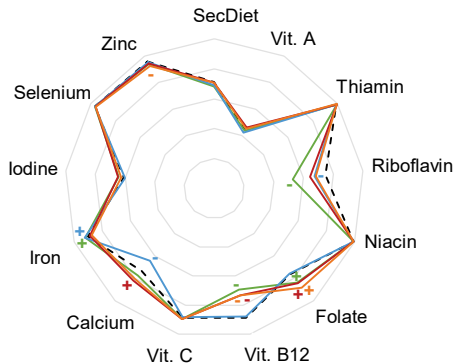
▨ D-s-high

■ D-s-low

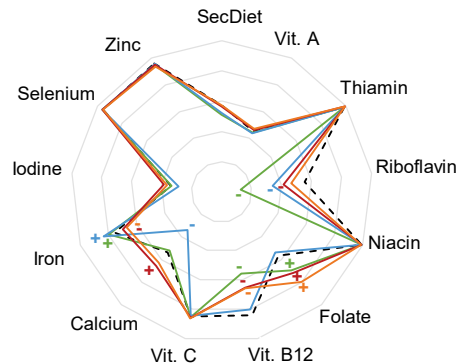
A



B



C



----- Observed

— M&D-s-avg

— D-s-avg

— M-s-avg

— M-s-Leg

1.00

0.95

0.90

0.85

0.80

0.75

